Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-Q

(Mark One)

☑ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended September 30, 2019

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission file number 001-37359

BLUEPRINT MEDICINES CORPORATION
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**26-3632015**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
45 Sidney Street Cambridge, Massachusetts	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

(617) 374-7580
(Registrant's Telephone Number, Including Area Code)

(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☑ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☑ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☑	Accelerated filer ☐
Non-accelerated filer ☐	Smaller reporting company ☐
	Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☑

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	BPMC	Nasdaq Global Select Market

Number of shares of the registrant's common stock, $0.001 par value, outstanding on October 31, 2019: 49,202,122

TABLE OF CONTENTS

Unless otherwise stated, all references to "us," "our," "Blueprint," "Blueprint Medicines," "we," the "Company" and similar designations in this Quarterly Report on Form 10-Q refer to Blueprint Medicines Corporation and its consolidated subsidiaries.

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Quarterly Report on Form 10-Q are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "seek," "should," "target," "will," "would" or the negative of these words or other comparable terminology, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Quarterly Report on Form 10-Q include, but are not limited to, statements about:

- the initiation, timing, progress and results of our pre-clinical studies and clinical trials, including our ongoing clinical trials and any planned clinical trials for avapritinib, pralsetinib, fisogatinib and BLU-263, and our research and development programs;
- our ability to advance drug candidates into, and successfully complete, clinical trials;
- the timing or likelihood of regulatory actions, filings and approvals for our drug candidates;
- the commercialization of our drug candidates, if approved;
- the pricing and reimbursement of our drug candidates, if approved;
- the implementation of our business model, strategic plans for our business, drug candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our drug candidates and technology;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the potential benefits of our existing cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. and our collaboration with CStone Pharmaceuticals, as well as our ability to maintain these collaborations and establish other strategic collaborations;
- the potential benefits of our exclusive license agreement with Clementia Pharmaceuticals, Inc. to develop and commercialize BLU-782;
- the development of companion diagnostic tests for our drug candidates;
- our financial performance; and
- developments relating to our competitors and our industry.

Any forward-looking statements in this Quarterly Report on Form 10-Q reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. We have included important factors in the cautionary statements included in this Quarterly Report on Form 10-Q, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or enter into.

You should read this Quarterly Report on Form 10-Q and the documents that we have filed as exhibits to this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results, performance or achievements may be materially different from what we expect. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Quarterly Report on Form 10-Q also contains estimates, projections and other information concerning our industry, our business and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

Blueprint Medicines Corporation
Condensed Consolidated Balance Sheets
(in thousands, except share and per share data)
(Unaudited)

	September 30, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 89,237	$ 68,064
Investments, available-for-sale	404,205	425,948
Accounts receivable	2,414	64
Unbilled accounts receivable	2,662	151
Prepaid expenses and other current assets	15,208	5,560
Total current assets	513,726	499,787
Investments, available-for-sale	101,017	—
Property and equipment, net	38,310	29,627
Operating lease right-of-use assets, net	73,967	—
Restricted cash	5,164	5,154
Other assets	5,741	5,556
Total assets	$ 737,925	$ 540,124
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	2,203	3,298
Accrued expenses	80,419	51,711
Current portion of operating lease liabilities	6,587	—
Current portion of deferred revenue	4,933	3,600
Current portion of lease incentive obligation	—	1,714
Total current liabilities	94,142	60,323
Deferred rent, net of current portion	—	5,130
Operating lease liabilities, net of current portion	90,921	—
Deferred revenue, net of current portion	36,398	42,567
Lease incentive obligation, net of current portion	—	12,903
Other long-term liabilities	120	192
Total liabilities	221,581	121,115
Commitments (Note 12)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.001 par value; 120,000,000 shares authorized; 49,175,442 and 44,037,026 shares issued and outstanding at September 30, 2019 and December 31, 2018, respectively	49	44
Additional paid-in capital	1,394,566	1,016,690
Accumulated other comprehensive income (loss)	637	(180)
Accumulated deficit	(878,908)	(597,545)
Total stockholders' equity	516,344	419,009
Total liabilities and stockholders' equity	$ 737,925	$ 540,124

Blueprint Medicines Corporation
Condensed Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except per share data)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Collaboration revenue	$ 9,139	$ 1,095	$ 14,979	$ 43,488
Operating expenses:				
Research and development	81,453	64,562	242,804	173,089
General and administrative	25,647	12,041	64,123	34,285
Total operating expenses	107,100	76,603	306,927	207,374
Other income (expense):				
Other income (expense), net	3,692	2,799	10,595	7,635
Interest expense	(6)	(14)	(10)	(69)
Total other income	3,686	2,785	10,585	7,566
Net loss	$ (94,275)	$ (72,723)	$ (281,363)	$ (156,320)
Other comprehensive loss:				
Changes in foreign currency translation adjustments	(3)	—	(10)	—
Changes in unrealized gain (losses) related to available-for-sale investments	(287)	44	828	(68)
Comprehensive loss	$ (94,565)	$ (72,679)	$ (280,545)	$ (156,388)
Net loss per share — basic and diluted	$ (1.93)	$ (1.66)	$ (5.94)	$ (3.57)
Weighted-average number of common shares used in net loss per share — basic and diluted	48,921	43,915	47,361	43,825

Blueprint Medicines Corporation
Condensed Consolidated Statements of Stockholders' Equity
(in thousands)
(Unaudited)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2018	44,037,026	44	1,016,690	(180)	(597,545)	419,009
Issuance of common stock under stock plan	134,439	—	2,061	—	—	2,061
Stock-based compensation expense	—	—	10,295	—	—	10,295
Cumulative translation adjustment	—	—	—	(15)	—	(15)
Unrealized gain (loss) on available-for-sale securities	—	—	—	270	—	270
Net loss	—	—	—	—	(87,407)	(87,407)
Balance at March 31, 2019	44,171,465	$ 44	$ 1,029,046	$ 75	$ (684,952)	$ 344,213
Issuance of common stock under stock plan	215,299	—	5,813	—	—	5,813
Purchase of common stock under ESPP	10,718	—	522	—	—	522
Stock-based compensation expense	—	—	13,666	—	—	13,666
Cumulative translation adjustment	—	—	—	7	—	7
Unrealized gain (loss) on available-for-sale securities	—	—	—	845	—	845
Follow on offering, net of issuance costs	4,662,162	5	327,437	—	—	327,442
Net loss	—	—	—	—	(99,681)	(99,681)
Balance at June 30, 2019	49,059,644	$ 49	$ 1,376,484	$ 927	$ (784,633)	$ 592,827
Issuance of common stock under stock plan	115,798	—	3,089	—	—	3,089
Stock-based compensation expense	—	—	14,993	—	—	14,993
Cumulative translation adjustment	—	—	—	(3)	—	(3)
Unrealized gain (loss) on available-for-sale securities	—	—	—	(287)	—	(287)
Net loss	—	—	—	—	(94,275)	(94,275)
Balance at September 30, 2019	49,175,442	$ 49	$ 1,394,566	$ 637	$ (878,908)	$ 516,344
Balance at December 31, 2017	43,577,526	$ 43	$ 979,785	$ (269)	$ (355,589)	$ 623,970
Issuance of common stock under stock plan	243,721	1	3,552	—	—	3,553
Stock-based compensation expense	—	—	5,549	—	—	5,549
Adoption of new accounting standard	—	—	—	—	(5,314)	(5,314)
Unrealized gain (loss) on available-for-sale securities	—	—	—	(322)	—	(322)
Other	—	—	(14)	—	—	(14)
Net loss	—	—	—	—	(56,549)	(56,549)
Balance at March 31, 2018	43,821,247	$ 44	$ 988,872	$ (591)	$ (417,452)	$ 570,873
Issuance of common stock under stock plan	56,955	—	742	—	—	742
Purchase of common stock under ESPP	5,572	—	345	—	—	345
Stock-based compensation expense	—	—	7,762	—	—	7,762
Unrealized gain (loss) on available-for-sale securities	—	—	—	210	—	210
Other	—	—	49	—	—	49
Net loss	—	—	—	—	(27,048)	(27,048)
Balance at June 30, 2018	43,883,774	$ 44	$ 997,770	$ (381)	$ (444,500)	$ 552,933
Issuance of common stock under stock plan	61,542	—	651	—	—	651
Stock-based compensation expense	—	—	8,391	—	—	8,391
Unrealized gain (loss) on available-for-sale securities	—	—	—	44	—	44
Net loss	—	—	—	—	(72,723)	(72,723)
Balance at September 30, 2018	43,945,316	$ 44	$ 1,006,812	$ (337)	$ (517,223)	$ 489,296

Blueprint Medicines Corporation
Condensed Consolidated Statements of Cash Flows
(in thousands)
(Unaudited)

	Nine Months Ended September 30,	
	2019	**2018**
Cash flows from operating activities		
Net loss	$ (281,363)	$ (156,320)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	7,334	3,076
Stock-based compensation	38,954	21,702
Accretion of premiums and discounts on investments	(4,366)	(2,934)
Other	—	10
Changes in assets and liabilities:		
Prepaid expenses and other current assets	(7,175)	6,007
Other assets	(58)	(4,265)
Accounts receivable	(2,350)	413
Unbilled accounts receivable	(2,417)	(344)
Accounts payable	(1,095)	244
Accrued expenses	26,408	18,926
Deferred revenue	(4,836)	6,512
Deferred rent	—	(454)
Operating lease liabilities	(2,156)	—
Net cash used in operating activities	(233,120)	(107,427)
Cash flows from investing activities		
Purchases of property and equipment	(10,122)	(12,252)
Purchases of investments	(597,514)	(648,902)
Maturities of investments	523,434	443,825
Net cash used in investing activities	(84,202)	(217,329)
Cash flows from financing activities		
Principal payments on loan payable	—	(1,250)
Proceeds from public offering of common stock, net of issuance cost	327,466	—
Net proceeds from stock option exercises and employee stock purchase plan	11,454	5,341
Payment of offering costs	—	(281)
Other financing activities	(116)	(120)
Net cash provided by financing activities	338,804	3,690
Net increase (decrease) in cash, cash equivalents, and restricted cash	21,482	(321,066)
Cash, cash equivalents and restricted cash at beginning of period	73,429	405,072
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(10)	—
Cash, cash equivalents and restricted cash at end of period	$ 94,901	$ 84,006
Supplemental cash flow information		
Public offering costs incurred but unpaid at period end	$ 25	$ —
Property and equipment purchases unpaid at period end	$ 3,225	$ 128
Cash paid for interest	$ 5	$ 61
Cash paid for taxes, net	$ 130	$ 105

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the condensed consolidated balance sheets that sum to the total of the same such amounts shown in the condensed consolidated statements of cash flows (in thousands).

	September 30, 2019	September 30, 2018
Cash and cash equivalents	$ 89,237	$ 78,641
Restricted cash included in prepaid expenses and other current assets	500	211
Restricted cash	5,164	5,154
Total cash, cash equivalents, and restricted cash shown in condensed consolidated statements of cash flows	$ 94,901	$ 84,006

Blueprint Medicines Corporation
Notes to Condensed Consolidated Financial Statements
(Unaudited)

1. Nature of Business

Blueprint Medicines Corporation (the Company), a Delaware corporation incorporated on October 14, 2008, is a precision therapy company focused on genomically defined cancers, rare diseases and cancer immunotherapy. The Company's approach is to leverage its novel target discovery engine to systematically and reproducibly identify kinases that are drivers of diseases and to craft highly selective and potent drug candidates that may provide significant and durable clinical responses for patients without adequate treatment options.

The Company is devoting substantially all of its efforts to research and development, initial market development and raising capital. The Company is subject to a number of risks similar to those of other early stage companies, including dependence on key individuals; establishing safety and efficacy in clinical trials for its drug candidates; the need to develop commercially viable drug candidates; competition from other companies, many of which are larger and better capitalized; and the need to obtain adequate additional financing to fund the development of its drug candidates. If the Company is unable to raise capital when needed or on attractive terms, it would be forced to delay, reduce, eliminate or out-license certain of its research and development programs or future commercialization efforts.

On April 2, 2019, the Company closed an underwritten public offering of 4,662,162 shares of its common stock at a price to the public of $74.00 per share, including 608,108 shares of common stock sold by the Company pursuant to the exercise in full by the underwriters of their option to purchase additional shares in connection with the offering. The Company received net proceeds of $327.4 million, after deducting underwriting discounts and commissions and offering expenses.

As of September 30, 2019, the Company had cash, cash equivalents and investments of $594.5 million. Based on the Company's current operating plans, the Company believes that its existing cash, cash equivalents and investments, together with the $25.0 million upfront cash payment from Clementia Pharmaceuticals, Inc. (Clementia) and an $8.0 million research milestone achieved in the fourth quarter of 2019 under the collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, Roche), but excluding any additional potential option fees, milestone payments or other payments from Roche, CStone Pharmaceuticals (CStone) or Clementia, will be sufficient to enable it to fund its operating expenses and capital expenditure requirements into the second half of 2021. See Note 13, *Subsequent Events*.

2. Summary of Significant Accounting Policies and Recent Accounting Pronouncements

Basis of Presentation

The unaudited interim condensed consolidated financial statements of the Company included herein have been prepared in accordance with accounting principles generally accepted in the United States (GAAP) as found in the Accounting Standards Codification (ASC), Accounting Standards Update (ASU) of the Financial Accounting Standards Board (FASB) and the rules and regulations of the Securities and Exchange Commission (SEC). Certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these financial statements should be read in conjunction with the financial statements as of and for the year ended December 31, 2018 and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on February 26, 2019 (the 2018 Annual Report on Form 10-K).

The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited financial statements, and updated, as necessary, in this report. In the opinion of the Company's management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments that are necessary to present fairly the Company's financial position as of September 30, 2019, the results of its operations for the three and nine months ended September 30, 2019 and 2018, stockholder's equity for the three and nine months ended September 30, 2019 and 2018 and cash flows for the nine months ended September 30, 2019 and 2018. Such adjustments are of a

normal and recurring nature. The results for the three and nine months ended September 30, 2019 are not necessarily indicative of the results for the year ending December 31, 2019, or for any future period.

The accompanying condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, Blueprint Medicines Security Corporation, which is a Massachusetts subsidiary created to buy, sell and hold securities, Blueprint Medicines (Switzerland) GmbH, Blueprint Medicines (Netherlands) B.V., Blueprint Medicines (UK) Ltd, and Blueprint Medicines (Germany) GmbH. All intercompany transactions and balances have been eliminated. The accompanying condensed consolidated financial statements do not include the account of the Company's wholly-owned subsidiaries Blueprint Medicines Spain, S.L., which was formed in October 2019, and Blueprint Medicines (France) SAS, which was formed in November 2019.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires the Company's management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. Management's estimation process often may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: revenue recognition, operating lease right-of-use assets, operating lease liabilities, stock-based compensation expense, accrued expenses, and income taxes.

Significant Accounting Policies

The significant accounting policies used in preparation of these condensed consolidated financial statements for the three and nine months ended September 30, 2019 are consistent with those discussed in Note 2 to the consolidated financial statements in the 2018 Annual Report on Form 10-K, except as noted below with respect to the Company's accounting policies related to lease obligations and as noted within this Note 2 under the section titled "—New Accounting Pronouncements."

New Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies that the Company adopts as of the specified effective date. Unless otherwise discussed below, the Company does not believe that the adoption of recently issued standards have or may have a material impact on its condensed consolidated financial statements and disclosures.

Leases

In February 2016, the FASB issued Accounting Standards Update *ASU No. 2016-02, Leases (Topic 842)* or ASC 842, a new standard issued to increase transparency and comparability among organizations related to their leasing activities. This standard established a right-of-use model that requires all lessees to recognize right-of-use assets and lease liabilities on their balance sheet that arise from leases as well as provide disclosures with respect to certain qualitative and quantitative information related to a company's leasing arrangements to meet the objective of allowing users of financial statements to assess the amount, timing and uncertainty of cash flows arising from leases.

The FASB subsequently issued the following amendments to ASU 2016-02 that have the same effective date and transition date: *ASU No. 2018-01, Leases (Topic 842): Land Easement Practical Expedient for Transition to Topic 842, ASU No. 2018-10, Codification Improvements to Topic 842, Leases, ASU No. 2018-11, Leases (Topic 842): Targeted Improvements, ASU No. 2018-20, Narrow-Scope Improvement for Lessors, and ASU No. 2019-01, Leases (Topic 842): Codification Improvements.* The Company adopted these amendments with ASU 2016-02 (collectively, the new leasing standards, or ASC 842) effective January 1, 2019.

As permitted by the new leasing standards, the Company elected to adopt ASC 842 using the modified retrospective transition approach, with no restatement of prior periods or cumulative adjustment to retained earnings, and therefore, the consolidated balance sheet prior to January 1, 2019 continues to be reported under ASC Topic 840, *Leases*,

or ASC 840, which did not require the recognition of operating lease liabilities on the balance sheet, and is not comparative.

Upon adoption, the Company elected the package of transition practical expedients, which allowed it to carry forward prior conclusions related to whether any expired or existing contracts are or contain leases, the lease classification for any expired or existing leases and initial direct costs for existing leases. The leases that were classified as operating leases under ASC 840 were classified as operating leases under ASC 842, and the accounting for finance leases (capital leases) was substantially unchanged. The Company elected to apply the practical expedient not to separate lease and non-lease components for new and modified leases commencing after adoption. The Company also made an accounting policy election to not recognize leases with an initial term of 12 months or less within the condensed consolidated balance sheets and to recognize those lease payments on a straight-line basis in the condensed consolidated statements of operations over the lease term.

Impact of Adoption of ASC 842

Upon adoption of the new leasing standards, the Company recognized an adjustment of $54.2 million and $74.1 million to operating lease right-of-use assets and the related lease liabilities, respectively. The operating lease liabilities are based on the present value of the remaining minimum lease payments discounted using the Company's secured incremental borrowing rate at the effective date of January 1, 2019. The adoption of the new leasing standards did not have an impact on the Company's condensed consolidated statements of operations.

The impact of the adoption of ASC 842 on the condensed consolidated balance sheet was as follows:

	Impact of ASC 842 Adoption on Consolidated Balance Sheet as of January 1, 2019		
(in thousands)	Balances without adoption of ASC 842	ASC 842 Adjustment	Balances with adoption of ASC 842
Operating lease right-of-use assets, net	$ —	$ 54,245	$ 54,245
Total assets	540,124	54,245	594,369
Accrued expenses	51,711	(125)	51,586
Current portion of operating lease liabilities	—	4,730	4,730
Current portion of lease incentive obligation	1,714	(1,714)	—
Total current liabilities	60,323	2,891	63,214
Deferred rent, net of current portion	5,130	(5,130)	—
Operating lease liabilities, net of current portion	—	69,387	69,387
Lease incentive obligation, net of current portion	12,903	(12,903)	—
Total liabilities	121,115	54,245	175,360

Leases Accounting Policy

For contracts entered into on or after the effective date, at the inception of a contract, the Company assesses whether the contract is, or contains, a lease. The assessment is based on: (1) whether the contract involves the use of a distinct identified asset, (2) whether the Company obtains the right to substantially all the economic benefit from the use of the asset throughout the period, and (3) whether the Company has the right to direct the use of the asset. At inception of a lease, the Company allocates the consideration in the contract to each lease component based on its relative stand-alone price to determine the lease payments.

Leases are classified as either finance leases or operating leases. A lease is classified as a finance lease if any one of the following criteria are met: the lease transfers ownership of the asset by the end of the lease term, the lease contains an option to purchase the asset that is reasonably certain to be exercised, the lease term is for a major part of the remaining useful life of the asset or the present value of the lease payments equals or exceeds substantially all of the fair value of the asset. A lease is classified as an operating lease if it does not meet any of these criteria.

For all leases at the lease commencement date, a right-of-use asset and a lease liability are recognized. The right-of-use asset represents the right to use the leased asset for the lease term. The lease liability represents the present value of the lease payments under the lease.

The right-of-use asset is initially measured at cost, which primarily comprises the initial amount of the lease liability, plus any initial direct costs incurred if any, less any lease incentives received. All right-of-use assets are reviewed for impairment. The lease liability is initially measured at the present value of the lease payments, discounted using the interest rate implicit in the lease or, if that rate cannot be readily determined, the secured incremental borrowing rate for the same term as the underlying lease. For real estate leases, the Company uses its secured incremental borrowing rate. For finance leases, the Company uses the rate implicit in the lease or its secured incremental borrowing rate if the implicit lease rate cannot be determined.

Lease payments included in the measurement of the lease liability comprise the following: the fixed noncancelable lease payments, payments for optional renewal periods where it is reasonably certain the renewal period will be exercised, and payments for early termination options unless it is reasonably certain the lease will not be terminated early.

Lease cost for operating leases consists of the lease payments plus any initial direct costs, primarily brokerage commissions, and is recognized on a straight-line basis over the lease term. Included in lease cost are any variable lease payments incurred in the period that are not included in the initial lease liability and lease payments incurred in the period for any leases with an initial term of 12 months or less. Lease cost for finance leases consists of the amortization of the right-of-use asset on a straight-line basis over the lease term and interest expense determined on an amortized cost basis. The lease payments are allocated between a reduction of the lease liability and interest expense.

Credit Losses

In June 2016, the FASB issued *ASU No. 2016-13, Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. The FASB has subsequently issued amendments to ASU 2016-13, which have the same effective date and transition date of January 1, 2020. These standards require that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establish additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, these standards now require allowances to be recorded instead of reducing the amortized cost of the investment. These standards will be effective for the Company on January 1, 2020. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial position and results of operations.

Debt Securities

In March 2017, the FASB issued *ASU No. 2017-08, Receivables - Nonrefundable Fees and Other Costs (Subtopic 310-20): Premium Amortization on Purchased Callable Debt Securities.* This standard amends the amortization period for certain purchased callable debt securities held at a premium by shortening the amortization period to the earliest call date. This standard became effective for the Company on January 1, 2019, and was adopted using a modified retrospective transition approach. The adoption of this standard did not result in a significant adjustment to the Company’s marketable debt securities.

Fair Value Measurements

In August 2018, the FASB issued *ASU No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework Changes to the Disclosure Requirements for Fair Value Measurement*. This standard modifies certain disclosure requirements on fair value measurements. This standard will be effective for the Company on January 1, 2020. The Company does not expect that the adoption of this standard will have a material impact on the disclosures.

Collaborative Arrangements

In November 2018, the *FASB issued ASU No. 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606.* This standard makes targeted improvements for collaborative arrangements as follows:

- Clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue under *ASC 606, Revenue from Contracts with Customers*, when the collaborative arrangement participant is a customer in the context of a unit of account. In those situations, all the guidance in ASC 606 should be applied, including recognition, measurement, presentation and disclosure requirements;

- Adds unit-of-account guidance to *ASC 808, Collaborative Arrangements*, to align with the guidance in ASC 606 (that is, a distinct good or service) when an entity is assessing whether the collaborative arrangement or a part of the arrangement is within the scope of ASC 606; and

- Requires that in a transaction with a collaborative arrangement participant that is not directly related to sales to third parties, presenting that transaction together with revenue recognized under ASC 606 is precluded if the collaborative arrangement participant is not a customer.

This standard will be effective for the Company on January 1, 2020; however, early adoption is permitted. A retrospective transition approach is required for either all contracts or only for contracts that are not completed at the date of initial application of ASC 606, with a cumulative adjustment to opening retained earnings. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial position and results of operations.

Internal-Use Software

In August 2018, the FASB issued *ASU No. 2018-15, Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, which clarifies the accounting for implementation costs in cloud computing arrangements. This standard will be effective for the Company on January 1, 2020, however, early adoption is permitted. The Company currently is evaluating the impact the adoption may have on its consolidated financial position and results of operations.

3. Cash Equivalents and Investments

Cash equivalents and investments, available-for-sale, consisted of the following at September 30, 2019 and December 31, 2018 (in thousands):

September 30, 2019	**Amortized Cost**	**Unrealized Gain**	**Unrealized Losses**	**Fair Value**
Cash equivalents:				
Money market funds	$ 89,237	$ —	$ —	$ 89,237
Investments, available-for-sale:				
U.S. government agency securities and treasuries	504,559	693	(30)	505,222
Total	$ 593,796	$ 693	$ (30)	$ 594,459

December 31, 2018	Amortized Cost	Unrealized Gain	Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 68,064	$ —	$ —	$ 68,064
Investments, available-for-sale:				
U.S. government agency securities and treasuries	426,112	—	(164)	425,948
Total	$ 494,176	$ —	$ (164)	$ 494,012

At September 30, 2019 and December 31, 2018, the Company held eight and 54 debt securities, respectively, that were in an unrealized loss position. The aggregate fair value of debt securities in an unrealized loss position at September 30, 2019 and December 31, 2018 was $55.4 million and $397.5 million, respectively. There were no individual securities that were in a significant unrealized loss position as of September 30, 2019 and December 31, 2018. As of September 30, 2019, there was no securities in an unrealized loss position for more than twelve months. The Company has the intent and ability to hold such securities until recovery, and there was no material change in the credit risk of these investments. As a result, the Company determined it did not hold any investments with an other-than-temporary impairment as of September 30, 2019.

As of September 30, 2019, 14 securities with an aggregate fair value of $101.0 million have remaining maturities greater than one year. No available-for-sale securities held as of December 31, 2018 had remaining maturities greater than one year.

4. Fair Value of Financial Instruments

The following table summarizes cash equivalents and marketable securities measured at fair value on a recurring basis as of September 30, 2019 (in thousands):

Description	September 30, 2019	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Financial Assets				
Cash equivalents:				
Money market funds	$ 89,237	$ 89,237	$ —	$ —
Investments, available-for-sale:				
U.S. government agency securities and treasuries	505,222	505,222	—	—
Total	$ 594,459	$ 594,459	$ —	$ —

The following table summarizes cash equivalents and marketable securities measured at fair value on a recurring basis as of December 31, 2018 (in thousands):

Description	December 31, 2018	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Financial Assets				
Cash equivalents:				
Money market funds	$ 68,064	$ 68,064	$ —	$ —
Investments, available-for-sale:				
U.S. government agency securities and treasuries	425,948	425,948	—	—
Total	$ 494,012	$ 494,012	$ —	$ —

5. Restricted Cash

At September 30, 2019 and December 31, 2018, $5.7 million and $5.4 million, respectively, of the Company's cash is restricted by a bank primarily related to security deposits for the lease agreements for the Company's current and former corporate headquarters.

For additional information on these security deposits, see Note 11, *Leases.*

6. Property and Equipment, Net

Property and equipment and related accumulated depreciation are as follows (in thousands):

	Estimated Useful Life (Years)	September 30, 2019	December 31, 2018
Lab equipment	5	$ 8,370	$ 6,232
Furniture and fixtures	4	3,491	2,369
Computer equipment	3	1,632	1,805
Leasehold improvements	Term of lease	35,513	26,640
Software	3	408	280
Construction-in-progress		1,149	956
		50,563	38,282
Less: accumulated depreciation and amortization		(12,253)	(8,655)
Total		$ 38,310	$ 29,627

Property, plant and equipment are recorded at historical cost, net of accumulated depreciation. For the three and nine months ended September 30, 2019, depreciation expense totaled $1.3 million and $3.7 million, respectively, compared to $1.2 million and $3.1 million, respectively, for the three and nine months ended September 30, 2018.

7. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	September 30, 2019	December 31, 2018
External research and development	$ 55,270	$ 36,213
Employee compensation	10,960	8,071
Accrued professional fees	8,720	4,423
Property and equipment costs	3,225	912
Other	2,244	2,092
Total	$ 80,419	$ 51,711

8. Collaboration Agreements

CStone Pharmaceuticals

On June 1, 2018, the Company entered into a collaboration and license agreement (the CStone agreement) with CStone pursuant to which the Company granted CStone exclusive rights to develop and commercialize the Company's drug candidates avapritinib, pralsetinib and fisogatinib, including back-up forms and certain other forms thereof, in Mainland China, Hong Kong, Macau and Taiwan (each, a CStone region and collectively, the CStone territory), either as a monotherapy or as part of a combination therapy. The Company will retain exclusive rights to the licensed products outside the CStone territory.

The Company received an upfront cash payment of $40.0 million, and subject to the terms of the CStone agreement, will be eligible to receive up to approximately $346.0 million in milestone payments, including $118.5

million related to development and regulatory milestones and $227.5 million related to sales-based milestones. In addition, CStone will be obligated to pay the Company tiered percentage royalties on a licensed product-by-licensed product basis ranging from the mid-teens to low twenties on annual net sales of each licensed product in the CStone territory, subject to adjustment in specified circumstances. CStone will be responsible for costs related to the development of the licensed products in the CStone territory, other than specified costs related to the development of fisogatinib as a combination therapy in the CStone territory that will be shared by the Company and CStone.

Pursuant to the terms of the CStone agreement, CStone will be responsible for conducting all development and commercialization activities in the CStone territory related to the licensed products, and the Company and CStone plan to conduct a proof-of-concept clinical trial in China evaluating fisogatinib in combination with CS1001, a clinical-stage anti-programmed death ligand-1 immunotherapy being developed by CStone, as a first-line therapy for the treatment of patients with hepatocellular carcinoma.

The CStone agreement will continue on a licensed product-by-licensed product and CStone region-by-CStone region basis until the later of (i) 12 years after the first commercial sale of a licensed product in a CStone region in the CStone territory and (ii) the date of expiration of the last valid patent claim related to the Company's patent rights or any joint collaboration patent rights for the licensed product that covers the composition of matter, method of use or method of manufacturing such licensed product in such region. Subject to the terms of the CStone agreement, CStone may terminate the CStone agreement in its entirety or with respect to one or more licensed products for convenience by providing written notice to the Company after June 1, 2019, and CStone may terminate the CStone agreement with respect to a licensed product for convenience at any time by providing written notice to the Company following the occurrence of specified events. In addition, the Company may terminate the CStone agreement under specified circumstances if CStone or certain other parties challenges the Company's patent rights or any joint collaboration patent rights or if CStone or its affiliates do not conduct any material development or commercialization activities with respect to one or more licensed products for a specified period of time, subject to specified exceptions. Either party may terminate the CStone agreement for the other party's uncured material breach or insolvency. In certain termination circumstances, the parties are entitled to retain specified licenses to be able to continue to exploit the licensed products, and in the event of termination by CStone for the Company's uncured material breach, the Company will be obligated to pay CStone a low single digit percentage royalty on a licensed product-by-licensed product basis on annual net sales of such licensed product in the CStone territory, subject to a cap and other specified exceptions.

The Company evaluated the CStone agreement to determine whether it is a collaborative arrangement for purposes of ASC 808. The Company determined that there were two material components of the CStone agreement: (i) the CStone territory-specific license and related activities in the CStone territory, and (ii) the parties' participation in global development of the licensed products. The Company concluded that the CStone territory-specific license and related activities in the CStone territory are not within the scope of ASC 808 because the Company is not exposed to significant risks and rewards. The Company concluded that CStone is a customer with regard to the component that includes the CStone territory-specific license and related activities in CStone territory, which include manufacturing. For the parties' participation in global development of the licensed products, the Company concluded that the research and development activities and cost-sharing payments related to such activities are within the scope of ASC 808 as both parties are active participants exposed to the risk of the activities under the CStone agreement. The Company concluded that CStone is not a customer with regard to the global development component in the context of the CStone agreement. Therefore, payments received by the Company for global development activities under the CStone agreement, including manufacturing, will be accounted for as a reduction of related expenses.

A summary of manufacturing services related to the global development activities during the three and nine months ended September 30, 2019 and 2018 is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Manufacturing services related to global development activities	$ 1,275	$ 345	$ 2,403	$ 345

The Company evaluated the CStone territory-specific license and related activities in the CStone territory under ASC 606 as these transactions are considered transactions with a customer. The Company identified the following material promises under the arrangement: (1) the three exclusive licenses granted in the CStone territory to develop,

manufacture and commercialize the three licensed products; (2) the initial know-how transfer for each licensed product; (3) manufacturing activities related to development and commercial supply of the licensed products; (4) participation in the joint steering committee (JSC) and joint project teams (JPT); (5) regulatory responsibilities; and (6) manufacturing technology and continuing know-how transfers. The Company determined that each licensed product is distinct from the other licensed products. In addition, the Company determined that the exclusive licenses and initial know-how transfers for each licensed product were not distinct from each other, as each exclusive license has limited value without the corresponding initial know-how transfer. For purposes of ASC 606, the Company determined that that participation on the JSC and JPTs, the regulatory responsibilities and the manufacturing technology and continuing know-how transfers are qualitatively and quantitatively immaterial in the context of the CStone agreement and therefore are excluded from performance obligations. As such, the Company determined that these six material promises, described above, should be combined into one performance obligation for each of the three candidates.

The Company evaluated the provision of manufacturing activities related to development and commercial supply of the licensed products as an option for purposes of ASC 606 to determine whether these manufacturing activities provide CStone with any material rights. The Company concluded that the manufacturing activities were not issued at a significant and incremental discount, and therefore do not provide CStone with any material rights. As such, the manufacturing activities are excluded as performance obligations at the outset of the arrangement.

Based on these assessments, the Company identified three distinct performance obligations at the outset of the CStone agreement, which consists of the following for each licensed product: (1) the exclusive license and (2) the initial know-how transfer.

Under the CStone agreement, in order to evaluate the transaction price for purposes of ASC 606, the Company determined that the upfront amount of $40.0 million constituted the entirety of the consideration to be included in the transaction price as of the outset of the arrangement, which was allocated to the three performance obligations. The potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement. The Company satisfied the performance obligations upon delivery of the licenses, initial know-how transfers and product trademark and recognized the upfront payment of $40.0 million as revenue during the second quarter of 2018.

The Company will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and if necessary, the Company will adjust its estimate of the transaction price, and any addition to the transaction price would be recognized as revenue when it becomes probable that inclusion would not lead to a significant revenue reversal. During the three months ended September 30, 2019, three development and regulatory milestones were either achieved or deemed probable, and the associated aggregate cash consideration of $6.0 million for such milestones was added to the estimated transaction price for the CStone agreement.

A summary of revenue recognized under the CStone agreement during the three and nine months ended September 30, 2019 and 2018 is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
License milestone revenue	$ 6,000	$ —	$ 10,000	$ 40,000
Manufacturing services related to territory-specific activities	—	—	144	—
Total CStone collaboration revenue	$ 6,000	$ —	$ 10,144	$ 40,000

The following table presents the contract assets associated with the CStone agreement as of September 30, 2019 and December 31, 2018 (in thousands):

	September 30, 2019	December 31, 2018
Accounts receivables	$ 2,414	$ —

Unbilled accounts receivables	$ 2,662	$ 151

There was no revenue deferred as a contract liability associated with the CStone agreement as of September 30, 2019 and December 31, 2018.

Roche

In March 2016, the Company entered into a collaboration and license agreement (as amended, Roche agreement) with Roche for the discovery, development and commercialization of up to five small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy, as single products or possibly in combination with other therapeutics.

Under the Roche agreement, Roche was granted up to five option rights to obtain an exclusive license to exploit products derived from the collaboration programs in the field of cancer immunotherapy. Such option rights are triggered upon the achievement of Phase 1 proof-of-concept. As a result of an amendment to the Roche agreement in the fourth quarter of 2019, the parties are currently conducting activities for up to four programs under the collaboration. See Note 13, *Subsequent Events*. For up to two collaboration programs, if Roche exercises its option, Roche will receive worldwide, exclusive commercialization rights for the licensed products. For up to two collaboration programs, if Roche exercises its option, the Company will retain commercialization rights in the United States for the licensed products, and Roche will receive commercialization rights outside of the United States for the licensed products. The Company will also retain worldwide rights to any products for which Roche elects not to exercise its applicable option.

Prior to Roche's exercise of an option, the Company will have the lead responsibility for drug discovery and pre-clinical development of all collaboration programs. In addition, the Company will have the lead responsibility for the conduct of all Phase 1 clinical trials other than those Phase 1 clinical trials for any product in combination with Roche's portfolio of therapeutics, for which Roche will have the right to lead the conduct of such Phase 1 clinical trials. Pursuant to the Roche agreement, the parties will share the costs of Phase 1 development for each collaboration program. In addition, Roche will be responsible for post-Phase 1 development costs for each licensed product for which it retains global commercialization rights, and the Company and Roche will share post-Phase 1 development costs for each licensed product for which the Company retains commercialization rights in the United States.

The Company received an upfront cash payment of $45.0 million in March 2016 upon execution of the Roche agreement, and subject to the terms of the Roche agreement, the Company will be eligible to receive up to approximately $965.0 million in contingent option fees and milestone payments related to specified research, pre-clinical, clinical, regulatory and sales-based milestones. Of the total contingent payments, up to approximately $215.0 million are for option fees and milestone payments for research, pre-clinical and clinical development events prior to licensing across all five potential collaboration programs, including contingent milestone payments for initiation of each of the collaboration programs for which the parties will work together to select targets (pre-option exercise milestones). In June 2018, the Company achieved and received a $10.0 million research milestone payment.

In addition, for any licensed product for which Roche retains worldwide commercialization rights, the Company will be eligible to receive tiered royalties ranging from low double-digits to high-teens on future net sales of the licensed product. For any licensed product for which the Company retains commercialization rights in the United States, the Company and Roche will be eligible to receive tiered royalties ranging from mid-single-digits to low double-digits on future net sales in the other party's respective territories in which it commercializes the licensed product. The upfront cash payment and any payments for milestones, option fees and royalties are non-refundable, non-creditable and not subject to set-off.

The Roche agreement will continue until the date when no royalty or other payment obligations are or will become due, unless earlier terminated in accordance with the terms of the Roche agreement. Prior to its exercise of its first option, Roche may terminate the Roche agreement at will, in whole or on a collaboration target-by-collaboration target basis, upon 120 days' prior written notice to the Company. Following its exercise of an option, Roche may terminate the Roche agreement at will, in whole, on a collaboration target-by-collaboration target basis, on a collaboration program-by-collaboration program basis or, if a licensed product has been commercially sold, on a country-by-country basis, (i) upon 120 days' prior written notice if a licensed product has not been commercially sold or (ii) upon 180 days' prior written notice if a licensed product has been commercially sold. Either party may terminate the

Roche agreement for the other party's uncured material breach or insolvency and in certain other circumstances agreed to by the parties. In certain termination circumstances, the Company is entitled to retain specified licenses to be able to continue to exploit the licensed products.

The Company assessed this arrangement in accordance with ASC 606 upon the adoption of the new standard on January 1, 2018, and concluded that the contract counterparty, Roche, is a customer prior to the exercise, if any, of an option by Roche. The Company identified the following material promises under the arrangement: (1) a non-transferable, sub-licensable and non-exclusive license to use the Company's intellectual property and collaboration compounds to conduct research activities; (2) research and development activities through Phase 1 clinical trials under the research plan; (3) five option rights for licenses to develop, manufacture, and commercialize the collaboration targets; (4) participation on a joint research committee (JRC) and joint development committee (JDC); and (5) regulatory responsibilities under Phase 1 clinical trials. The Company determined that the license and research and development activities were not distinct from another, as the license has limited value without the performance of the research and development activities. Participation on the JRC and JDC to oversee the research and development activities was determined to be quantitatively and qualitatively immaterial and therefore is excluded from performance obligations. The regulatory responsibilities related to filings and obtaining approvals related to the products that may result from each program do not represent separate performance obligations based on their dependence on the research and development efforts. As such, the Company determined that these promises should be combined into a single performance obligation.

The Company evaluated the option rights for licenses to develop, manufacture, and commercialize the collaboration targets to determine whether it provides Roche with any material rights. The Company concluded that the options were not issued at a significant and incremental discount, and therefore do not provide material rights. As such, they are excluded as performance obligations at the outset of the arrangement.

Based on these assessments, the Company identified one performance obligation at the outset of the Roche agreement, which consists of: (1) the non-exclusive license; (2) the research and development activities through Phase 1; and (3) regulatory responsibilities under Phase 1 clinical trials.

Under the Roche agreement, in order to evaluate the appropriate transaction price, the Company determined that as of January 1, 2018, the upfront amount of $45.0 million constituted the entirety of the consideration to be included in the transaction price as of the outset of the arrangement, which was allocated to the single performance obligation. The option exercise payments that may be received are excluded from the transaction price until each customer option is exercised as it was determined that the options are not material rights. The potential milestone payments that the Company is eligible to receive prior to the exercise of the options were initially excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement. The Company will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

In June 2018, the Company achieved and received a $10.0 million research milestone payment related to the Roche agreement, and it became probable that a significant reversal of cumulative revenue would not occur for the $10.0 million research milestone achieved. At such time, the associated consideration was added to the estimated transaction price and allocated to the existing performance obligation.

The Company recognizes revenue associated with the performance obligation as the research and development services are provided using an input method, according to the costs incurred as related to the research and development activities on each program and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurs over this time period and, in management's judgment, is the best measure of progress towards satisfying the performance obligation. The amounts received that have not yet been recognized as revenue are deferred as a contract liability on the Company's consolidated balance sheet and will be recognized over the remaining research and development period until the performance obligation is satisfied.

During the three months ended September 30, 2019, a reduction in the costs expected to be incurred in the future to satisfy certain performance obligations under the collaboration became probable. Accordingly, the Company recorded a cumulative revenue catch-up of $2.0 million during the three months ended September 30, 2019. For additional information, see Note 13, *Subsequent Events*.

A summary of revenue recognized under the Roche agreement during the three and nine months ended September 30, 2019 and 2018 is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Roche collaboration research and development services revenue	$ 3,139	$ 1,095	$ 4,836	$ 3,488

During the three and nine months ended September 30, 2019 and 2018, the Company recognized the following revenue due to the changes in the contract liability balances (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Amounts included in the contract liability at the beginning of the period	$ 1,149	$ 1,129	$ 3,470	$ 3,240

As of September 30, 2019, the Company had revenue deferred as a contract liability related to the Roche agreement of $41.3 million, of which $4.9 million was included in current liabilities, and the research and development services related to the performance obligation are expected to be performed over a remaining period of approximately 5.5 years.

9. Stock-based compensation

2015 Stock Option and Incentive Plan

In 2015, the Company's board of directors and stockholders approved the 2015 Stock Option and Incentive Plan (the 2015 Plan), which replaced the Company's 2011 Stock Option and Grant Plan, as amended (the 2011 Plan). The 2015 Plan includes incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units, unrestricted stock, performance share awards and cash-based awards. The Company initially reserved a total of 1,460,084 shares of common stock for the issuance of awards under the 2015 Plan. The 2015 Plan provides that the number of shares reserved and available for issuance under the 2015 Plan will be cumulatively increased on January 1 of each calendar year by 4% of the number of shares of common stock issued and outstanding on the immediately preceding December 31 or such lesser amount as specified by the compensation committee of the board of directors. For the calendar year beginning January 1, 2019, the number of shares reserved for issuance under the 2015 Plan was increased by 1,761,481 shares. In addition, the total number of shares reserved for issuance is subject to adjustment in the event of a stock split, stock dividend or other change in the Company's capitalization. At September 30, 2019, there were 1,653,349 shares available for future grant under the 2015 Plan.

Stock options

The following table summarizes the stock option activity for the nine months ended September 30, 2019:

	Shares	Weighted-Average Exercise Price
Outstanding at December 31, 2018	4,557,800	$ 44.64
Granted	1,673,749	84.12
Exercised	(462,806)	23.69
Canceled	(137,266)	68.03
Outstanding at September 30, 2019	5,631,477	$ 57.53
Exercisable at September 30, 2019	2,527,772	$ 36.67

At September 30, 2019, the total unrecognized compensation expense related to unvested stock option awards was $135.3 million, which is expected to be recognized over a weighted-average period of approximately 2.82 years.

Restricted stock units

The following table summarizes the restricted stock units activity for the nine months ended September 30, 2019:

	Shares	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2018	36,868	$ 66.28
Granted	356,915	85.30
Vested	(2,730)	66.40
Forfeited	(9,261)	80.53
Unvested shares at September 30, 2019	381,792	$ 83.72

At September 30, 2019, the total unrecognized compensation expense related to unvested restricted stock units was $27.7 million, which is expected to be recognize over a weighted-average period of approximately 3.39 years.

2015 Employee Stock Purchase Plan

In 2015, the Company's board of directors and stockholders approved the 2015 Employee Stock Purchase Plan (the 2015 ESPP), which became effective upon the closing of the Company's initial public offering in May 2015. The Company initially reserved a total of 243,347 shares of common stock for issuance under the 2015 ESPP. The 2015 ESPP provides that the number of shares reserved and available for issuance under the 2015 ESPP will be cumulatively increased on January 1 of each calendar year by 1% of the number of shares of common stock issued and outstanding on the immediately preceding December 31 or such lesser amount as specified by the compensation committee of the board of directors. For the calendar year beginning January 1, 2019, the number of shares reserved for issuance under the 2015 ESPP was increased by 440,370 shares. The Company issued 10,718 and 5,572 shares under the 2015 ESPP during the nine months ended September 30, 2019 and 2018, respectively.

Stock-based compensation expense

The Company recognized stock-based compensation expense totaling $15.0 million and $39.0 million for the three and nine months ended September 30, 2019, respectively. The Company recognized stock-based compensation expense totaling $8.4 million and $21.7 million for the three and nine months ended September 30, 2018, respectively. Stock-based compensation expense by award type included within the unaudited condensed consolidated statements of operations and comprehensive loss was as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Stock options	$ 12,778	$ 8,278	$ 34,373	$ 21,468
Restricted stock units	2,076	42	4,243	42
Employee stock purchase plan	139	71	338	192
Total stock-based compensation expense	$ 14,993	$ 8,391	$ 38,954	$ 21,702

Stock-based compensation expense by classification within the unaudited condensed consolidated statements of operations and comprehensive loss is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Research and development	$ 7,678	$ 4,770	$ 20,971	$ 12,054
General and administrative	7,315	3,621	17,983	9,648
Total stock-based compensation expense	$ 14,993	$ 8,391	$ 38,954	$ 21,702

10. Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period. For purposes of the dilutive net loss per share calculation, stock options, unvested restricted stock units and ESPP shares are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share were the same for all periods presented as a result of the Company's net loss.

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect.

	Nine Months Ended September 30,	
	2019	2018
Stock options	5,631,477	4,458,508
Restricted stock units	381,792	12,195
ESPP shares	11,641	5,860
Total	6,024,910	4,476,563

The weighted average number of common shares used in net loss per share on a basic and diluted basis were 48,921,445 and 43,915,376 for the three months ended September 30, 2019 and 2018, respectively. The weighted average number of common shares used in net loss per share on a basic and diluted basis were 47,360,675 and 43,824,773 for the nine months ended September 30, 2019 and 2018, respectively.

11. Leases

38 Sidney Street

On February 12, 2015, the Company entered into a lease for approximately 38,500 rentable square feet of office and laboratory space at 38 Sidney Street in Cambridge, Massachusetts, which the Company gained control over on June 15, 2015, and occupancy commenced in October 2015. The initial term of the lease agreement will expire on October 31, 2022, unless terminated sooner. The Company has an option to extend the lease for five additional years. The lease has a

total commitment of $17.8 million over the initial seven-year term. The Company has agreed to pay an initial annual base rent of approximately $2.3 million, which rises periodically until it reaches approximately $2.8 million. The lease provided the Company with an allowance for leasehold improvements of $4.3 million. Prior to adoption of ASC 842, the Company recorded rent expense on a straight-line basis through the end of the lease term and the associated deferred rent on the consolidated balance sheet. The Company also recorded the leasehold improvement incentives as a reduction to rent expense ratably over the lease term, and the balance from the leasehold improvement incentives was included in lease incentive obligations on the consolidated balance sheet as of December 31, 2018. The lease agreement required the Company to pay a security deposit of $1.3 million, of which $0.2 million was released in February 2018 and February 2019, respectively. The remaining $0.9 million is recorded in restricted cash on the Company's condensed consolidated balance sheet as of September 30, 2019.

In the first quarter of 2018, the Company subleased its former corporate headquarters at 38 Sidney Street, Cambridge, Massachusetts through October 31, 2020. Subject to the terms of the sublease agreement and the master lease agreement, including a right of recapture by the Company, the sublessee has the option to extend the sublease through October 31, 2022. The sublease includes a total commitment by the sublessee of $8.2 million over the 32 month term of the sublease agreement. During the 32 month term, the Company will be responsible for total rental payments of $6.9 million and an additional $0.7 million in total payments related to the Company's profit on the sublease income which are payable by the Company to the landlord. As of September 30, 2019, the remaining minimum sublease rental commitment by the sublessee was $3.4 million.

45 Sidney Street

On April 28, 2017, the Company entered into a lease agreement for approximately 99,833 rentable square feet of office and laboratory space located at 45 Sidney Street in Cambridge, Massachusetts. The initial term of the lease agreement commenced on October 1, 2017 and will expire on November 30, 2029, unless terminated sooner. The lease agreement also provides the Company with an option to extend the lease agreement for two consecutive five-year periods at the then fair market annual rent, as defined in the lease agreement.

During the initial term of the lease agreement, the Company has agreed to pay an initial annual base rent of approximately $7.7 million, which increases annually until it reaches approximately $10.6 million in the last year of the initial term. The lease provided the Company with a tenant improvement allowance of approximately $14.2 million for improvements to be made to the premises. Prior to adoption of ASC 842, the Company recorded rent expense on a straight-line basis through the end of the lease term and the associated deferred rent on the consolidated balance sheet. The Company also recorded the leasehold improvement incentives as a reduction to rent expense ratably over the lease term, and the balance from the leasehold improvement incentives was included in lease incentive obligations on the consolidated balance sheet as of December 31, 2018. The lease agreement required the Company to pay a security deposit of $3.5 million, of which $3.0 million is recorded in restricted cash on the Company's condensed consolidated balance sheet as of September 30, 2019, and an additional $0.5 million is due to be released in October 2019 in accordance with the terms of the lease agreement.

On September 19, 2018, the Company entered into an amendment to the lease agreement for its office and laboratory space located at 45 Sidney Street in Cambridge, Massachusetts to expand the rentable square footage from approximately 99,833 square feet to approximately 139,216 square feet. The initial term of the lease with respect to the expansion premises commenced on March 1, 2019 and will expire on November 30, 2029, unless terminated sooner. Pursuant to the lease amendment, the rent commencement date for the expansion premises was July 1, 2019.

The Company has agreed to pay an initial annual base rent of approximately $3.2 million for the expansion premises, which increases annually until it reaches approximately $4.2 million in the last year of the initial term for the expansion premises. Pursuant to the lease amendment, the landlord has also agreed to provide the Company with a tenant improvement allowance of approximately $3.2 million for improvements to be made to the expansion premises. The lease amendment required the Company to pay an additional security deposit of $0.8 million to the landlord for the expansion premises, which is recorded in restricted cash on the Company's condensed consolidated balance sheet as of September 30, 2019.

The lease agreements do not contain residual value guarantees and the components of lease cost for the three and nine months ended September 30, 2019 were as follows (in thousands):

Operating leases:	Three Months Ended September 30, 2019	Nine Months Ended September 30, 2019
Lease cost	$ 4,167	$ 11,906
Sublease income	(708)	(2,117)
Net lease cost	$ 3,459	$ 9,789

For the three and nine months ended September 30, 2018, rent expenses under ASC 840, net of sublease income, was $1.7 million and $5.6 million, respectively.

The Company has not entered into any material short-term leases or financing leases as of September 30, 2019.

Supplemental cash flow information related to leases for the three and nine months ended September 30, 2019 was as follows (in thousands):

	Three Months Ended September 30, 2019	Nine Months Ended September 30, 2019
Cash paid for amounts included in the measurement of lease liabilities:	$ 3,485	$ 8,727
Lease liabilities arising from obtaining right-of-use assets:		
Operating leases	$ -	$ 23,300

The weighted average remaining lease term and weighted average discount rate of the operating leases are as follows:

	Operating leases
Weighted average remaining lease term in years	9.50
Weighted average discount rate	8.2%

Future minimum lease payments under non-cancellable leases as of September 30, 2019 were as follows (in thousands):

2019 (excluding the 9 months ended September 30, 2019)	$ 3,521
2020	14,341
2021	14,764
2022	14,719
2023	12,746
Thereafter	83,471
Total future minimum lease payments (1)	143,562
Less imputed interest	(46,054)
Total	$ 97,508

(1) Minimum lease payments have not been reduced by minimum sublease rentals of $3.1 million due in the future under the Company's non-cancelable sublease for the office and laboratory space located at 38 Sidney Street, Cambridge, Massachusetts. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

Under the prior lease guidance minimum rental commitments under non-cancelable leases for each of the next five years and total thereafter as of December 31, 2018, were as follows (in thousands):

2019	$ 12,247
2020	14,341
2021	14,764
2022	14,719
2023	12,746
Thereafter	83,471
Total minimum lease payments (1)	$ 152,288

(1) Minimum lease payments have not been reduced by minimum sublease rentals of $5.3 million due in the future under the Company's non-cancelable sublease for the office and laboratory space located at 38 Sidney Street, Cambridge, Massachusetts. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

12. Commitments

The Company has no other commitments other than the minimum lease payments commitment as disclosed in Note 11, *Leases*.

13. Subsequent Events

License Agreement with Clementia

On October 15, 2019, the Company entered into a license agreement (the Clementia agreement) with Clementia, a wholly-owned subsidiary of Ipsen S.A. Under the Clementia agreement, the Company granted an exclusive, worldwide, royalty-bearing license to Clementia to develop and commercialize BLU-782, the Company's oral, highly selective investigational ALK2 inhibitor in Phase 1 clinical development for the treatment of fibrodysplasia ossificans progressiva, as well as specified other compounds related to the BLU-782 program.

Subject to the terms of the Clementia agreement, the Company will be eligible to receive up to $535.0 million in upfront, milestone and other payments, including an upfront cash payment of $25.0 million, a $20.0 million cash milestone payment due in the third quarter of 2020 and up to $490.0 million in other payments and potential development, regulatory and sales-based milestone payments for licensed products. In addition, Clementia is obligated to pay to the Company royalties on aggregate annual worldwide net sales of licensed products at tiered percentage rates ranging from the low- to mid-teens, subject to adjustment in specified circumstances under the Clementia agreement, and to purchase specified manufacturing inventory from the Company.

The Company is currently evaluating the revenue recognized under the Clementia agreement and expects to recognize revenue during the fourth quarter of 2019 related to a majority of the $25.0 million upfront cash payment and the $20.0 million cash milestone payment anticipated in the third quarter of 2020.

Collaboration with Roche

In the fourth quarter of 2019, the Company achieved an $8.0 million research milestone under the Roche agreement.

On November 1, 2019, the Company entered into a sixth amendment to the Roche agreement, pursuant to which the Company and Roche agreed to, among other things, modify certain cost-sharing arrangements related to certain preclinical development activities for the collaboration programs and terminate one of the collaboration targets. As a result of the termination of such collaboration target, the parties are currently conducting activities for up to four programs under the collaboration.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our unaudited consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and the unaudited consolidated financial statements and related notes thereto and management's discussion and analysis of financial condition and results of operations included in our Annual Report on Form 10-K for the year ended December 31, 2018, filed with the Securities and Exchange Commission, or the SEC, on February 26, 2019. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report on Form 10-Q, our actual results or timing of certain events could differ materially from the results or timing described in, or implied by, these forward-looking statements.

Overview

We are a precision therapy company focused on genomically defined cancers, rare diseases and cancer immunotherapy. Our approach is to leverage our novel target discovery engine to systematically and reproducibly identify kinases that are drivers of diseases and to craft highly selective and potent drug candidates that may provide significant and durable clinical responses for patients without adequate treatment options. This integrated biology and chemistry approach enables us to identify, characterize and design drug candidates to inhibit novel kinase targets that have been difficult to selectively inhibit. We believe that our uniquely targeted, scalable approach empowers the rapid design and development of new treatments and increases the likelihood of success. Our lead drug candidates are avapritinib and pralsetinib, and our other drug candidates are fisogatinib and BLU-263.

Avapritinib: KIT and PDGFRA

Avapritinib is an orally available, potent and highly selective inhibitor that targets KIT and PDGFRA mutations. These mutations abnormally activate receptor tyrosine kinases that are drivers of cancer and proliferative disorders, including gastrointestinal stromal tumors, or GIST, and systemic mastocytosis, or SM. GIST is a rare disease that is a sarcoma, or tumor of bone or connective tissue, of the gastrointestinal tract, and SM is a rare disorder that causes an overproduction of mast cells and the accumulation of mast cells in the bone marrow and other organs, which can lead to a wide range of debilitating symptoms and organ dysfunction and failure.

Gastrointestinal stromal tumors (GIST)

We are currently evaluating avapritinib for the treatment of GIST in an ongoing Phase 1 clinical trial in advanced GIST, which we refer to as our NAVIGATOR trial, and an ongoing global, randomized Phase 3 clinical trial comparing avapritinib to regorafenib in third-line GIST, which we refer to as our VOYAGER trial. We have completed enrollment of the NAVIGATOR trial, and in June 2019, we reported updated data from the NAVIGATOR trial at the 2019 American Society of Clinical Oncology, or ASCO, Annual Meeting. In July 2019, as part of our collaboration with CStone Pharmaceuticals, or CStone, we dosed the first patient in China in our ongoing VOYAGER trial. We have completed patient screening in the VOYAGER trial, and we recently achieved the target enrollment for this trial. We expect to report top-line data from the VOYAGER trial in the second quarter of 2020. We plan to continue to evaluate opportunities for the development of avapritinib in second-line GIST and provide an update in 2020 on those plans and our previously announced planned Phase 3 clinical trial in second-line GIST, which we refer to as our COMPASS-2L trial.

In June 2019, we submitted a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for avapritinib for the treatment of adult patients with PDGFRA Exon 18 mutant GIST, regardless of prior therapy, and fourth-line GIST. In August 2019, the FDA accepted this NDA and granted priority review. The FDA set a Prescription Drug User Fee Act, or PDUFA, action date of February 14, 2020 for the NDA. In October 2019, we announced that the FDA informed us in writing that it intends to administratively split the proposed indications for avapritinib into two separate NDAs: one for PDGFRA Exon 18 mutant GIST, regardless of prior therapy, and one for fourth-line GIST. Given the acceleration of the VOYAGER trial and the anticipated availability of top-line data in the second quarter of 2020, the FDA requested top-line data from the VOYAGER trial and indicated these data would be informative in its review of the proposed fourth-line indication and potential clinical benefit in this population, including

its evaluation of response rate and safety for the fourth-line indication. Assuming the FDA administratively splits the fourth-line GIST indication into a separate NDA, an extension of up to three months for the PDUFA action date for the fourth-line indication will likely be required to provide the top-line VOYAGER data to the FDA for the FDA to render a decision on the NDA for the fourth-line indication. Assuming an approval of an initial NDA for avapritinib, we plan to submit a supplemental NDA to the FDA for avapritinib for the treatment of third-line GIST in the second half of 2020. In July 2019, the European Medicines Agency, or EMA, validated our marketing authorization application, or MAA, for avapritinib for the treatment of adult patients with PDGFRa D842V mutant GIST, regardless of prior therapy, and fourth-line GIST. Validation of the MAA confirms that the application is sufficiently complete to begin the formal review process. The FDA has granted orphan drug designation to avapritinib for the treatment of GIST, and the European Commission has granted orphan medicinal product designation to avapritinib for the treatment of GIST. The FDA has granted fast track designation to avapritinib for (i) the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and (ii) the treatment of patients with unresectable or metastatic GIST with the PDGFRA D842V mutation regardless of prior therapy. In addition, the FDA has granted breakthrough therapy designation to avapritinib for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRA D842V mutation.

Systemic Mastocytosis (SM)

We are also currently evaluating avapritinib for the treatment of SM in an ongoing Phase 1 clinical trial in advanced SM, which we refer to as our EXPLORER trial, an ongoing registration-enabling Phase 2 clinical trial in advanced SM, which we refer to as our PATHFINDER trial, and an ongoing registration-enabling Phase 2 clinical trial in indolent and smoldering SM, which we refer to as our PIONEER trial. In June 2019, we reported updated data from the EXPLORER trial in advanced SM at the 24th Congress of the European Hematology Association. We recently completed enrollment in the dose-finding portion of the PIONEER trial and plan to present initial data from the dose-finding portion (part 1) of the PIONEER trial in a poster presentation at the 61st American Society of Hematology Annual Meeting & Exposition in December 2019.

Based on discussions with the FDA regarding the data required to support an NDA submission, we plan to submit an NDA to the FDA for avapritinib for the treatment of advanced SM in the first quarter of 2020 based on the combined data from our EXPLORER and PATHFINDER trials. In the second half of 2019, we amended the protocol for the PATHFINDER trial to include additional patients and expect to continue enrolling patients for the PATHFINDER trial. The FDA has granted orphan drug designation to avapritinib for the treatment of mastocytosis, and the European Commission has granted orphan medicinal product designation to avapritinib for the treatment of mastocytosis. In addition, the FDA has granted breakthrough therapy designation to avapritinib for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia.

Pralsetinib: RET

Pralsetinib is an orally available, potent and highly selective inhibitor that targets RET, a receptor tyrosine kinase that is abnormally activated by mutations or fusions and RET resistance mutations that we predict will arise from treatment with first generation therapies. RET drives disease in subsets of patients with non-small cell lung cancer, or NSCLC, and cancers of the thyroid, including medullary thyroid carcinoma, or MTC, and papillary thyroid cancer, or PTC, and our research suggests that RET may drive disease in subsets of patients with colon cancer, breast cancer and other cancers.

We are currently evaluating pralsetinib in an ongoing Phase 1/2 clinical trial in patients with RET-altered NSCLC, MTC and other advanced solid tumors, which we refer to as our ARROW trial. In June 2019, we reported updated RET-fusion NSCLC data and RET-mutant data at the 2019 ASCO Annual Meeting. In the fourth quarter of 2019, we plan to initiate a Phase 3 clinical trial evaluating pralsetinib in first-line RET-fusion NSCLC. In addition, we plan to submit an NDA to the FDA for pralsetinib for the treatment of patients with RET-fusion NSCLC previously treated with platinum-based chemotherapy in the first quarter of 2020, and we plan to submit an NDA to the FDA for pralsetinib for the treatment of patients with MTC previously treated with an approved multi-kinase inhibitor in the first half of 2020. In September 2018, we presented two clinical cases demonstrating proof-of-concept for pralsetinib in combination with osimertinib (Tagrisso®) in treatment-resistant, EGFR-mutant NSCLC at the International Association for the Study of Lung Cancer 19th World Conference on Lung Cancer and published online in *Cancer Discovery*. We now plan to initiate a Phase 2 clinical trial evaluating pralsetinib in combination with osimertinib in treatment-resistant,

EGFR-mutant NSCLC harboring an acquired RET fusion in 2020.

The FDA has granted orphan drug designation to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC, and the FDA has granted breakthrough therapy designation to pralsetinib for the treatment of patients with RET-fusion positive NSCLC that has progressed following platinum-based chemotherapy and to pralsetinib for the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments.

Fisogatinib: FGFR4

Fisogatinib is an orally available, potent and highly selective inhibitor that targets FGFR4, a kinase that is aberrantly activated in a defined subset of patients with hepatocellular carcinoma, or HCC, the most common type of liver cancer. We are currently evaluating fisogatinib in an ongoing Phase 1 clinical trial in patients with advanced HCC. In May 2019, as part of the collaboration with CStone, we dosed the first patient in China in our ongoing Phase 1 trial of fisogatinib in advanced HCC. In the second quarter of 2019, the China National Medicinal Products Administration approved a clinical trial application for a proof-of-concept clinical trial evaluating fisogatinib in combination with CS1001, a clinical-stage anti-programmed death ligand-1 immunotherapy being developed by CStone, as a first-line therapy for the treatment of patients with HCC, and we and CStone plan to initiate this clinical trial in the fourth quarter of 2019. The FDA has granted orphan drug designation to BLU-554 for the treatment of HCC.

BLU-263: KIT

BLU-263 is an orally available, potent and highly selective KIT inhibitor currently in the discovery stage for the treatment of mast cell disorders. BLU-263 is designed to have equivalent potency as avapritinib, improved selectivity for KIT, with low off-target activity, and lower penetration of the central nervous system relative to avapritinib based on preclinical data, which may provide BLU-263 flexibility to expand into indolent SM and a broader set of mast cell disorders. We plan to submit an investigational new drug application for BLU-263 for indolent SM in the first half of 2020.

Discovery Platform

We also plan to continue to leverage our discovery platform to systematically and reproducibly identify kinases that are drivers of diseases in genomically defined patient populations and craft drug candidates that potently and selectively target these kinases. We currently have five wholly-owned discovery programs, consisting of the following: BLU-263; pre-development candidate programs targeting EGFR Exon 19/L858R+C797S and EGFR Exon 19/L858R+T790M+C797S, which are acquired resistance mutations in NSCLC patients following treatment with osimertinib; and pre-development candidate programs for two undisclosed kinase targets. We anticipate nominating two development candidates in the first half of 2020: one for EGFR Exon 19/L858R+T790M+C797S and one for MAP4K1 under the Roche collaboration.

Collaborations and Licenses

We currently have worldwide development and commercialization rights to avapritinib, pralsetinib and fisogatinib, other than the rights licensed to CStone for these drug candidates in Mainland China, Hong Kong, Macau and Taiwan, or the CStone territory. We currently have worldwide development and commercialization rights to BLU-263 and all of our other discovery programs, other than the discovery-stage cancer immunotherapy programs under collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., which we collectively refer to as Roche.

Roche. We entered into a collaboration with Roche in March 2016. Under our collaboration agreement with Roche, we agreed to work with Roche to discover, develop and commercialize up to five small molecule therapeutics targeting kinases believed to be important in cancer immunotherapy, as single products or possibly in combination with other therapeutics. In the fourth quarter of 2019, we and Roche announced one of the kinase targets under the collaboration, MAP4K1, which is believed to play a role in T cell regulation. In addition, in the fourth quarter of 2019, we and Roche mutually agreed to terminate one of the other collaboration targets and as a result are currently conducting activities for up to four programs under the collaboration.

CStone. We entered into a collaboration with CStone in June 2018. Under our collaboration agreement with CStone, we are seeking to develop and commercialize avapritinib, pralsetinib and fisogatinib, including back-up forms and certain other forms, in the CStone territory either as a monotherapy or as part of a combination therapy.

Clementia. In October 2019, we entered into a license agreement with Clementia Pharmaceuticals, Inc., or Clementia, a wholly-owned subsidiary of Ipsen S.A., and granted an exclusive, worldwide, royalty-bearing license to Clementia to develop and commercialize BLU-782, as well as specified other compounds related to the BLU-782 program. BLU-782 is an orally available, potent and highly selective inhibitor that targets mutant activin-like kinase 2, or ALK2, in development for the treatment of fibrodysplasia ossificans progressiva, or FOP. We recently completed enrollment in the Phase 1 trial for BLU-782 in healthy volunteers, and Clementia is planning to commence a potentially pivotal Phase 2 trial of BLU-782 for the treatment of FOP in 2020 as monotherapy. The FDA has granted a rare pediatric disease designation, orphan drug designation and fast track designation to BLU-782.

We will continue to evaluate additional collaborations, partnerships and licenses that could maximize the value for our programs and allow us to leverage the expertise of strategic collaborators, partners and licensors. We are also focused on engaging in collaborations, partnerships and license agreements to capitalize on our discovery platform outside of our primary strategic focus area of cancer.

Financial Operations Overview

General

To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred stock, collaborations, a license agreement and a debt financing. Through September 30, 2019, we have received an aggregate of $1.5 billion from such transactions, including $1.2 billion in aggregate gross proceeds from the sale of common stock in our May 2015 initial public offering, or IPO, and December 2016, April 2017, December 2017 and April 2019 follow-on public offerings, $115.1 million in gross proceeds from the issuance of convertible preferred stock, $18.8 million in upfront and milestone payments under our former collaboration with Alexion Pharma Holding, or Alexion, $55.0 million in upfront and milestone payments under our collaboration with Roche, $46.0 million in upfront and milestone payments under our collaboration with CStone, and $10.0 million in gross proceeds from the debt financing. In addition, we received the $25.0 million upfront payment under our license agreement with Clementia in October 2019 and expect to receive $8.0 million in the fourth quarter of 2019 related to a research milestone achieved under the Roche collaboration in the fourth quarter of 2019.

Since inception, we have incurred significant operating losses. Our net losses were $281.4 million for the nine months ended September 30, 2019 and $236.6 million, $148.1 million and $72.5 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of September 30, 2019, we had an accumulated deficit of $878.9 million. We expect to continue to incur significant expenses and operating losses over the next several years. We anticipate that our expenses will increase significantly in connection with our ongoing activities, particularly as we:

- continue to advance and initiate clinical development activities for our lead drug candidates, avapritinib and pralsetinib, as well as our other drug candidates, fisogatinib and BLU-263;
- continue to manufacture increasing quantities of the active pharmaceutical ingredient, or API, drug substance and drug product material for use in pre-clinical studies, clinical trials, compassionate use program and for any potential commercial inventory;
- seek marketing approvals for avapritinib and pralsetinib, as well as our other drug candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize avapritinib and pralsetinib, if approved, and any other medicines for which we may obtain marketing approval;
- conduct development and commercialization activities for companion diagnostic tests for current or future drug candidates;

- continue to discover, validate and develop additional drug candidates;
- conduct research and development activities under our collaborations with Roche and CStone;
- maintain, expand and protect our intellectual property portfolio;
- acquire or in-license other drug candidates or technologies;
- establish our operations outside the United States;
- hire additional research, clinical, quality, manufacturing, regulatory, commercial and general and administrative personnel; and
- incur additional costs associated with operating as a public company.

Revenue

To date, we have not generated any revenue from drug sales. As of September 30, 2019, our revenue consists of collaboration revenue under our collaborations with Roche and CStone, including amounts that are recognized related to upfront payments, milestone payments and amounts due to us for research and development services. Subsequent revenue will include the $25.0 million upfront payment under our license agreement with Clementia, which we received in October 2019, and the $20.0 million cash milestone payment due in the third quarter of 2020 under our license agreement with Clementia. In addition, subsequent revenue may include revenues related to the supply of our drug candidates or products to CStone for development and commercialization activities in the CStone territory and milestone, royalty or other payments from Roche, CStone or Clementia. We do not expect to generate any revenue from the sale of avapritinib until 2020, assuming we receive marketing approval for avapritinib in the United States. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of product sales, if any, license fees, research and development services and related reimbursements, payments for manufacturing services, and milestone and other payments.

In the future, subject to obtaining marketing approval for one or more of our drug candidates or our licensed drug candidates, we expect to generate revenue from a combination of product sales, royalties on product sales and cost reimbursements, as well as upfront, milestone, royalty and other payments, if any, under any current or future collaborations and licenses.

Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research and development activities, including our drug discovery efforts, and the development of our drug candidates, which include:

- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with third parties that conduct research and development, pre-clinical activities, clinical activities and manufacturing on our behalf;
- expenses incurred under agreements with third parties for the development and commercialization of companion diagnostic tests;
- the cost of consultants;
- the cost associated with regulatory quality assurance and quality control operations;

- the cost of lab supplies and acquiring, developing and manufacturing pre-clinical study materials, clinical trial materials and commercial supply materials; and

- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other operating costs in support of research and development activities.

Research and development costs are expensed as incurred. Costs for certain activities are recognized based on an evaluation of the progress to completion of specific tasks. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

The successful development of our drug candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these drug candidates. We are also unable to predict when, if ever, material net cash inflows will commence from our drug candidates. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- establishing an appropriate safety profile with IND-enabling toxicology studies;

- successful enrollment in, and completion of clinical trials;

- receipt of marketing approvals from applicable regulatory authorities;

- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;

- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our drug candidates;

- commercializing the drug candidates, if and when approved, whether alone or in collaboration with others;

- market acceptance of any drug candidates we commercialize; and

- continued acceptable safety profile of the drugs following approval.

A change in the outcome of any of these variables with respect to the development of any of our drug candidates would significantly change the costs and timing associated with the development of that drug candidate.

Research and development activities are central to our business model. Drug candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our drug candidate development programs progress. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our drug candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. In addition, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

A significant portion of our research and development expenses have been external expenses, which we track on a program-by-program basis following nomination as a development candidate. Our internal research and development expenses are primarily personnel-related expenses, including stock-based compensation expense. Except for internal research and development expenses related to collaboration agreements, we do not track our internal research

and development expenses on a program-by-program basis as they are deployed across multiple projects under development.

The following table summarizes our external research and development expenses by program for the three and nine months ended September 30, 2019 and 2018. Other development and pre-development candidate expenses, unallocated expenses and internal research and development expenses have been classified separately.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
	(in thousands)		(in thousands)	
Avapritinib external expenses	$ 18,290	$ 21,409	$ 69,953	$ 60,623
Pralsetinib external expenses	21,963	11,968	59,850	26,424
Fisogatinib external expenses	2,446	2,219	4,694	9,226
BLU-782 external expenses	2,816	2,891	9,130	7,772
BLU-263 external expenses	1,654	—	2,019	—
Other development and pre-development candidate expenses and unallocated expenses	14,734	12,856	42,762	33,924
Internal research and development expenses	19,550	13,219	54,396	35,120
Total research and development expenses	$ 81,453	$ 64,562	$ 242,804	$ 173,089

We expect that our research and development expenses will increase in future periods as we expand our operations and incur additional costs in connection with our clinical trials and preparing regulatory filings. These increases will likely include the costs related to the implementation and expansion of clinical trial sites and related patient enrollment, monitoring, program management and manufacturing expenses for API, drug product and drug substance for current and future clinical trials and potential commercial inventory. In addition, we expect that our research and development expenses will increase in future periods as we incur additional costs in connection with research and development activities under our collaboration with Roche, development activities under our collaboration with CStone and development activities for companion diagnostic tests for current and future drug candidates. Following the completion of specified transition activities under our license agreement with Clementia, we will not incur additional research and development activities related to BLU-782.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, commercial, business development, information technology, legal, compliance and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, pre-commercial development activities, legal fees relating to intellectual property and corporate matters and fees for accounting and consulting services.

We expect that our general and administrative expenses will increase in the future to support continued research and development activities and planned commercialization activities, including establishing a sales, marketing and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval and establishing our operations outside the United States. These increases will likely include increased costs related to the hiring of additional personnel, legal, auditing and filing fees and general compliance and consulting expenses, among other expenses. We have incurred and will continue to incur additional costs associated with operating as a public company and expanding the scope of our operations.

Other Income (Expense), net

Other income (expense), net consists primarily of income earned on cash equivalents and investments.

Interest Expense

For the three and nine months ended September 30, 2018, interest expense consisted primarily of interest expense on amounts outstanding under the loan and security agreement that we entered into with Silicon Valley Bank in

May 2013 and amortization of debt discount. We repaid the loan in full in November 2018. For the three and nine months ended September 30, 2019, interest expense consisted primarily of interest expense related to an insignificant finance lease.

Critical Accounting Policies and Estimates

Our critical accounting policies are those policies that require the most significant judgments and estimates in the preparation of our financial statements. Management has determined that our most critical accounting policies are those relating to revenue recognition, accrued research and development expenses, available-for-sale investments, leases and stock-based compensation.

For a description of our critical accounting policies, please see "Management's Discussion and Analysis of Financial Condition and Results of Operations—Financial Operations Overview—Critical Accounting Policies and Estimates" in our Annual Report on Form 10-K for the year ended December 31, 2018. Other than as described below, there have been no significant changes to our critical accounting policies since December 31, 2018.

Leases

On January 1, 2019, we adopted *ASU No. 2016-02, Leases (Topic 84)*, or ASC 842, which requires the recognition of the right-of-use assets and related operating and finance lease liabilities on the balance sheet. We adopted ASC 842 using a modified retrospective approach for all leases existing at January 1, 2019. The adoption of ASC 842 had a substantial impact on our condensed consolidated balance sheet and no impact to our condensed consolidated statements of operations. Upon adoption of ASC 842, we recognized an adjustment of $54.2 million and $74.1 million to operating lease right-of-use assets and the related lease liabilities, respectively. The operating lease liabilities are based on the present value of the remaining minimum lease payments discounted using our secured incremental borrowing rate at the effective date of January 1, 2019.

For contracts entered into on or after the effective date, at the inception of a contract, we assess whether the contract is, or contains, a lease. The assessment is based on: (1) whether the contract involves the use of a distinct identified asset, (2) whether we obtain the right to substantially all the economic benefit from the use of the asset throughout the period, and (3) whether we have the right to direct the use of the asset. At inception of a lease, we allocate the consideration in the contract to each lease component based on its relative stand-alone price to determine the lease payments.

Leases are classified as either finance leases or operating leases. A lease is classified as a finance lease if any one of the following criteria are met: the lease transfers ownership of the asset by the end of the lease term, the lease contains an option to purchase the asset that is reasonably certain to be exercised, the lease term is for a major part of the remaining useful life of the asset or the present value of the lease payments equals or exceeds substantially all of the fair value of the asset. A lease is classified as an operating lease if it does not meet any of these criteria.

For all leases at the lease commencement date, a right-of-use asset and a lease liability are recognized. The right-of-use asset represents the right to use the leased asset for the lease term. The lease liability represents the present value of the lease payments under the lease.

The right-of-use asset is initially measured at cost, which primarily comprises the initial amount of the lease liability, plus any initial direct costs incurred if any, less any lease incentives received. All right-of-use assets are reviewed for impairment. The lease liability is initially measured at the present value of the lease payments, discounted using the interest rate implicit in the lease or, if that rate cannot be readily determined, our secured incremental borrowing rate for the same term as the underlying lease. For real estate leases and other operating leases, we use its secured incremental borrowing rate. For finance leases, we use the rate implicit in the lease or its secured incremental borrowing rate if the implicit lease rate cannot be determined.

Lease payments included in the measurement of the lease liability comprise the following: the fixed noncancelable lease payments, payments for optional renewal periods where it is reasonably certain the renewal period will be exercised, and payments for early termination options unless it is reasonably certain the lease will not be terminated early.

Lease cost for operating leases consists of the lease payments plus any initial direct costs, primarily brokerage commissions, and is recognized on a straight-line basis over the lease term. Included in lease cost are any variable lease payments incurred in the period that are not included in the initial lease liability and lease payments incurred in the period for any leases with an initial term of 12 months or less. Lease cost for finance leases consists of the amortization of the right-of-use asset on a straight-line basis over the lease term and interest expense determined on an amortized cost basis. The lease payments are allocated between a reduction of the lease liability and interest expense.

We made an accounting policy election to not recognize leases with an initial term of 12 months or less within our condensed consolidated balance sheets and to recognize those lease payments on a straight-line basis in our condensed consolidated statements of income over the lease term.

Results of Operations

Comparison of Three Months Ended September 30, 2019 and 2018

The following table summarizes our results of operations for the three months ended September 30, 2019 and 2018, together with the changes in those items in dollars and as a percentage:

	Three Months Ended September 30,			
	2019	2018	Dollar Change	% Change
	(in thousands)			
Collaboration revenue	$ 9,139	$ 1,095	$ 8,044	735 %
Operating expenses:				
Research and development	81,453	64,562	16,891	26
General and administrative	25,647	12,041	13,606	113
Total operating expenses	107,100	76,603	30,497	40
Other income (expense):				
Other income (expense), net	3,692	2,799	893	32
Interest expense	(6)	(14)	8	(57)
Total other income	3,686	2,785	901	32
Net loss	$ (94,275)	$ (72,723)	$ (21,552)	30 %

Collaboration Revenue

Collaboration revenue increased by $8.0 million from $1.1 million for the three months ended September 30, 2018 to $9.1 million for the three months ended September 30, 2019. Collaboration revenue for the three months ended September 30, 2019 and 2018 was related to the CStone and Roche agreements. Revenue recognized under the CStone agreement for the three months ended September 30, 2019 consisted of $6.0 million in milestone revenue related to three development and regulatory milestones that were either achieved or deemed probable during the third quarter of 2019. For the three months ended September 30, 2018, no revenue was recognized under the CStone agreement. We recorded collaboration revenue of $3.1 million and $1.1 million under the Roche agreement for the three months ended September 30, 2019 and 2018, respectively, related to amortization of the total $55.0 million of upfront and milestone payments received as of such periods.

Research and Development Expense

Research and development expense increased by $16.9 million from $64.6 million for the three months ended September 30, 2018 to $81.5 million for the three months ended September 30, 2019. The increase in research and development expense was primarily related to the following:

- approximately $8.0 million in increased personnel-related expense, primarily due to an increase in headcount, which was driven by growth in the clinical and manufacturing organizations and an increase of $2.9 million in stock-based compensation expense;

- approximately $6.3 million in increased expenses for external clinical activities related to clinical trials for avapritinib, pralsetinib and BLU-782; and

- approximately $2.6 million in increased expenses associated with manufacturing activities related to clinical and commercial drug supply.

General and Administrative Expense

General and administrative expense increased by $13.6 million from $12.0 million for the three months ended September 30, 2018 to $25.6 million for the three months ended September 30, 2019. The increase in general and administrative expense was primarily related to the following:

- approximately $7.9 million in increased personnel expenses, primarily due to an increase in general and administrative headcount related to building our commercial infrastructure and to support the overall growth of our business and an increase of $3.7 million in stock-based compensation expense; and

- approximately $5.6 million in increased professional fees, including commercial planning activities.

Other Income (Expense), Net

Other income, net, increased by $0.9 million from $2.8 million for the three months ended September 30, 2018 to $3.7 million for the three months ended September 30, 2019. The increase was primarily related to higher average investment balances and a higher rate of return on investments.

Interest Expense

Interest expense for the three months ended September 30, 2018 was less than $0.1 million and was primarily related to interest under our loan and security agreement with Silicon Valley Bank, which we repaid in full in November 2018. Interest expense for the three months ended September 30, 2019 was less than $0.1 million and was primarily related to interest expense for an insignificant finance lease.

Comparison of Nine Months Ended September 30, 2019 and 2018

The following table summarizes our results of operations for the nine months ended September 30, 2019 and 2018, together with the changes in those items in dollars and as a percentage:

	Nine Months Ended September 30,			
	2019	2018	Dollar Change	% Change
	(in thousands)			
Collaboration revenue	$ 14,979	$ 43,488	$ (28,509)	(66)%
Operating expenses:				
Research and development	242,804	173,089	69,715	40
General and administrative	64,123	34,285	29,838	87
Total operating expenses	306,927	207,374	99,553	48
Other income (expense):				
Other income (expense), net	10,595	7,635	2,960	39
Interest expense	(10)	(69)	59	(86)
Total other income	10,585	7,566	3,019	40
Net loss	$ (281,363)	$ (156,320)	$ (125,043)	80 %

Collaboration Revenue

Collaboration revenue decreased by $28.5 million from $43.5 million for the nine months ended September 30, 2018 to $15.0 million for the nine months ended September 30, 2019. Collaboration revenue for the nine months ended September 30, 2019 and 2018 was related to the CStone and Roche agreements. Revenue recorded under the CStone agreement for the nine months ended September 30, 2019 primarily consisted of $10.0 million in milestone revenue related to four development and regulatory milestones that were either achieved or deemed probable. Revenue recorded under the CStone agreement for in the nine months ended September 30, 2018 consisted of a $40.0 million upfront payment was recognized upon the execution of the CStone collaboration agreement. We recorded collaboration revenue of $4.8 million and $3.5 million under the Roche agreement for the nine months ended September 30, 2019 and 2018, respectively, related to amortization of the total $55.0 million of upfront and milestone payments received as of such periods.

Research and Development Expense

Research and development expense increased by $69.7 million from $173.1 million for the nine months ended September 30, 2018 to $242.8 million for the nine months ended September 30, 2019. The increase in research and development expense was primarily related to the following:

- approximately $25.9 million in increased expenses for external clinical activities related to clinical trials for avapritinib, pralsetinib and BLU-782;
- approximately $22.6 million in increased personnel-related expense primarily due to an increase in headcount, which was driven by growth in the clinical and manufacturing organizations and an increase of $8.9 million in stock-based compensation expense;
- approximately $16.4 million in increased expenses associated with clinical and commercial manufacturing activities; and
- approximately $4.8 million in increased expenses associated with continuing to build our discovery platform and advance our discovery pipeline.

General and Administrative Expense

General and administrative expense increased by $29.8 million from $34.3 million for the nine months ended September 30, 2018 to $64.1 million for the nine months ended September 30, 2019. The increase in general and administrative expense was primarily related to the following:

- approximately $17.1 million in increased personnel expenses due to an increase in general and administrative headcount, primarily due to an increase in general and administrative headcount related to building our commercial infrastructure and to support the overall growth of our business and an increase of $8.3 million in stock-based compensation expense; and
- approximately $12.7 million in increased professional fees, including commercial planning activities.

Other Income (Expense), Net

Other income (expense), net, increased by $3.0 million from $7.6 million of expense for the nine months ended September 30, 2018 to $10.6 million of income for the nine months ended September 30, 2019. The increase was primarily related to higher average investment balances and a higher rate of return on investments.

Interest Expense

Interest expense for the nine months ended September 30, 2018 was less than $0.1 million and was primarily related to interest under our loan and security agreement with Silicon Valley Bank, which we repaid in full in November 2018. Interest expense for the nine months ended September 30, 2019 was less than $0.1 million and was primarily related to interest expense for an insignificant finance lease.

Liquidity and Capital Resources

Sources of Liquidity

To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred stock, collaborations, a license agreement and a debt financing. Through September 30, 2019, we have received an aggregate of $1.5 billion from such transactions, including $1.2 billion in aggregate gross proceeds from the sale of common stock in our May 2015 IPO and December 2016, April 2017, December 2017 and April 2019 follow-on public offerings, $115.1 million in gross proceeds from the issuance of convertible preferred stock, $18.8 million in upfront and milestone payments from Alexion, $55.0 million in upfront and milestone payments under our collaboration with Roche, $46.0 million in upfront and milestone payments under our collaboration with CStone and $10.0 million in gross proceeds from the debt financing. In addition, we received the $25.0 million upfront payment under our license agreement with Clementia in October 2019.

As of September 30, 2019, we had cash, cash equivalents and investments of $594.5 million.

Cash Flows

The following table provides information regarding our cash flows for the nine months ended September 30, 2019 and 2018:

	Nine Months Ended September 30,	
(in thousands)	**2019**	**2018**
Net cash used in operating activities	$ (233,120)	$ (107,427)
Net cash used in investing activities	(84,202)	(217,329)
Net cash provided by financing activities	338,804	3,690
Net increase (decrease) in cash and cash equivalents	$ 21,482	$ (321,066)

Net Cash Used in Operating Activities. For the nine months ended September 30, 2019, compared to the same period in 2018, the $125.7 million increase in net cash used in operating was primarily due to the increased net loss during this period of $125.0 million, which was driven by increased headcount and headcount-related expenses and spending on pre-clinical, clinical and pre-commercial activities.

Net Cash Used in Investing Activities. For the nine months ended September 30, 2019, compared to the same period in 2018, the $133.1 million decrease in net cash used in investing activities was primarily due to a decrease in the net purchases and maturities of investments and a decrease in purchases of property and equipment.

Net Cash Provided by Financing Activities. For the nine months ended September 30, 2019, compared to the same period in 2018, the $335.1 million increase in net cash provided by financing activities was primarily due to $327.4 million in gross proceeds received from our April 2019 follow-on public offering, net of underwriting discounts and commissions and offering expenses paid by us, and an increase in net proceeds received from stock options exercises and our employee stock purchase plan.

Borrowings

In May 2013, we entered into a loan and security agreement with Silicon Valley Bank. Under the terms of the loan and security agreement, we borrowed $5.0 million. Loan advances under the loan and security agreement accrue interest at a fixed rate of 2.0% above the prime rate. In November 2014, we amended the loan and security agreement

and borrowed an additional $5.0 million. Each loan advance included an interest-only payment period, and we were required to pay a fee of 4% of the total loan advances at the end of the term of the loan. There were no financial covenants associated with the loan and security agreement. We repaid the loan in full in November 2018.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue and initiate clinical trials of, and seek marketing approval for, our drug candidates. In addition, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of potential collaborators. Furthermore, we expect to continue to incur additional costs associated with operating as a public company and with establishing our operations outside the United States. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

As of September 30, 2019, we had cash, cash equivalents and investments of $594.5 million. Based on our current operating plans, we believe that our existing cash, cash equivalents and investments, together with the $25.0 million upfront cash payment from Clementia and an $8.0 million research milestone achieved in the fourth quarter of 2019 under the Roche collaboration, but excluding any additional potential option fees, milestone payments or other payments from Roche, CStone or Clementia, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the second half of 2021. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of drug discovery, pre-clinical development, laboratory testing and clinical trials for our drug candidates;
- the costs of securing manufacturing arrangements for development activities and commercial production, including API, drug substance and drug product material for use in pre-clinical studies, clinical trials, our compassionate use program and for use as commercial supply;
- the costs, timing and outcome of regulatory review of our drug candidates;
- the costs of establishing or contracting for sales, marketing and distribution capabilities if we obtain regulatory approvals to market our drug candidates;
- the success of our collaborations with Roche and CStone and our license agreement with Clementia, as well as our ability to establish and maintain additional collaborations, partnerships or licenses on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under our collaboration agreements with Roche and CStone or license agreement with Clementia, or any collaboration, partnership or license agreements that we may enter into in the future;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the extent to which we acquire or in-license other drug candidates and technologies;
- the success of our current or future collaborations for the development of companion diagnostic tests;
- the success of our commercialization efforts and market acceptance for any approved drug candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and

- the costs of establishing operations outside the United States.

Identifying potential drug candidates and conducting pre-clinical development and testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, our drug candidates, if approved, may not achieve commercial success or market acceptance. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial drug revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. At this time, we do not have any committed external source of funds other than potential funds to be earned under our collaborations with Roche and CStone or license agreement with Clementia. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or drug candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

As of September 30, 2019, there have been no material changes to our contractual obligations and commitments from those described under “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in the Annual Report on Form 10-K for the year ended December 31, 2018.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

As of September 30, 2019, and December 31, 2018, we had cash, cash equivalents and investments of $594.5 million and $494.0 million, respectively, consisting primarily of money market funds and investments in U.S. treasury obligations.

Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term marketable securities. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we believe an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We have the ability to hold our investments until maturity, and therefore, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investment portfolio.

We are also exposed to market risk related to changes in foreign currency exchange rates. From time to time, we contract with vendors that are located in Asia and Europe, which are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk. As of September 30, 2019 and December 31, 2018, we had minimal or no liabilities denominated in foreign currencies.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the three and nine months ended September 30, 2019 and 2018.

Item 4. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2019. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of September 30, 2019, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the fiscal quarter covered by this report that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II – OTHER INFORMATION

Item 1. Legal Proceedings

We are not currently a party to any material legal proceedings.

Item 1A. Risk Factors

The following risk factors and other information included in this Quarterly Report on Form 10-Q should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see the Section titled "Forward-Looking Statements" of this Quarterly Report on Form 10-Q for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

We are a precision therapy company with a limited operating history and have not generated any revenue from drug sales. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

We are a precision therapy company with a limited operating history on which investors can base an investment decision. Biopharmaceutical drug development is a highly speculative undertaking and involves a substantial degree of risk. We commenced operations in April 2011. Our operations to date have been limited primarily to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential drug candidates, undertaking pre-clinical studies and conducting clinical trials for our lead drug candidates, avapritinib and pralsetinib, our other drug candidates fisogatinib and BLU-263, and BLU-782 prior to entering into the license agreement with Clementia Pharmaceuticals, Inc., or Clementia.

We have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale drug, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes many years to develop one new drug from the time it is discovered to when it is available for treating patients. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Since inception, we have focused substantially all of our efforts and financial resources on organizing and staffing our company, business planning, raising capital, establishing our intellectual property, building our discovery platform, including our proprietary compound library and new target discovery engine, identifying kinase drug targets and potential drug candidates, producing the active pharmaceutical ingredient, or API, drug substance and drug product material for use in pre-clinical studies and clinical trials, conducting pre-clinical studies and commencing clinical development and pre-commercial activities. To date, we have financed our operations primarily through public offerings of our common stock, private placements of our convertible preferred stock, collaborations, a license agreement and a debt financing. Through September 30, 2019, we have received an aggregate of $1.5 billion from such transactions, including $1.2 billion in aggregate gross proceeds from the sale of common stock in our May 2015 initial public offering, or IPO, and December 2016, April 2017, December 2017 and April 2019 follow-on public offerings, $115.1 million in gross proceeds from the issuance of convertible preferred stock, $18.8 million in upfront and milestone payments under our former collaboration with Alexion Pharma Holding, or Alexion, $55.0 million in upfront and milestone payments under our collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., which we refer to collectively as Roche, a $46.0 million in upfront and milestone payments under our collaboration with CStone Pharmaceuticals, or CStone, and $10.0 million in gross proceeds from the debt financing. In addition, we received the $25.0 million upfront payment under our license agreement with Clementia in October 2019.

Since inception, we have incurred significant operating losses. Our net losses were $281.4 million for the nine months ended September 30, 2019 and $236.6 million, $148.1 million and $72.5 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of September 30, 2019, we had an accumulated deficit of $878.9 million. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect our research and development expenses to significantly increase in connection with continuing our existing clinical trials and beginning additional clinical trials. In addition, if we obtain marketing approval for our drug candidates, we will incur significant sales, marketing and outsourced-manufacturing expenses. We have incurred and will continue to incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceuticals, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis. Our ability to become profitable depends upon our ability to generate revenue.

To date, we have not generated any revenue from our drug candidates, including our lead drug candidates, avapritinib and pralsetinib. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to sell, avapritinib, pralsetinib, fisogatinib, BLU-263 or our future drug candidates. We do not expect to generate any revenue from the sale of avapritinib until 2020, assuming we receive marketing approval for avapritinib in the United States. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- initiate and successfully complete clinical trials that meet their clinical endpoints;
- initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for our drug candidates;
- establish commercial manufacturing capabilities or make arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- commercialize our drug candidates, if approved, by developing a sales force or entering into additional collaborations with third parties; and
- achieve market acceptance of our drug candidates in the medical community and with third-party payors.

We expect to incur significant sales and marketing costs as we prepare to commercialize our drug candidates. Even if we initiate and successfully complete pivotal clinical trials of our drug candidates, and our drug candidates are approved for commercial sale, and despite expending these costs, our drug candidates may not be commercially successful. We may not achieve profitability soon after generating drug sales, if ever. If we are unable to generate drug revenue, we will not become profitable and may be unable to continue operations without continued funding.

We may need to raise substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate some of our drug development programs or commercialization efforts.

The development of pharmaceuticals is capital-intensive. We are currently advancing avapritinib, pralsetinib and fisogatinib through clinical development, and we plan to submit an investigational new drug application for BLU-263 for indolent SM in the first half of 2020. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate or continue clinical trials of, and seek marketing approval for, our drug candidates. In addition, depending on the status of regulatory approval or, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of Roche, CStone or other collaborators. We may also need to raise additional funds sooner if we choose to pursue additional indications or geographies for our drug candidates or otherwise expand

more rapidly than we presently anticipate. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts.

As of September 30, 2019, we had cash, cash equivalents and investments of $594.5 million. Based on our current operating plans, we believe that our existing cash, cash equivalents and investments, together with the $25.0 million upfront cash payment from Clementia and the $8.0 million research milestone achieved in the fourth quarter of 2019 under the collaboration with Roche, but excluding any additional potential option fees, milestone payments or other payments from Roche, CStone or Clementia, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the second half of 2021. Our future capital requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, results and costs of drug discovery, pre-clinical development, laboratory testing and clinical trials for our drug candidates;
- the costs of securing manufacturing arrangements for development activities and commercial production, including API, drug substance and drug product material for use in pre-clinical studies, clinical trials, our compassionate use program and for use as commercial supply;
- the costs, timing and outcome of regulatory review of our drug candidates;
- the costs of establishing or contracting for sales, marketing and distribution capabilities if we obtain regulatory approvals to market our drug candidates;
- the success of our collaborations with Roche and CStone and our license agreement with Clementia, as well as our ability to establish and maintain additional collaborations, partnerships or licenses on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under our collaboration agreements with Roche and CStone or license agreement with Clementia, or any collaboration, partnership or license agreements that we may enter into in the future;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the extent to which we acquire or in-license other drug candidates and technologies;
- the success of our current or future collaborations for the development of companion diagnostic tests;
- the success of our commercialization efforts and market acceptance for any approved drug candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- the costs of establishing operations outside the United States.

Identifying potential drug candidates and conducting pre-clinical development and testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, our drug candidates, if approved, may not achieve commercial success or market acceptance. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our drug candidates. Dislocations in the financial markets have

generally made equity and debt financing more difficult to obtain and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through collaborations, partnerships, licensing arrangements or otherwise at an earlier stage than would be desirable and we may be required to relinquish rights to some of our technologies or drug candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any drug candidate or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates.

Until such time, if ever, as we can generate substantial drug revenues, we expect to finance our cash needs through a combination of public and private equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaborations with Roche and CStone and the license agreement with Clementia, which are limited in scope and duration and subject to the achievement of milestones or royalties on sales of licensed products, if any. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that materially adversely affect the rights of our common stockholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or drug candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Drug Development and Regulatory Approval

We remain early in our development efforts as a clinical-stage company with only three drug candidates in clinical development: avapritinib, pralsetinib and fisogatinib. All of our other drug candidates are currently in pre-clinical or earlier stages of development. If we are unable to advance our other drug candidates to clinical development, obtain regulatory approval for our lead drug candidates or other drug candidates and ultimately commercialize our lead drug candidates or other drug candidates, or experience significant delays in doing so, our business will be materially harmed.

We remain early in our development efforts as a clinical-stage company with only three drug candidates in clinical development: avapritinib, pralsetinib and fisogatinib. All of our other drug candidates are currently in pre-clinical or earlier stages of development. We have invested substantially all of our efforts and financial resources in the identification and pre-clinical development of kinase inhibitors, including the development of our drug candidates avapritinib, pralsetinib and fisogatinib. Our ability to generate drug revenues, if ever, will depend heavily on the successful development and eventual commercialization of our drug candidates, which may never occur. We currently generate no revenues from sales of any drugs, and we do not expect to generate any revenue from the sale of avapritinib until 2020, assuming we receive marketing approval for avapritinib in the United States. We may never be able to

develop or commercialize a marketable drug. Each of our drug candidates will require additional pre-clinical or clinical development, management of clinical, pre-clinical and manufacturing activities, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenues from drug sales. In addition, for some of our drug candidates, in order to select patients most likely to respond to treatment and rapidly confirm mechanistic and clinical proof-of-concept, or to identify appropriate patients for any drug candidates for which we obtain approval, we may be required or we may seek to develop companion diagnostic tests, which are assays or tests to identify an appropriate patient population. For example, we have entered into agreements with third parties to develop and commercialize companion diagnostics for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, fisogatinib in order to identify HCC patients with FGFR4 pathway activation and pralsetinib in order to identify NSCLC patients with RET fusions. Companion diagnostic tests are subject to regulation as medical devices and must themselves be cleared or approved for marketing by the FDA or certain other foreign regulatory agencies before we may commercialize our drug candidates. The success of our lead drug candidates and other drug candidates will depend on several factors, including the following:

- successful enrollment in, and completion of, clinical trials, including our current clinical trials for avapritinib, pralsetinib and fisogatinib;
- successful completion of pre-clinical studies for our other drug candidates;
- approval of investigational new drug applications for future clinical trials for our other drug candidates;
- successful development of any companion diagnostic tests for use with our current or future drug candidates;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers for clinical supply and commercial manufacturing and the receipt by such third-party manufacturers of requisite approvals to supply commercial inventories of our drug candidates;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our drug candidates;
- successful commercialization launching sales of our drug candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the drug candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- enforcing and defending intellectual property rights and claims; and
- maintaining a continued acceptable safety profile of the drug candidates following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our drug candidates, which would materially harm our business. If we do not receive regulatory approvals for our drug candidates, we may not be able to continue our operations.

We do not know whether we will be able to develop any drugs of commercial value.

Our scientific approach focuses on using our novel target discovery engine and our proprietary compound library to identify new kinase targets in disease indications. Our focus on using our novel target discovery engine to identify potential kinase targets in disease indications may not result in the discovery and development of commercially viable drugs for these diseases. The use of our proprietary compound library may not lead to the development of commercially viable drugs. Even if we are able to develop a drug candidate that successfully targets these kinases in pre-clinical studies, we may not succeed in demonstrating safety and efficacy of the drug candidate in clinical trials.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

Our drug candidates avapritinib, pralsetinib and fisogatinib are in clinical development, and our other drug candidate BLU-263 is in pre-clinical development. The risk of failure for our drug candidates is high. It is impossible to predict when or if any of our drug candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must complete pre-clinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of pre-clinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drug candidates. Our pre-clinical studies, current clinical trials and future clinical trials may not be successful.

Successful completion of our clinical trials is a prerequisite to submitting a new drug application, or NDA, to the FDA and a marketing authorization application, or MAA, in the European Union for each drug candidate and, consequently, the ultimate approval and commercial marketing of our drug candidates, including our lead drug candidates, avapritinib and pralsetinib. We do not know whether any of our clinical trials for our drug candidates will be completed on schedule, if at all, or will provide clinical data sufficient to support regulatory submissions for or approval of such drug candidates.

We may experience delays in completing our pre-clinical studies and initiating or completing clinical trials, and we may experience numerous unforeseen events during, or as a result of, any current or future clinical trials that we could conduct that could delay or prevent our ability to receive marketing approval or commercialize our drug candidates, including:

- regulators or institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional pre-clinical studies or clinical trials or we may decide to abandon drug development programs;
- patients treated with our drug candidates may develop mutations that confer resistance to treatment, which may limit the market opportunity for our drug candidates or prevent us from completing our clinical trials, obtaining regulatory approval for or commercializing our drug candidates;
- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may

drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;

- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators or IRBs or ethics committees may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our drug candidates may be greater than we anticipate;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate;
- our drug candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from pre-clinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our drug candidates; and
- the FDA or other regulatory authorities may require us to submit additional data or impose other requirements before permitting us to initiate a clinical trial.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates. Further, the FDA may disagree with our clinical trial design and our interpretation of data from clinical trials, or the FDA may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

If we are required to conduct additional clinical trials or other testing of our drug candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our drug candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- be subject to post-marketing testing requirements; or
- fail to achieve market acceptance or have the drug removed from the market after obtaining marketing approval.

Our drug development costs will also increase if we experience delays in testing or regulatory approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant pre-clinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our drug candidates and may harm our business and

results of operations. Any delays in our pre-clinical or future clinical development programs may harm our business, financial condition and prospects significantly.

We may choose not to develop a potential drug candidate, or we may suspend, deprioritize or terminate one or more discovery programs or pre-clinical drug candidates or programs.

At any time and for any reason, we may determine that one or more of our discovery programs or pre-clinical drug candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or drug candidate. Accordingly, we may choose not to develop a potential drug candidate or elect to suspend, deprioritize or terminate one or more of our discovery programs or pre-clinical drug candidates or programs. For example, we have previously determined to suspend our discovery program for inhibitors of neurotrophic tyrosine receptor kinase, or NTRK, and predicted NTRK resistant mutants, and to deprioritize our discovery program targeting protein kinase cAMP-activated catalytic subunit alpha fusions for the treatment of fibrolamellar carcinoma. If we suspend, deprioritize or terminate a program or drug candidate in which we have invested significant resources, we will have expended resources on a program that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or drug candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In particular, because we are focused on diseases in genomically defined patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates.

Patient enrollment may be affected by other factors including:

- the severity of the disease under investigation;
- the size of the target patient population;
- the eligibility criteria for the clinical trial;
- the availability of an appropriate genomic screening test;
- the perceived risks and benefits of the drug candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Because the target patient populations for our drug candidates are relatively small, it may be difficult to successfully identify patients, could delay enrollment for our trials. If the market opportunities for our drug candidates are smaller than we believe they are, our product revenues may be adversely affected, and our business may suffer.

We focus our research and product development on treatments for cancer and rare genetic diseases, including genomically defined cancer and diseases driven by abnormal kinase activation. Because the target patient populations for our drug candidates are relatively small, it may be difficult to successfully identify patients. We have entered into

agreements with third parties to develop a companion diagnostic test for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, fisogatinib in order to identify HCC patients with FGFR4 pathway activation and pralsetinib in order to identify NSCLC patients with RET fusions, and we may engage third parties to develop companion diagnostic tests for use in some of our other current or future clinical trials. However, we may experience delays in reaching, or fail to reach, agreement on acceptable terms to develop companion diagnostic tests with third parties, and any third parties whom we engage to develop companion diagnostic tests may experience delays or may not be successful in developing such companion diagnostic tests, furthering the difficulty in identifying patients for our clinical trials. In addition, current commercially available diagnostic tests to identify appropriate patients for our clinical trials or any approved drug candidates may become unavailable in the future.

Our inability to enroll a sufficient number of patients in our clinical trials, or to identify patients appropriate for enrollment in our clinical trials, would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our drug candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. If we are unable to include patients with the driver of the disease, including the applicable genomic alteration for diseases in genomically defined patient populations, this could compromise our ability to seek participation in the FDA's expedited review and approval programs, including breakthrough therapy designation and fast track designation, or otherwise to seek to accelerate clinical development and regulatory timelines. In addition, our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our drug candidates, are based on estimates. These estimates may prove to be incorrect, and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States, European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our drug candidates or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, prospects and ability to achieve or sustain profitability.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals both for our drug candidates and for any related companion diagnostic tests, we will not be able to commercialize, or will be delayed in commercializing, our drug candidates, and our ability to generate revenue will be materially impaired.

Our drug candidates and any related companion diagnostic tests, including the companion diagnostic tests that we are developing for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, fisogatinib in order to identify HCC patients with FGFR4 pathway activation and pralsetinib in order to identify NSCLC patients with RET fusions, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Before we can commercialize any of our drug candidates, we must obtain marketing approval. We may also need marketing clearance or approval for any related companion diagnostic tests, including the companion diagnostic tests that we are developing for avapritinib, pralsetinib and fisogatinib. We have not received regulatory authorization to market any of our drug candidates or related companion diagnostic tests from regulatory authorities in any jurisdiction, and it is possible that none of our current or future drug candidates or related companion diagnostic tests will ever obtain regulatory approval. We have only limited experience in filing and supporting the applications necessary to gain regulatory approvals and expect to rely on third-party CROs and/or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive pre-clinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our drug candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining regulatory approvals, if approval is obtained at all, both in the United States and abroad is expensive, may take many years if additional clinical trials are required and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted NDA for a drug candidate, pre-market approval, or PMA, application for a companion diagnostic test or equivalent application types, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process

and may refuse to accept any application or may decide that our data are insufficient for approval and require additional pre-clinical, clinical or other studies. For example, in October 2019, the FDA informed us in writing that it intends to administratively split the proposed indications for avapritinib into two separate NDAs: one for PDGFRA Exon 18 mutant GIST, regardless of prior therapy, and one for fourth-line GIST. Given the acceleration of the VOYAGER trial and the anticipated availability of top-line data in the second quarter of 2020, the FDA requested top-line data from the VOYAGER trial and indicated these data would be informative in its review of the proposed fourth-line indication and potential clinical benefit in this population, including its evaluation of response rate and safety for the fourth-line indication. Assuming the FDA administratively splits the fourth-line GIST indication into a separate NDA, an extension of up to three months for the PDUFA action date for the fourth-line indication will likely be required to provide the top-line VOYAGER data to the FDA for the FDA to render a decision on the NDA for the fourth-line indication.

Our drug candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug candidate is safe and effective for its proposed indication or a related companion diagnostic test is suitable to identify appropriate patient populations;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate’s clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from pre-clinical studies or clinical trials;
- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our drugs and related companion diagnostic tests, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our drug candidates and related companion diagnostic tests, the commercial prospects for our drug candidates may be harmed and our ability to generate revenues will be materially impaired.

Our drug candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our drug candidates could cause us to interrupt, delay or halt pre-clinical studies or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. As is the case with all oncology drugs, it is likely that there may be side effects associated with the use of our drug candidates. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our drug candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, our drug candidates could cause undesirable side effects in pre-clinical studies or clinical trials related to on-target toxicity. For example, the FGF19/FGFR4 signaling axis has been shown to play a role in the regulation of de novo bile acid synthesis. Modulation of this signaling axis by treatment with a small molecule FGFR4 inhibitor could lead to the clinical symptoms that were observed with administration of an FGF19 antibody. If on-target toxicity is observed, or if our drug candidates have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in early stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our drug candidates may only be uncovered with a significantly larger number of patients exposed to the drug candidate. If our drug candidates receive marketing approval and we or others identify undesirable side effects caused by such drug candidates (or any other similar drugs) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such drug candidates;
- regulatory authorities may require the addition of labeling statements, such as a “boxed” warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way such drug candidates are distributed or administered, conduct additional clinical trials or change the labeling of the drug candidates;
- regulatory authorities may require a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such drug candidates from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our drug candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected drug candidates and could substantially increase the costs of commercializing our drug candidates, if approved, and significantly impact our ability to successfully commercialize our drug candidates and generate revenues.

A breakthrough therapy designation by the FDA for our drug candidates, including avapritinib and pralsetinib, may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our drug candidates will receive marketing approval.

The FDA has granted breakthrough therapy designation to avapritinib for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRA D842V mutation, and the FDA has granted breakthrough therapy designation to avapritinib for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia. In addition, the FDA has granted breakthrough therapy designation to pralsetinib for the treatment of patients with RET-fusion positive NSCLC that has progressed following platinum-based chemotherapy and to pralsetinib for the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments. We may also seek breakthrough therapy designation for some of our other drug candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our drug candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a drug candidate may not result in a faster development process, review or approval compared to other drugs and does not assure ultimate approval by the FDA. In addition, even if one or more of our drug candidates qualify as breakthrough therapies, the FDA may later decide that the drugs no longer meet the conditions for qualification.

A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process for our drug candidates.

The FDA has granted fast track designation to avapritinib for (i) the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and (ii) the treatment of patients with unresectable or metastatic GIST with the PDGFRA D842V mutation regardless of prior therapy. We may also seek fast track designation for some of our other drug candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular drug candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even though we have received fast track designation for avapritinib for the treatment of patients with unresectable or metastatic GIST that progressed following treatment with imatinib and a second tyrosine kinase inhibitor and for the treatment of patients with unresectable or metastatic GIST with the PDGFRA D842V mutation regardless of prior therapy, or even if we receive fast track designation for our other drug candidates, we may not experience a faster development process, review or approval. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

While we have received orphan drug designation for our drug candidates, avapritinib, pralsetinib and fisogatinib, for specified indications, we may seek orphan drug designation for some of our other drug candidates. However, we may be unsuccessful in obtaining or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

The FDA has granted orphan drug designation to avapritinib for the treatment of GIST and the treatment of mastocytosis, to fisogatinib for the treatment of HCC and to pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC. In addition, the European Commission has granted medicinal product designation to avapritinib for the treatment of GIST and the treatment of mastocytosis. As part of our business

strategy, we may seek orphan drug designation for some of our other drug candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

Similarly, in the European Union, the European Commission grants medicinal product designation after receiving the opinion of the European Medicines Agency, or EMA, Committee for Orphan Medicinal Products on an orphan medicinal product designation application. Orphan medicinal product designation is intended to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). In addition, designation is granted for drugs intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug. In the European Union, orphan medicinal product designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States and ten years in the European Union. The European Union exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain orphan drug exclusivity for a drug, that exclusivity may not effectively protect the designated drug from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. While we intend to seek orphan drug designation for our other drug candidates in addition to avapritinib for the treatment of GIST and the treatment of mastocytosis, fisogatinib for the treatment of HCC and pralsetinib for the treatment of RET-rearranged NSCLC, JAK1/2-positive NSCLC or TRKC-positive NSCLC, we may never receive such designations. Even if we receive orphan drug designation for any of our drug candidates, there is no guarantee that we will enjoy the benefits of those designations.

Even if we receive regulatory approval for any of our drug candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. In addition, our drug candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our drugs.

If the FDA or a comparable foreign regulatory authority approves any of our drug candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the drug will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current Good Manufacturing Practices, or cGMPs, and Good Clinical Practices, or GCPs, for any clinical trials that we conduct post-approval. Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to

monitor the safety and efficacy of the drug. Later discovery of previously unknown problems with a drug, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the drug, withdrawal of the drug from the market, or voluntary drug recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of marketing approvals;
- drug seizure or detention, or refusal to permit the import or export of drugs; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We may not be successful in our efforts to use and expand our discovery platform to build a pipeline of drug candidates.

A key element of our strategy is to use our novel target discovery engine to identify kinases that are drivers of diseases in genomically defined patient populations with high unmet medical need in order to build a pipeline of drug candidates. Although our research and development efforts to date have resulted in a pipeline of drug candidates, we may not be able to continue to identify novel kinase drivers and develop drug candidates. Even if we are successful in continuing to build our pipeline, the potential drug candidates that we identify may not be suitable for clinical development. For example, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will be successful in clinical trials or receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize drug candidates based upon our approach, we will not be able to obtain drug revenues in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate.

Risks Related to Commercialization

The incidence and prevalence for target patient populations of our drug candidates have not been established with precision. If the market opportunities for our drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.

The precise incidence and/or prevalence for GIST, SM, RET-altered NSCLC and MTC, and HCC are unknown. Our projections of the number of people who have these diseases, the frequency of the genetic alterations targeted by our drug candidates and the subset of people with these diseases who have the potential to benefit from treatment with our drug candidates are based on estimates. We estimate that in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan, or the Major Markets, there are approximately: 75,000 patients with SM, including 3,750 patients with advanced SM and 71,250 patients with indolent SM or smoldering SM (regardless of severity of symptoms); 500 first-line patients with PDGFRA D842V mutant GIST (including resectable, metastatic and unresectable GIST); 7,500 second-line patients with GIST, including approximately 75%-80% of second-line patients with GIST who do not have a KIT V654A or T670I mutation; 7,400 third-line and later patients with GIST (regardless of alteration); 8,900 first- and second-line patients with RET-altered NSCLC; 1,300 patients with MTC (regardless of line of therapy or alteration); and 25,900 first- and second-line patients with FGFR4-activated HCC.

The total addressable market opportunity for avapritinib for the treatment of patients with GIST and SM, pralsetinib for the treatment of patients with RET-altered NSCLC and MTC and fisogatinib for the treatment of patients with advanced HCC will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each of avapritinib, pralsetinib and fisogatinib, if our drug candidates are approved for sale for these indications, acceptance by the medical community and patient access, drug pricing and reimbursement. The number of patients in the Major Markets and elsewhere, including the number of addressable patients in those markets, may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drugs, patients treated with our drug candidates may develop mutations that confer resistance to treatment or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.

The development and commercialization of new drugs is highly competitive. We face competition with respect to our current clinical-stage drug candidates, and we will face competition with respect to any drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of therapies in the field of kinase inhibition for cancer and other diseases. Some of these competitive drugs and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Specifically, there are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. If avapritinib receives marketing approval for advanced SM, it will face competition from Novartis AG's midostaurin, a multi-kinase inhibitor with KIT D816V inhibitory activity. If avapritinib receives marketing approval for third-line GIST, it will face competition from Bayer AG's regorafenib, and if avapritinib receives marketing approval for second-line GIST, it will face competition from Pfizer Inc.'s sunitinib. In addition, if avapritinib receives marketing approval for advanced SM, GIST and/or for GIST patients with the PDGFRA D842V mutation, it may face competition from other drug candidates in development for these indications, including drug candidates in development by AB Science S.A., Allakos Inc., ARIAD Pharmaceuticals, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, AROG Pharmaceuticals, Inc., Celldex Therapeutics, Inc., and Deciphera Pharmaceuticals, LLC.

If pralsetinib receives marketing approval for patients with RET-driven cancers, it may face competition from other drug candidates in development, including drug candidates in development by AstraZeneca plc, Boston

Pharmaceuticals, Inc., Eisai Inc., Exelixis, Inc., GlaxoSmithKline plc, Loxo Oncology, Inc., a wholly-owned subsidiary of Eli Lilly and Company, Mirati Therapeutics, Inc., Novartis AG, Pfizer Inc. Roche, Stemline Therapeutics, Inc., and Turning Point Therapeutics, Inc., as well as several approved multi-kinase inhibitors with RET activity being evaluated in clinical trials, including alectinib, apatinib, cabozantinib, dovitinib, lenvatinib, sorafenib, sunitinib and vandetinib.

If fisogatinib receives marketing approval for patients with FGFR4-activated HCC, it will face competition from Bristol-Myers Squibb Company's nivolumab and Merck & Co., Inc.'s pembrolizumab, immune checkpoint inhibitors approved by the FDA for the treatment of HCC, as well as sorafenib, cabozantinib, regorafenib and lenvatinib, multi-kinase inhibitors approved for the treatment of HCC. In addition, fisogatinib may face competition from other drug candidates in development by Abbisko Therapeutics Co., Ltd, AstraZeneca plc, Bayer AG, Celgene Corporation, Eisai Inc., H3 Biomedicine Inc., Incyte Corporation, Johnson & Johnson, Novartis AG, Sanofi S.A., Taiho Pharmaceutical Co., Ltd., U3 Pharma GmbH, a wholly-owned subsidiary of Daiichi Sankyo Company, Limited, and Xoma Ltd.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we or our collaborators may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our drug candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of any related companion diagnostic tests, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any drug candidates that we may develop.

We face an inherent risk of product liability exposure related to the testing of our drug candidates in human clinical trials and use of our drug candidates through compassionate use programs, and we will face an even greater risk if we commercially sell any drug candidates that we may develop. If we cannot successfully defend ourselves against claims that our drug candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any drug candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any drug candidates that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we begin later-stage clinical trials and if we successfully commercialize any drug candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If we or our collaborators are unable to successfully develop and commercialize companion diagnostic tests for our drug candidates, or experience significant delays in doing so we may not realize the full commercial potential of our drug candidates.

Because we are focused on precision medicine, in which predictive biomarkers will be used to identify the right patients for our drug candidates, we believe that our success may depend, in part, on the development and commercialization of companion diagnostic tests. There has been limited success to date industrywide in developing and commercializing these types of companion diagnostic tests. To be successful, we need to address a number of scientific, technical and logistical challenges. We have entered into agreements to develop and commercialize companion diagnostic tests with third parties for avapritinib in order to identify GIST patients with the PDGFRA D842V mutation, fisogatinib in order to identify HCC patients with FGFR4 pathway activation and pralsetinib in order to identify NSCLC patients with RET fusions. If we decide to initiate the COMPASS-2L trial, prior to initiation we will need to enter into an agreement with a third party to develop a companion diagnostic test for avapritinib in order to select patients with PDGFRA- and KIT-driven second-line GIST who do not test positive for the KIT V654A or T670I mutations. We have not yet initiated commercialization of these companion diagnostic tests or development and commercialization of companion diagnostic tests for any of our other programs. We have little experience in the development and commercialization of companion diagnostic tests and may not be successful in developing and commercializing appropriate companion diagnostic tests to pair with any of our drug candidates that receive marketing approval. In addition, current commercially available diagnostic tests may become unavailable in the future. Companion diagnostic tests are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices and require separate regulatory clearance or approval prior to commercialization. Given our limited experience in developing and commercializing companion diagnostic tests, we are relying on third parties to design, manufacture, obtain regulatory clearance or approval for and commercialize the companion diagnostic tests for avapritinib, pralsetinib and fisogatinib, and we expect to rely in whole or in part on third parties to design, manufacture, obtain regulatory clearance or approval for and commercialize any other companion diagnostic tests for our drug candidates. We and our collaborators may encounter difficulties in developing and obtaining clearance or approval for the companion diagnostic tests, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. In addition, our collaborators for any companion diagnostic test that we may seek to develop:

- may not perform their respective obligations as expected or as required under our agreements with them;
- may not pursue commercialization of a companion diagnostic test even if it receives any required regulatory clearances or approvals;
- may elect not to continue the development of a companion diagnostic test based on changes in their or other third parties' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- may not commit sufficient resources to the marketing and distribution of a companion diagnostic test; and
- may terminate their relationship with us.

Any delay or failure by us or our collaborators to develop or obtain regulatory clearance or approval of the companion diagnostic tests could delay or prevent approval of our drug candidates. If we, or any third parties that we

have engaged or may in the future engage to assist us are unable to successfully develop and commercialize companion diagnostic tests for our drug candidates, or experience delays in doing so:

- the development of our drug candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- our drug candidates may not receive marketing approval if safe and effective use of a therapeutic drug candidate depends on an *in vitro* diagnostic;
- regulatory authorities may impose post-marketing requirements regarding the development and commercialization of companion diagnostic tests for our drug candidates; and
- we may not realize the full commercial potential of any drug candidates that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from treatment with our drugs.

As a result, our business would be harmed, possibly materially.

In addition, third party collaborators may encounter production difficulties that could constrain the supply of the companion diagnostic tests, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostic tests in the clinical community. If such companion diagnostic tests fail to gain market acceptance, it would have an adverse effect on our ability to derive revenues from sales of our drug candidates, if approved. In addition, the diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of our drug candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our drug candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our drug candidates.

Even if we are able to commercialize any drug candidates, such drugs may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.

The regulations that govern regulatory approvals, pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a drug candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the drug candidate, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the drug candidate in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

Our ability to commercialize any drug candidates successfully also will depend in part on the extent to which coverage and reimbursement for these drug candidates and related treatments will be available from government authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drugs. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. We cannot be sure that coverage will be available for any drug candidate that we commercialize and, if coverage is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any drug candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any drug candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower-cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Affordable Care Act, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts (increased to 70% by the Bipartisan Budget Act of 2018, effective January 1, 2019) off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2027 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, the Middle Class Tax Relief and Job Creation Act of 2012 required that the Centers for Medicare and Medicaid Services, or CMS, reduce the Medicare clinical laboratory fee schedule by 2% in 2013, which served as a base for 2014 and subsequent years. In addition, effective January 1, 2014, CMS also began bundling the Medicare payments for certain laboratory tests ordered while a patient received services in a hospital outpatient setting. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or companion diagnostic tests or additional pricing pressures.

Since its enactment, some of the provisions of the Affordable Care Act have yet to be fully implemented, while certain provisions have been subject to judicial, congressional, and executive challenges. Since January 2017, President Trump has signed two executive orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed repeal legislation to date, it has enacted laws that modify certain provisions of the Affordable Care Act. The Tax Cuts and Jobs Act of 2017, or TCJA, included a

provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the Affordable Care Act is an essential and inseverable feature of the Affordable Care Act, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the Affordable Care Act are invalid as well. The current U.S. President's Administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018, the Texas District Court judge issued an order staying the judgment pending appeal. On July 9, 2019, a Fifth Circuit U.S. Court of Appeals held a hearing to determine whether certain states and the U.S. House of Representatives have standing to appeal the lower court decision, but it is unclear when the court will render its decision on this hearing, and what effect it will have on the status of the Affordable Care Act. Litigation and legislation over the Affordable Care Act are likely to continue, with unpredictable and uncertain results. We will continue to evaluate the effect that the Affordable Care Act and its possible repeal and replacement has on our business.

Further, on January 20, 2017, U.S. President Donald Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the Affordable Care Act. Several state Attorneys General filed suit to stop the administration from terminating these subsidies, but on October 25, 2017, a federal judge in California denied their request for a restraining order. On June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in Affordable Care Act risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the Affordable Care Act marketplace, providers, and potentially our business, are not yet known.

Moreover, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act -mandated fees, including the so called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share. In July 2018, the Centers for Medicare & Medicaid Services, the agency responsible for administering the Medicare program, or CMS, published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. In addition, CMS published regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the health benefits required under the Affordable Care Act for plans sold through these marketplaces.

There has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal years 2019 and 2020 contain further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients.

Additionally, the Trump administration released a "blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. HHS has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. Congress and the Trump administration will likely continue to consider subsequent legislation and further action to repeal, replace or modify the Affordable Care Act. It is unclear what impact any changes to the

Affordable Care Act will have on the availability of healthcare and containing or lowering the cost of healthcare. We plan to continue to evaluate the effect that the Affordable Care Act and its possible repeal and replacement may have on our business.

In addition, individual states have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, to encourage importation from other countries and bulk purchasing.

Healthcare reforms stemming from the repeal of, and potential replacement for, the Affordable Care Act may result in more rigorous coverage criteria and lower reimbursement among regulated third-party payors, and in additional downward pressure on the prices that we receive for sales of our products, if approved. Any reduction in reimbursement from Medicare or other government-funded federal programs, including the Veterans Health Administration, or state healthcare programs could lead to a similar reduction in payments from private commercial payors. The implementation of cost containment measures or other healthcare reforms may thus prevent us from being able to generate revenue or attain profitability.

Beyond challenges to the Affordable Care Act, other legislative measures have also been enacted that may impose additional pricing and product development pressures on our business. For example, on May 30, 2018, the Right to Try Act, was signed into law. Among other things, this law provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy. We expect that additional foreign, federal and state healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our products, once approved, or additional pricing pressures.

The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize any products for which we obtain marketing approval.

We are currently unable to predict what additional legislation or regulation, if any, relating to the health care industry may be enacted in the future or what effect recently enacted federal legislation or any such additional legislation or regulation would have on our business. The pendency or approval of such proposals or reforms could result in a decrease in our stock price or limit our ability to raise capital or to enter into collaboration agreements for the further development and potential commercialization of our products.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our drug candidates, we may not be successful in commercializing our drug candidates if and when they are approved, and we may not be able to generate any revenue.

We have not completed building our sales or marketing infrastructure and have limited experience in the sale, marketing or distribution of drugs. To achieve commercial success for any approved drug candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial, and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our drug candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any drug launch. If the commercial launch of a drug candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our drug candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future drugs;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our drug revenues or the profitability of these drug revenues to us are likely to be lower than if we were to market and sell any drug candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our drug candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our drug candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our drug candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Although we do not currently have any drugs on the market, once we begin commercializing our drug candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any drug candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our drug candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal False Claims Act imposes civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In

addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the federal physician payment transparency requirements, sometimes referred to as the "Sunshine Act" under the Affordable Care Act require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report to the Department of Health and Human Services information related to physician payments and other transfers of value and the ownership and investment interests of such physicians and their immediate family members;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services (similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation);

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and

- analogous state laws and regulations, such as state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, were to be found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our drug candidates in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our drug candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our drug candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials, manufacturing, commercial sales, pricing and distribution of our drug candidates, and we cannot predict success in these jurisdictions. If we seek to develop our drug candidates or obtain approval of our drug candidates and ultimately commercialize our drug candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our drug candidates in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, including the European General Data Protection Regulation 2016/679, commonly referred to as GDPR;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our drug candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly countries in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our drug candidate to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed. In addition, in 2016, the United Kingdom referendum on its membership in the European Union resulted in a majority of United Kingdom voters voting to exit the European Union, often referred to as Brexit. Brexit has already and may continue to adversely affect European and/or worldwide regulatory conditions. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations, including those related to the pricing of prescription pharmaceuticals, as the United Kingdom determines which European Union laws to replicate or replace. If the United Kingdom were to significantly alter its regulations

affecting the pricing of prescription pharmaceuticals, we could face significant new costs. As a result, Brexit could impair our ability to transact business in the European Union and the United Kingdom.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

Risks Related to Our Dependence on Third Parties

We may seek to establish additional collaborations and licensing arrangements, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our drug candidates will require substantial additional cash to fund expenses. For some of our drug candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those drug candidates or to license the development and commercialization rights of those drug candidates to third parties.

We face significant competition in seeking appropriate collaborators and licensing partners. Whether we reach a definitive agreement for a collaboration or license will depend, among other things, upon our assessment of the collaborator's or licensing partner's resources and expertise, the terms and conditions of the proposed agreement and the proposed partner's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator or licensing partner may also consider alternative drug candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration or licensing arrangement could be more attractive than the one with us for our drug candidate. The terms of any additional collaborations, licenses or other arrangements that we may establish may not be favorable to us. We may also be restricted under our collaboration agreements with Roche and CStone from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations and licensing arrangements on a timely basis, on acceptable terms or at all. If we are unable to do so, we may have to curtail the development of the drug candidate for which we are seeking to collaborate or license, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate drug revenue.

In addition, our collaborations with Roche and CStone and our license agreement with Clementia, as well as any future collaborations or licenses that we enter into, may not be successful. The success of these arrangements will depend heavily on the efforts and activities of our collaborators and licensing partners. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable drug candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Licensors generally have sole discretion in determining the efforts and resources that they will apply to the licensed products. Collaborations and licenses with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. For example, in the fourth quarter of 2017, Alexion terminated our collaboration related to fibrodysplasia ossificans progressiva for convenience following a strategic review by Alexion of its research and development portfolio. Any termination or expiration of our collaboration agreements with Roche and CStone, our license agreement with Clementia or any future collaboration or license agreement could adversely affect us financially or harm our business reputation.

We rely on third parties to conduct our clinical trials for our drug candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed.

We do not have the ability to independently conduct clinical trials. We rely on medical institutions, clinical investigators, CROs, contract laboratories and other third parties to conduct or otherwise support clinical trials for our drug candidates. We rely heavily on these parties for execution of clinical trials for our drug candidates and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

We and our CROs are required to comply with regulations, including GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any drugs in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that our current or future clinical trials comply with GCPs. In addition, our clinical trials must be conducted with drug candidates produced under cGMPs regulations. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we intend to design the clinical trials for our drug candidates, CROs will conduct all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct current or future clinical trials will also result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;

- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our drug candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our drug candidates, or our development program materially and irreversibly harmed. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, we believe that our financial results and the commercial prospects for our drug candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We contract with third parties for the manufacture of our drug candidates for pre-clinical development and clinical trials, and we expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities or personnel. We rely, and expect to continue to rely, on third parties for the manufacture of our drug candidates for pre-clinical development and clinical testing, as well as for the commercial manufacture of our drugs if any of our drug candidates receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or drugs or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

The facilities used by our contract manufacturers to manufacture our drug candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our marketing applications to the FDA. We do not control the manufacturing process of, and will be completely dependent on, our contract manufacturers for compliance with cGMPs in connection with the manufacture of our drug candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our drug candidates, if approved. Further, our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or drugs, if approved, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business and supplies of our drug candidates.

We do not have any long-term supply agreements with our contract manufacturers, and we purchase our required drug supply, including the API, drug product and drug substance used in our lead drug candidates, on a purchase order basis. In addition, we may be unable to establish or maintain any agreements with third-party

manufacturers or to do so on acceptable terms. Even if we are able to establish and maintain agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Our drug candidates and any drugs that we may develop may compete with other drug candidates and approved drugs for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for bulk drug substances. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our drug candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our drug candidates or drugs could result in significant delays or gaps in availability of such drug candidates or drugs and may adversely affect our future profit margins and our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis.

The third parties upon whom we rely for the supply of the API, drug substance and drug product used in our lead drug candidates are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.

The API, drug substance and drug product used in our lead drug candidates are currently supplied to us from single-source suppliers. Our ability to successfully develop our drug candidates, supply our drug candidates for clinical trials and to ultimately supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the API, drug substance and drug product for these drugs in accordance with regulatory requirements and in sufficient quantities for clinical testing and commercialization. Although we have entered into arrangements to establish redundant or second-source supply of some of the API, drug product or drug substance for our lead drug candidates, if any of our suppliers ceases its operations for any reason or is unable or unwilling to supply API, drug product or drug substance in sufficient quantities or on the timelines necessary to meet our needs, it could significantly and adversely affect our business, the supply of our drug candidates and our financial condition.

For all of our drug candidates, we intend to identify and qualify additional manufacturers to provide such API, drug substance and drug product prior to submission of an NDA to the FDA and/or an MAA to the EMA. We are not certain, however, that our single-source suppliers will be able to meet our demand for their products, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers.

Establishing additional or replacement suppliers for the API, drug substance and drug product used in our drug candidates, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory approval, which could result in further delay. While we seek to maintain adequate inventory of the API, drug substance and drug product used in our drug candidates, any interruption or delay in the supply of components or materials, or our inability to obtain such API, drug substance

and drug product from alternate sources at acceptable prices in a timely manner could impede, delay, limit or prevent our development efforts, which could harm our business, results of operations, financial condition and prospects.

Risks Related to Intellectual Property

If we are unable to adequately protect our proprietary technology or obtain and maintain patent protection for our technology and drugs or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and drugs may be impaired.

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection in the United States and other countries for our drug candidates, including our lead drug candidates, avapritinib and pralsetinib, and our core technologies, including our novel target discovery engine and our proprietary compound library and other know-how. We seek to protect our proprietary and intellectual property position by, among other methods, filing patent applications in the United States and abroad related to our proprietary compounds, technologies, inventions and improvements that are important to the development and implementation of our business. We also rely on copyright, trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We own patents and patent applications that relate to our drug candidates, avapritinib, pralsetinib, fisogatinib and BLU-263, as well as our licensed drug candidate, BLU-782, as composition of matter. We also own applications relating to composition of matter for KIT inhibitors with multiple compound families, composition of matter for FGFR4 inhibitors with multiple compound families, composition of matter for inhibitors of RET, including predicted RET resistance mutations, with multiple compound families, and composition of matter for inhibitors of ALK2, with multiple compound families, as well as methods of use for these novel compounds. The issued U.S. patent directed to avapritinib composition of matter has a statutory expiration date in 2034, the issued U.S. patent directed to pralsetinib composition of matter has a statutory expiration date in 2036, the issued U.S. patent directed to fisogatinib composition of matter has a statutory expiration date in 2034, and the issued U.S. patent directed to BLU-782 composition of matter has a statutory expiration date in 2037.

As of October 15, 2019, we owned nine issued U.S. patents, nine issued foreign patents, including one European patent validated in 38 countries, two pending U.S. non-provisional patent applications, seven pending U.S. provisional patent applications, 20 pending foreign patent applications directed to our KIT program, including avapritinib and BLU-263. Our foreign patent filings are in a number of jurisdictions, including Australia, Argentina, Brazil, Bolivia, Canada, China, the European Union, Hong Kong, Israel, India, Japan, Lebanon, Macau, Mexico, New Zealand, Pakistan, Paraguay, Philippines, Russia, Singapore, South Africa, South Korea, Taiwan, Uruguay and Venezuela. Any U.S. or ex-U.S. patents issuing from the pending applications covering avapritinib will have a statutory expiration date between October 2034 and April 2040. Any U.S. or ex-U.S. patents issuing from the pending applications covering BLU-263 will have a statutory expiration date of April 2040. Patent term adjustments or patent term extensions could result in later expiration dates for avapritinib or BLU-263.

As of October 15, 2019, we owned five issued U.S. patents, two pending U.S. non-provisional patent applications, three pending PCT international applications, and 27 pending foreign patent applications directed to our RET program, including pralsetinib. Our foreign patent filings are in a number of jurisdictions, including Argentina, Australia, Brazil, Canada, China, Chile, Ecuador, Eurasia, the European Union, Israel, India, Japan, Malaysia, Mexico, New Zealand, Philippines, Saudi Arabia, Singapore, South Africa, South Korea, Taiwan, Thailand, the United Arab Emirates and Uruguay. Any U.S. or ex-U.S. patent issuing from the pending applications covering pralsetinib will have a statutory expiration date between November 2036 and August 2039. Patent term adjustments or patent term extensions could result in later expiration dates.

As of October 15, 2019, we owned eight issued U.S. patents, three pending U.S. non-provisional patent applications, sixteen issued foreign patents and 33 pending foreign patent applications directed to our FGFR4 program, including fisogatinib. Our foreign patent filings are in a number of jurisdictions, including Argentina, Australia, Bolivia, Brazil, Canada, China, Egypt, the European Union, Hong Kong, Israel, India, Indonesia, Japan, South Korea, Lebanon, Mexico, New Zealand, Pakistan, Paraguay, Philippines, Russia, Singapore, South Africa, Taiwan, Thailand, Uruguay, Venezuela and Vietnam. Any U.S. or ex-U.S. patent issuing from the pending applications covering fisogatinib will have

a statutory expiration date between July 2033 and September 2037. Patent term adjustments or patent term extensions could result in later expiration dates.

As of October 15, 2019, we owned one issued U.S. patent, one pending U.S. non-provisional patent application, two pending U.S. provisional applications, one pending PCT international application and 16 pending foreign patent applications directed to the ALK2 program, including our licensed drug candidate BLU-782. Our foreign patent filings are in a number of jurisdictions, including Australia, Brazil, Canada, China, Chile, the European Union, Israel, Japan, South Korea, Mexico, New Zealand, Philippines, Eurasia and South Africa. Any U.S. or ex-U.S. patent issuing from pending applications covering BLU-782 will have a statutory expiration date between April 2037 and October 2040. Patent term adjustments or patent term extensions could result in later expiration dates.

The intellectual property portfolio directed to our platform includes patent applications directed to novel gene fusions and the uses of these fusions for detecting and treating conditions implicated with these fusions. As of October 15, 2019, we owned six issued U.S. patents, seven pending U.S. non-provisional patent applications, seven pending European Union patent applications and four issued European patents (validated in the UK) directed to this technology. Any U.S. or ex-U.S. patent issuing from the pending applications directed to this technology, if issued, will have statutory expiration dates ranging from 2034 to 2035.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation.

The degree of patent protection we require to successfully commercialize our drug candidates may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect avapritinib, pralsetinib, fisogatinib, BLU-263, or our licensed drug candidate, BLU-782. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally twenty years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing drugs similar or identical to our drug candidates, including generic versions of such drugs.

Other parties have developed technologies that may be related or competitive to our own, and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents, with respect to either the same methods or formulations or the same subject matter, in either case, that we may rely upon to dominate our patent position in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first-to-file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights cannot be predicted with any certainty. For example, we are aware of patents owned by third parties that have generic composition of matter, method of inhibition and method of treatment claims that may cover fisogatinib or generic method of treatment claims that may cover pralsetinib. If the claims of any of these third-party patents are asserted against us, we do not believe fisogatinib, pralsetinib or our proposed activities related to such compounds would be found to infringe any valid claim of these patents. While we may decide to initiate proceedings to challenge the validity of these patents in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patents. If we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent’s claims.

In addition, the patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Further, with respect

to some of the pending patent applications covering our drug candidates, prosecution has yet to commence. Patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U.S. Patent and Trademark Office, or USPTO, have been significantly narrowed by the time they issue, if at all. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Even if we acquire patent protection that we expect should enable us to maintain such competitive advantage, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third-party submission of prior art to the USPTO challenging the priority of an invention claimed within one of our patents, which submissions may also be made prior to a patent's issuance, precluding the granting of any of our pending patent applications. We may become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others from whom we have obtained licenses to such rights. Competitors may claim that they invented the inventions claimed in our issued patents or patent applications prior to us or may file patent applications before we do. Competitors may also claim that we are infringing on their patents and that we therefore cannot practice our technology as claimed under our patents, if issued. Competitors may also contest our patents, if issued, by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose our rights to those challenged patents.

In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although we generally require all of our employees, consultants and advisors and any other third parties who have access to our proprietary know-how, information or technology to assign or grant similar rights to their inventions to us, we cannot be certain that we have executed such agreements with all parties who may have contributed to our intellectual property, nor can we be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy.

An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, without payment to us, or could limit the duration of the patent protection covering our technology and drug candidates. Such challenges may also result in our inability to manufacture or commercialize our drug candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates.

Even if they are unchallenged, our issued patents and our pending patents, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our owned or licensed patents by developing similar or alternative technologies or drugs in a non-infringing manner. For example, a third party may develop a competitive drug that provides benefits similar to one or more of our drug candidates but that has a different composition that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our drug candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our drug candidates could be negatively affected, which would harm our business.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our drug candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and

frequent litigation regarding patents and other intellectual property rights. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our drug candidates and technology, including interference proceedings before the USPTO. Our competitors or other third parties may assert infringement claims against us, alleging that our drugs are covered by their patents. Given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Many companies have filed, and continue to file, patent applications related to kinase inhibitors. Some of these patent applications have already been allowed or issued, and others may issue in the future. For example, we are aware of patents owned by third parties that have generic composition of matter, method of inhibition and method of treatment claims that may cover fisogatinib or generic method of treatment claims that may cover pralsetinib. If the claims of any of these third-party patents are asserted against us, we do not believe fisogatinib, pralsetinib or our proposed activities related to such compounds would be found to infringe any valid claim of these patents. While we may decide to initiate proceedings to challenge the validity of these patents in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patents. If we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims.

Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our drug candidates. If a patent holder believes our drug or drug candidate infringes on its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our drug candidates and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby providing our competitors and other third parties access to the same technologies licensed to us. Without such a license, we could be forced, including by court order, to cease developing and commercializing the infringing technology or drug candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed such third-party patent rights. A finding of infringement could prevent us from commercializing our drug candidates or force us to cease some of our business operations, which could materially harm our business.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims. A court may disagree with our allegations, however, and may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the third-party technology in question. Further, such third parties could counterclaim that we infringe their intellectual property or that a patent we have asserted against them is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. In addition, third parties may initiate legal proceedings against us to assert such challenges to our intellectual property rights. The outcome of any such proceeding is generally unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. It is possible that prior art of which we and the patent examiner were unaware during prosecution exists, which could render our patents invalid. Moreover, it is also possible that prior art may exist that we are aware of but do not believe is relevant to our current or future patents, but that could nevertheless be determined to render our patents invalid.

An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering one of our drug candidates, we would lose at least part, and perhaps all, of the patent protection covering such drug candidate. Competing drugs may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit, alleging our infringement of a competitor's patents, we could be prevented from marketing our drugs in one or more foreign countries. Any of these outcomes would have a materially adverse effect on our business.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our drugs or procedures, we may not be able to stop a competitor from marketing drugs that are the same as or similar to our drug candidates, which would have a material adverse effect on our business.

We may not be able to effectively enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our drug candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. In addition, the patent laws of some foreign countries do not afford intellectual property protection to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to

prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own drugs and, further, may export otherwise infringing drugs to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These drugs may compete with our drug candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in the major markets for our drug candidates, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our drug candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our drug candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time-consuming and inherently uncertain. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a “first-to-file” system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed.

In addition to the protection afforded by patents, we rely upon unpatented trade secret protection, unpatented know-how and continuing technological innovation to develop and maintain our competitive position. With respect to the building of our proprietary compound library, we consider trade secrets and know-how to be our primary intellectual property. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our consultants and employees. We may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets.

Our trade secrets could otherwise become known or be independently discovered by our competitors. Competitors could purchase our drug candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' drugs, our competitive position could be adversely affected, as could our business.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of our competitors or are in breach of non-competition or non-solicitation agreements with our competitors.

We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other proprietary information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may in the future be subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our drug candidates if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. An inability to incorporate such technologies or features would have a material adverse effect on our business and may prevent us from successfully commercializing our drug candidates. In addition, we may lose valuable intellectual property rights or personnel as a result of such claims. Moreover, any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent sales representatives. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our drug candidates, which would have an adverse effect on our business, results of operations and financial condition.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, business development, financial and legal expertise of Jeffrey W. Albers, our President and Chief Executive Officer, Anthony L. Boral, our Chief Medical Officer, Marion Dorsch, our Chief Scientific Officer, Kathryn Haviland, our Chief Operating Officer, Michael Landsittel, our Chief Financial Officer, Tracey McCain, our Chief Legal and Compliance Officer, Christopher Murray, our Senior Vice President of Technical Operations, and Christina Rossi, our Chief Commercial Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of our executive officers may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to continue hiring qualified development personnel. Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing key employees and executive officers may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is

intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As of October 15, 2019, we had 320 full-time employees, and we expect to continue to increase our number of employees and expand the scope of our operations. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Physical expansion of our operations in the future may lead to significant costs, including capital expenditures, and may divert financial resources from other projects, such as the development of our drug candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our drug candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including, weakened demand for our drug candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services.

Following its June 23, 2016 vote to leave the European Union, on March 29, 2017, the United Kingdom invoked Article 50 of the Lisbon Treaty and formally began the process of exiting the European Union. In March 2018, the parties agreed to a transition period of 21 months — from March 29, 2019 until the end of 2020 — before the United Kingdom leaves the European Union completely, assuming approval of a withdrawal agreement. Withdrawal from the European Union is controversial in the United Kingdom notwithstanding the 2016 vote. In December 2018, the European Court of Justice ruled that, subject to certain conditions, a member state could revoke notification of its intention to withdraw from the European Union. The British government and the European Union negotiated a withdrawal agreement, but the British Parliament did not approve that agreement. On October 17, 2019, the British government and the European Union announced that a new withdrawal agreement had been negotiated, but the Parliament must approve the new withdrawal agreement before it will become effective. As a result, there remains considerable uncertainty around the withdrawal. If the British Parliament does not approve the new withdrawal agreement on or before October 19, 2019, then British Prime Minister Boris Johnson must request an extension of Article 50 from the European Union. Failure to obtain parliamentary approval of the new withdrawal agreement would mean that the United Kingdom would leave the European Union on October 31, 2019 with no agreement, or a “hard” Brexit, unless the United Kingdom requests, and is granted, an extension of Article 50 from the European Union. An extension of Article 50 would need to be unanimously approved by the 27 European Union member states. Although Brexit has already and may continue to adversely affect European and/or worldwide economic or market, political or regulatory conditions and may contribute to instability in the global financial markets, political institutions and regulatory agencies, the resulting immediate changes in foreign currency exchange rates have had a limited overall impact due to natural hedging. Given the lack of comparable precedent, it is unclear what financial, trade and legal implications the withdrawal of the United Kingdom from the European Union, especially in the case of a “hard” Brexit, would have and how such withdrawal would affect us. The long-term impact of Brexit, including on our business and

our industry, will depend on the terms that are negotiated in relation to the United Kingdom's future relationship with the European Union, and we are closely monitoring the Brexit developments in order to determine, quantify and proactively address changes as they become clear.

For example, Brexit could result in the United Kingdom or the European Union significantly altering its regulations affecting the clearance or approval of our product candidates that are developed in the United Kingdom. Any new regulations could add time and expense to the conduct of our business, as well as the process by which our products receive regulatory approval in the United Kingdom, the European Union and elsewhere. In addition, the announcement of Brexit and the withdrawal of the United Kingdom from the European Union have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these effects of Brexit, among others, could adversely affect our business, our results of operations, liquidity and financial condition.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business.

Our internal computer systems, or those of our third-party collaborators, service providers, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drug candidates' development programs and have a material adverse effect on our reputation, business, financial condition or results of operations.

Our internal computer systems and those of our current or future third-party collaborators, service providers, contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and they are being conducted by increasingly sophisticated and organized groups and individuals with a wide range of motives and expertise. In addition to extracting sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. The prevalent use of mobile devices also increases the risk of data security incidents. While we have not experienced any material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or the operations of third-party collaborators, service providers, contractors and consultants, it could result in a material disruption of our drug candidates' development programs and significant reputational, financial, legal, regulatory, business or operational harm. For example, the loss of clinical trial data for our drug candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or drug candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our drug candidates could be delayed. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related breaches.

Any failure or perceived failure by us or any third-party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations to third parties, or any data security incidents or other security breaches that result in the unauthorized access, release or transfer of sensitive information, including physician data, patient data, or any personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us, could cause third parties to lose trust in us or could result in claims by third parties asserting that we have breached our privacy,

confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations. Moreover, data security incidents and other security breaches can be difficult to detect, and any delay in identifying them may lead to increased harm. While we have implemented data security measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or data security incidents.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.

Privacy and data security have become significant issues in the United States, Europe and in many other jurisdictions where we conduct or may in the future conduct our operations. The regulatory framework for the collection, use, safeguarding, sharing and transfer of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. On May 25, 2018, the European General Data Protection Regulation 2016/679, which is commonly referred to as GDPR, took effect. The GDPR applies to any company established in the European Union as well as any company outside the European Union that collects or otherwise processes personal data in connection with the offering goods or services to individuals in the European Union or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach notification requirements and onerous new obligations on services providers. The GDPR imposes additional obligations and risk upon our business and substantially increase the penalties to which we could be subject in the event of any non-compliance, including fines of up to €20 million or 4% of total worldwide annual turnover, whichever is higher. Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR requirements has required and will continue to require significant time, resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. If enacted, we will be subject to the EU ePrivacy Regulation, which is a proposed regulation of privacy and electronic communications. In addition, we will be subject to the California Consumer Privacy Act, which takes effect January 1, 2020 and will impose sweeping privacy and security obligations on many companies doing business in California and provides for substantial fines for non-compliance and, in some cases, a private right of action to consumers who are victims of data breaches involving their unredacted or unencrypted personal information. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could lead to government enforcement actions and significant penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Our employees, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our pre-clinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. In addition, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending

ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We may acquire businesses or drugs, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.

We may acquire additional businesses or drugs, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drugs resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the IRS and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. In recent years, many such changes have been made and changes are likely to continue to occur in the future. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or decided, which could result in an increase in our, or our stockholders', tax liability or require changes in the manner in which we operate in order to minimize increases in our tax liability.

On December 22, 2017, TCJA was enacted. The TCJA significantly reforms the Internal Revenue Code of 1986, as amended. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards and allows for the expensing of capital expenditures. Our net deferred tax assets and liabilities were revalued as of December 31, 2017 at the newly enacted U.S. corporate rate, and the impact was recognized in our tax expense in the year of enactment but was offset by a corresponding reduction to the valuation allowance. We continue to examine the impact this tax reform legislation may have on our business. The impact of this tax reform is uncertain and could be adverse.

Risks Related to Our Common Stock

The price of our common stock has been and may in the future be volatile and fluctuate substantially.

Our stock price has been and may in the future be subject to substantial volatility. In addition, the stock market in general, and Nasdaq listed and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. For example, our stock traded within a range of a high price of $109.00 and a low price of $13.04 per share for the period beginning on April 30, 2015, our first day of trading on The Nasdaq Global Select Market, through October 31, 2019. As a result of this volatility, our stockholders could incur substantial losses. In addition, the market price for our common stock may be influenced by many factors, including:

- the success of competitive drugs or technologies;
- results of clinical trials of our drug candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;

- the recruitment or departure of key personnel;
- the level of expenses related to any of our drug candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional drug candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

These and other market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

An active trading market for our common stock may not be sustained, and investors may not be able to resell their shares at or above the price they paid.

Although we have listed our common stock on The Nasdaq Global Select Market, an active trading market for our shares may not be sustained. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the price at which they acquired their shares or at the time that they would like to sell. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

If equity research analysts publish negative evaluations of or downgrade our common stock, the price of our common stock could decline.

The trading market for our common stock relies in part on the research and reports that equity research analysts publish about us or our business. We do not control these analysts. If one or more of the analysts covering our business downgrade their evaluations of our common stock, the price of our common stock could decline. If one or more of these analysts cease to cover our common stock, we could lose visibility in the market for our common stock, which in turn could cause our common stock price to decline.

Our executive officers, directors, principal stockholders and their affiliates maintain the ability to exercise significant influence over our company and all matters submitted to stockholders for approval.

Our executive officers, directors and stockholders who own more than 5% of our outstanding common stock, together with their affiliates and related persons, beneficially own shares of common stock representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders

may desire. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of us.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Future sales of our common stock, including by us or our directors and executive officers or shares issued upon the exercise of currently outstanding options, could cause our stock price to decline.

A substantial portion of our outstanding common stock can be traded without restriction at any time. In addition, a portion of our outstanding common stock is currently restricted as a result of federal securities laws, but can be sold at any time subject to applicable volume limitations. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, by us or others, could reduce the market price of our common stock or impair our ability to raise adequate capital through the sale of additional equity securities. In addition, we have a significant number of shares that are subject to outstanding options. The exercise of these options and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. We cannot predict the number, timing or size of future issuances or the effect, if any, that any future issuances may have on the market price for our common stock.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we have incurred and expect to continue to incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission, or SEC, and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and make some activities more time-consuming and costlier.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish an annual report by our management on our internal control over financial reporting. To achieve compliance with Section 404 within the prescribed period, we have been and will continue to be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need

to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting.

Despite our efforts, there is a risk that in the future neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404 or that we will not be able to comply with the requirements of Section 404 in a timely manner. If this were to occur, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources. Furthermore, investor perceptions of our company may suffer if deficiencies are found, and this could cause a decline in the market price of our stock. Irrespective of compliance with Section 404, any failure of our internal control over financial reporting could have a material adverse effect on our stated operating results and harm our reputation. If we are unable to implement these requirements effectively or efficiently, it could harm our operations, financial reporting, or financial results and could result in an adverse opinion on our internal control over financial reporting from our independent registered public accounting firm.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an “ownership change” (generally defined as a greater than 50% change (by value) in the ownership of its equity over a three-year period), the corporation’s ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income may be limited. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. As of December 31, 2018, we had federal net operating loss carryforwards of approximately $464.9 million, and our ability to utilize those net operating loss carryforwards could be limited by an “ownership change” as described above, which could result in increased tax liability to us. In addition, pursuant to the TCJA, we may not use net operating loss carry-forwards to reduce our taxable income in any year by more than 80%, and we may not carry back any net operating losses to prior years. These new rules apply regardless of the occurrence of an ownership change.

Item 5. Other Information

On November 1, 2019, we entered into a sixth amendment to our collaboration and license agreement, as amended, with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., which we refer to collectively as Roche, pursuant to which we and Roche agreed to, among other things, modify certain cost-sharing arrangements related to certain preclinical development activities for the collaboration programs and terminate one of the collaboration targets. As a result of the termination of such collaboration target, the parties are currently conducting activities for up to four programs under the collaboration.

The foregoing description of the sixth amendment to the collaboration and license agreement with Roche is qualified in its entirety by reference to the complete text of such agreement, a copy of which is attached as Exhibit 10.2 to this Quarterly Report on Form 10-Q.

Item 6. Exhibits

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
10.1*†	License Agreement, effective October 15, 2019, by and between Blueprint Medicines Corporation and Clementia Pharmaceuticals, Inc.
10.2*†	Sixth Amendment to Collaboration and License Agreement, effective November 1, 2019, by and among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc. and Blueprint Medicines Corporation
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1+	Certifications of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File – The cover page interactive data file does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document

* Filed herewith.

† Certain portions of the exhibit have been omitted pursuant to Regulation S-K Item 601(b) because it is both (i) not material to investors and (ii) likely to cause competitive harm to the Company if publicly disclosed.

\+ The certifications furnished in Exhibit 32.1 hereto are deemed to be furnished with this Quarterly Report on Form 10-Q and will not be deemed to be "filed" for purposes of Section 18 of the Exchange Act. Such certifications will not be deemed to be incorporated by reference into any filing under the Securities Act or the Exchange Act, except to the extent that the Registrant specifically incorporates it by reference.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

BLUEPRINT MEDICINES CORPORATION

Date: November 5, 2019

By: /s/ Jeffrey W. Albers
Jeffrey W. Albers
President, Chief Executive Officer and Director (Principal Executive Officer)

Date: November 5, 2019

By: /s/ Michael Landsittel
Michael Landsittel
Chief Financial Officer
(Principal Financial Officer)

Exhibit 10.1

[***] CERTAIN INFORMATION IN THIS DOCUMENT HAS BEEN OMITTED FROM THIS EXHIBIT BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

LICENSE AGREEMENT

by and between

Blueprint Medicines Corporation

and

Clementia Pharmaceuticals, Inc.

Dated as of October 15, 2019

TABLE OF CONTENTS

LICENSE AGREEMENT

This License Agreement (this "**Agreement**") is effective as of October 15, 2019 (the "**Effective Date**"), by and between Blueprint Medicines Corporation, a Delaware corporation with offices at 45 Sidney Street, Cambridge, MA, 02139 U.S.A. ("**Blueprint**"), and Clementia Pharmaceuticals, Inc., 1000 de la Gauchetière Street West, Suite 1200, Montreal, QC, H3B 4W5, Canada ("**Clementia**"). Blueprint and Clementia are each sometimes referred to herein as a "**Party**" or collectively as the "**Parties**." Capitalized terms used but not defined in this paragraph and the Recitals below will have the meanings ascribed to such terms in Article 1 or elsewhere in this Agreement.

RECITALS

WHEREAS, Blueprint Controls Licensed Technology related to the proprietary compound known as "BLU-782" and identified on Exhibit A-1 ("**BLU-782**") and other Blueprint Compounds and has the exclusive right to grant licenses under such Licensed Technology;

WHEREAS, Clementia desires to obtain, and Blueprint desires to grant, an exclusive license under the Blueprint Product-Specific Technology and a non-exclusive license to the Blueprint Platform Technology to Exploit Blueprint Compounds and Licensed Products on the terms and conditions set forth herein; and

WHEREAS, the Parties desire that the activities performed under this Agreement will accelerate the development and availability of treatment options for patients suffering from FOP and other diseases.

NOW, THEREFORE, in consideration of the mutual covenants contained herein, and for other good and valuable consideration, the amount and sufficiency of which are hereby acknowledged, Blueprint and Clementia hereby agree as follows:

ARTICLE 1
DEFINITIONS

As used in this Agreement, the following terms will have the meanings set forth below:

1.1 "**Acceptance**" means (a) with respect to an NDA, in the United States, the receipt of written notice from the FDA in accordance with 21 C.F.R. § 314.101(a)(2) (or its successor regulation) that such NDA is officially "filed"; or (b) with respect to an MAA, the receipt of written validation of the filing of such MAA from the EMA or acceptance or validation by the MHRA (as applicable).

1.2 "**Accounting Standards**" means, with respect to a Person, the generally accepted accounting principles as practiced in the United States ("**GAAP**"), or the international standards that are promulgated by the IFRS® Foundation or its successor organization, in each case as consistently applied by such Person.

1.3 "**Acquiring Party**" has the meaning set forth in Section 2.7.2.

1.4 "**Action**" means any claim, action, cause of action or suit (whether in contract or tort or otherwise), litigation (whether at law or in equity, whether civil or criminal), assessment, arbitration, investigation, hearing, charge, complaint, demand, notice or proceeding of, to, from, by or before any Governmental Authority.

1.5 "**Adverse Event**" has the meaning set forth in 21 C.F.R. § 312.32(a) and generally means any untoward medical occurrence associated with the use of a product in human subjects, whether or not considered related to such product.

1.6 "**Affiliate**" means, with respect to a specified Person, any other Person which (directly or indirectly) is controlled by, controls or is under common control with such Person. For the purposes of this definition, the term "control" (including, with correlative meanings, the terms "controlled by" and "under common control with") as used with respect to a Person means (a) in the case of a corporation, direct or indirect ownership of voting securities entitled to cast more than fifty percent (50%) of the votes in the election of directors, (b) in the case of a non-corporate Person, direct or indirect ownership of more than fifty percent (50%) of the equity interests with the power to direct the management and policies of such entity or (c) the power to direct the management or policies of a Person, whether through ownership of voting securities or by contract relating to voting rights or corporate governance, resolution, regulation or otherwise.

1.7 "**Agreement**" has the meaning set forth in the introductory paragraph of this Agreement.

1.8 "**Alexion**" means Alexion Pharma Holding and its Affiliates.

1.9 "**Alternative Breach Recovery**" has the meaning set forth in Section 11.8(a).

1.10 "**Anti-Corruption Laws**" means the U.S. Foreign Corrupt Practices Act of 1977 (the "**FCPA**") and similar Laws in any jurisdiction as applicable to either Party.

1.11 "**Bankruptcy Code**" has the meaning set forth in Section 2.5.

1.12 "**BLA**" means a biologics license application submitted to the FDA pursuant to the Public Health Service Act, 42 U.S.C. § 262.

"**Blocking Third Party Patent Payments**" means [***].

1.13 paid to a Third Party who Controls Blocking Third Party Patent(s) in order to obtain a license or otherwise acquire the relevant rights to such Blocking Third Party Patent(s).

"**Blocking Third Party Patent(s)**" means, with respect to a Licensed Product in any country in the Territory, any Patent(s) owned or in-licensed by a Third Party that are [***].

1.14 such Licensed Product in such country.

1.15 "**BLU-782**" has the meaning set forth in the Recitals.

1.16 "**Blueprint**" has the meaning set forth in the introductory paragraph of this Agreement.

1.17 "**Blueprint Change of Control Program**" has the meaning set forth in Section 2.7.2.

1.18 "**Blueprint CMO**" means, as of the Effective Date, any CMO that manufactures and supplies BLU-782 to Blueprint or its designee and identified on Schedule 1.18.

1.19 "**Blueprint Compounds**" means (a) BLU-782 and the other compounds identified in Exhibit A-1; (b) [***] ; (c) [***]; (d) [***] ("**Metabolites**") that are identified in Exhibit A-2; (e) [***]; and (f) [***].

1.20 **"Blueprint Development Know-How**" means any Know-How that is [***].

1.21 "**Blueprint Future Technology**" means [***].

1.22 "**Blueprint Indemnified Parties**" has the meaning set forth in Section 9.2.

1.23 "**Blueprint Platform Know-How**" means (a) any and all Know-How Controlled by Blueprint as of the Effective Date [***], (b) Blueprint Development Know-How, and (c) Blueprint's interest in any and all Joint Know-How, in each case (clauses (a), (b) and (c)) that is not Blueprint Product-Specific Know-How.

1.24 "**Blueprint Platform Patents**" means (a) any and all Patents identified on Exhibit C-2, (b) [***]; and (c) Blueprint's interest in any and all Joint Patents that are not Blueprint Product-Specific Patents (such Joint Patents, "**Joint Platform Patents**").

1.25 "**Blueprint Platform Technology**" means, collectively, the Blueprint Platform Know-How and Blueprint Platform Patents.

1.26 **"Blueprint Product-Specific Know-How**" means (a) any and all Know-How [***], (b) Blueprint Development Know-How, and (c) Blueprint's interest in any and all Joint Know-How, in each case (clauses (a), (b) and (c)) that is solely applicable to the Exploitation of Blueprint Compounds or Licensed Products in the Field in the Territory.

1.27 "**Blueprint Product-Specific Patents**" means (a) any and all Patents identified on Exhibit C-1, (b) [***], and (c) Blueprint's interest in any and all Joint Patents that solely Cover Joint Know-How that is Blueprint Product-Specific Know-How (such Patents, "**Joint Product-Specific Patents**").

1.28 "**Blueprint Product-Specific Technology**" means, collectively, the Blueprint Product-Specific Know-How and Blueprint Product-Specific Patents.

1.29 "**Breaching Party**" has the meaning set forth in Section 11.3.

1.30 "**Business Day**" means any day other than a Saturday or a Sunday or other bank or public holiday in Boston, Massachusetts or Montreal, Quebec.

1.31 "**Calendar Quarter**" means each of the three (3) month periods ending on March 31, June 30, September 30, and December 31 of any Calendar Year.

1.32 "**Calendar Year**" means each twelve (12) month period commencing on January 1 and ending on December 31.

1.33 "**Change of Control**" means with respect to a Party (or its Affiliate), any of the following events: (a) any Third Party (or group of Third Parties acting in concert) acquires in a transaction or series of transactions (including by way of a tender or exchange offer or issuance by such Party (or its Affiliate)), directly or indirectly, beneficial ownership or a right to acquire beneficial ownership of shares of such Party (or its Affiliate) representing fifty percent (50%) or more of the then outstanding voting shares (where voting refers to being entitled to vote for the election of directors) of such Party (or its Affiliate); (b) such Party (or its Affiliate) consolidates with or merges into another corporation or entity which is a Third Party, or any corporation or entity which is a Third Party consolidates with or merges into such Party (or its Affiliate), in either event, pursuant to a transaction or series of transactions in which more than fifty percent (50%) of the voting shares of the acquiring or resulting entity outstanding immediately after such

consolidation or merger is not held by the holders (or Affiliates of the holders) of the outstanding voting shares of such Party (or its Affiliate) immediately preceding such consolidation or merger; or (c) such Party (or its Affiliate) sells, transfers, exclusively licenses or otherwise disposes of all or substantially all of the assets to which this Agreement relates to a Third Party.

1.34 "**Clementia**" has the meaning set forth in the introductory paragraph of this Agreement.

1.35 "**Clementia Development Know-How**" means all Know-How conceived, discovered, developed, invented or created solely by or on behalf of Clementia or any of its Affiliates or Sublicensees, or jointly with a Third Party, (a) [***] and (b) [***].

1.36 "**Clementia Development Patents**" means all Patents that Cover any of the Clementia Development Know-How.

1.37 "**Clementia Development Technology**" means, collectively, the Clementia Development Know-How and Clementia Development Patents.

1.38 "**Clementia Indemnified Parties**" has the meaning set forth in Section 9.1.

1.39 "**Clementia Technology**" means any and all Know-How and Patents [***].

1.40 "**Clinical Study**" means a study in which human subjects or patients are dosed with a drug, whether approved or investigational, including any Phase I Clinical Study, Phase II Clinical Study, Phase III Clinical Study or any Pivotal Study.

1.41 "**Clinical Trial Application**" or "**CTA**" has the meaning set forth in Section 1.89.

1.42 "**CMC Data**" means any data included in the Chemistry, Manufacturing and Controls ("**CMC**") portion of a Regulatory Filing or in any supporting development reports thereto, in each case, with respect to any Licensed Product in any country in the world.

1.43 "**CMO**" means a contract manufacturing organization.

1.44 "**Code**" means the Internal Revenue Code of 1986, as amended from time to time (or any corresponding provisions of succeeding law).

1.45 "**Combination Product**" means: (a) a single pharmaceutical formulation [***] or (b) a combination therapy comprised of [***].

1.46 "**Commercialization Report**" has the meaning set forth in Section 4.4.2.

1.47 "**Commercialize**" or "**Commercializing**" means (a) to market, promote, distribute, offer for sale, sell, have sold, import or export for commercial purposes or otherwise commercialize a pharmaceutical or biologic product, (b) to conduct activities, other than Research, Development and Manufacturing, in preparation for the foregoing activities, including obtaining Pricing and Reimbursement Approval, or (c) to conduct post-Regulatory Approval studies (including Clinical Studies). When used as a noun, "Commercialization" means any activities involved in Commercializing. "Commercialization" excludes Development and Manufacturing.

1.48 "**Commercially Reasonable Efforts**" means, with respect to any Blueprint Compound or Licensed Product, that level of efforts, personnel and resources substantially similar to those commonly

dedicated by [***] to the Research, Development, Manufacture or Commercialization, as the case may be, of a product [***] (a "**Comparable Product**") to any Blueprint Compound or Licensed Product, in each case, taking into account [***]. Without limiting the foregoing, Commercially Reasonable Efforts requires that Clementia or any of its Affiliates or Sublicensees: [***].

1.49 "**Comparable Product**" has the meaning set forth in Section 1.48.

1.50 "**Competitive Infringement**" has the meaning set forth in Section 6.5.2(a).

1.51 "**Compulsory License**" means, with respect to a Licensed Product, in a country, a license or rights granted to a Third Party by a Governmental Authority within such country to sell or offer for sale such Licensed Product in such country under any Patents Controlled by Blueprint or its Affiliates, without direct or indirect authorization from Blueprint or its Affiliates including, for example, a right granted pursuant to requests under 30 August 2003 WTO decision.

1.52 "**Confidential Information**" means (a) all Know-How and any technical, scientific, trade, research, manufacturing, business, financial, marketing, product, supplier, intellectual property, and other non-public or proprietary data or information (including unpublished patent applications) of any kind whether in written, oral, graphical, electronic, machine-readable or other form, whether or not marked as confidential or proprietary that are disclosed, delivered or made available to the Receiving Party by or on behalf of the Disclosing Party, (b) "Proprietary Information" (as defined in the Prior CDA) that was disclosed by a Party or any of its Affiliates to the other Party or any of its Affiliates or Representatives under the Prior CDA, and (c) the terms and conditions of this Agreement; provided, however, that information of a Disclosing Party will not be Confidential Information of such Disclosing Party to the extent that the Receiving Party can demonstrate through competent evidence that such information:

(i) is known by the Receiving Party or any of its Affiliates without an obligation of confidentiality at the time of its receipt from the Disclosing Party, and not through a prior disclosure by or on behalf of the Disclosing Party;

(ii) was or is generally available to the public before the Receiving Party received such information from the Disclosing Party;

(iii) became generally available to the public or otherwise part of the public domain after its disclosure by the Disclosing Party and other than through any act or omission of the Receiving Party or any of its Affiliates or disclosees in breach of this Agreement;

(iv) is subsequently disclosed to the Receiving Party or any of its Affiliates without obligation of confidentiality by a Third Party who may rightfully do so and is not under a conflicting obligation of confidentiality to the Disclosing Party; or

(v) is developed by the Receiving Party or any of its Affiliates independently and without use of, reference to or reliance upon any Confidential Information received from the Disclosing Party.

No combination of features or disclosures will be deemed to fall within the foregoing exclusions merely because individual features are published or available to the general public or in the rightful possession of the Receiving Party unless the combination itself and principle of operation are published or available to the general public or in the rightful possession of the Receiving Party.

All Regulatory Filings and Know-How Controlled during the Term by a Party will be deemed to be the Confidential Information of such Party, and such Party will be deemed to be the Disclosing Party and the other Party will be deemed to be the Receiving Party with respect thereto.

1.53 "**Continuing Applications**" has the meaning set forth in Section 6.2.3.

1.54 "**Control**" or "**Controlled**" means, with respect to any Know-How, Patent, Regulatory Filing, Regulatory Approval, or other property (including intellectual property) right, the legal authority or right (whether by ownership, license (other than a license granted pursuant to this Agreement) or otherwise) of a Party or its Affiliate, to grant the right to access or use, or to grant a license or a sublicense to or under such Know-How, Patent, Regulatory Filing, Regulatory Approval or other property (including intellectual property) right as provided for herein (in whole or in part), without breaching the terms of any agreement or other arrangement between such Party (or any of its Affiliates) and a Third Party, in each case, existing at the time such Party would be required hereunder to grant the other Party such access, use, license or sublicense.

1.55 "**Cover**," "**Covering**" or "**Covered**" means: (a) with respect to a Patent, that, in the absence of a license granted to a Person under an issued Valid Claim included in such Patent, the practice by such Person of the subject matter at issue would infringe such Valid Claim, or (b) with respect to an application for Patents, that, in the absence of a license granted to a Person under a pending Valid Claim included in such application, the practice by such Person of the subject matter at issue would infringe such Valid Claim if such Patent application were to issue as a Patent.

1.56 "**Declined Patent**" has the meaning set forth in Section 6.2.4.

1.57 "**Delay or Suspension**" means a failure or delay in performance of Clementia's Research, Development, Manufacture and Commercialization obligations due to [***], in each case, that (x) [***] and (y) [***]. Notwithstanding the foregoing, a failure or delay in performance of Clementia's Research, Development, Manufacture and Commercialization obligations resulting from [***] shall not be deemed a "Delay or Suspension."

1.58 "**Develop**" or "**Developing**" means to conduct nonclinical and clinical drug development activities, whether before or after Regulatory Approval, including with respect to drug metabolism and pharmacokinetics, translational research, toxicology, pharmacology, test method development, conduct of in vitro and animal studies, stability testing, process and packaging development and improvement, process validation, process scale-up, formulation development, delivery system development, quality assurance and quality control development, statistical analysis, conduct of Clinical Studies, regulatory affairs, the preparation and submission of Regulatory Filings, Clinical Study regulatory activities, and any other activities directed towards obtaining Regulatory Approval of any Licensed Product. When used as a noun, "Development" means any activities involved in Developing. "Development" excludes Research, Commercialization and Manufacturing.

1.59 "**Development Milestone Event**" has the meaning set forth in Section 5.2.1.

1.60 "**Development Milestone Payment**" has the meaning set forth in Section 5.2.1.

1.61 "**Development Plan**" means the written Development plan intended to support Development and Regulatory Approval of Licensed Products in the Field in the Territory, as may be updated and amended periodically in accordance with Section 4.4. The initial Development Plan is attached hereto as Exhibit B.

1.62 "**Development Report**" has the meaning set forth in Section 4.4.

1.63 "**Disclosing Party**" means the Party disclosing or delivering Confidential Information or on whose behalf such Confidential Information is disclosed or delivered.

1.64 "**Disputes**" has the meaning set forth in Section 12.1.

1.65 "**DMF**" means any drug master file with the FDA, and any equivalent filing in other countries or regulatory jurisdictions.

1.66 "**Documents and Filings**" has the meaning set forth in Section 3.1.2.

1.67 "**Dollars**" or "**$**" means United States dollars.

1.68 "**Effective Date**" has the meaning set forth in the introductory paragraph of this Agreement.

1.69 "**EMA**" means the European Medicines Agency, or any successor Regulatory Authority thereto in the European Union having substantially the same function.

1.70 "**Employing Party**" has the meaning set forth in Section 13.2.

1.71 "**Exclusive Reversion License**" has the meaning set forth in Section 11.6.4(a)(i).

1.72 "**Executive Officers**" means (a) with respect to Blueprint, the Chief Executive Officer of Blueprint, and (b) with respect to Clementia, the Chief Executive Officer of Guarantor. If the position of any of the Executive Officers identified in this Section 1.72 no longer exists due to a corporate reorganization, corporate restructuring or the like that results in the elimination of the identified position, the applicable title of the Executive Officer set forth herein will be replaced with the title of another executive officer with responsibilities and seniority comparable to the eliminated Executive Officer, and the relevant Party will promptly provide notice of such replacement title to the other Party.

1.73 "**Exemplified Compounds**" means, excluding the Blueprint Compounds, the compounds (a) [***]; (b) [***]; (c) [***]; or (d) [***].

1.74 "**Existing Manufacturing Inventory**" has the meaning set forth in Section 3.2.2(a).

1.75 "**Exploit**" or "**Exploiting**" means to Research, Develop, Manufacture or Commercialize or have others do the same. When used as a noun, "Exploitation" means any activities involved in Exploiting.

1.76 "**FDA**" means the United States Food and Drug Administration or any successor agency thereto.

1.77 "**Field**" means all uses in humans and animals.

1.78 "**First Commercial Sale**" means, with respect to any Licensed Product in any country or jurisdiction, the first sale of such Licensed Product by Clementia or any of its Affiliates or Sublicensees to a Third Party for distribution, use or consumption in such country or jurisdiction after the applicable Regulatory Authority of such country or jurisdiction has granted Regulatory Approval of such Licensed Product in such country or jurisdiction.

1.79 "**FOP**" means fibrodysplasia ossificans progressiva.

1.80 "**Force Majeure Event**" has the meaning set forth in Section 13.8.

1.81 "**FTE**" means the equivalent of a full-time person's work time over a twelve (12) month period (including normal vacation, sick days and holidays) devoted to, and directly related to, conducting activities under this Agreement, in accordance with this Agreement, based on [***]. In the event that an individual devotes less than such full time to conducting activities under this Agreement in accordance with this Agreement during such twelve (12) month period, then for purposes of this Agreement, such individual will only count as a portion of an FTE which will be determined by dividing the number of full days during the applicable twelve (12) month period devoted to, and directly related to, conducting activities under this Agreement in accordance with this Agreement by the total number of working days during such twelve (12) month period. No individual may be charged at greater than [***] in a given Calendar Year.

1.82 "**FTE Rate**" means [***] per one (1) full FTE per full twelve (12) month Calendar Year; provided, that, starting January 1, 2020, such rate will adjust on January 1 of each Calendar Year by an amount equal to the change, if any, in the Consumer Price Index for All Urban Consumers (CPI-U) for the U.S. City Average, 1982-84 = 100, calculated by the Bureau of Labor Statistics during the immediately preceding Calendar Year. Notwithstanding the foregoing, for any Calendar Year during the Term that is less than a full year, the above referenced rate will be proportionately reduced to reflect such portion of such full Calendar Year.

1.83 "**Fully Burdened Costs**" means, with respect to any Blueprint Compound or Licensed Product (or component thereof), in each case, supplied by or on behalf of Blueprint or its Affiliates hereunder: (a) the actual costs of such Manufacturing incurred by Blueprint or its Affiliates, including [***], plus (b) any [***].

1.84 "**Generic Launch Quarter**" means, with respect to a Generic Product in a country in the Territory, the Calendar Quarter in which the First Commercial Sale of the applicable Generic Product in such country occurred following receipt of all necessary Regulatory Approvals from the applicable Regulatory Authorities in such country to market and sell such Generic Product as a pharmaceutical product for one or more Indication included in the approved labeling for such Licensed Product in such country.

1.85 "**Generic Product**" means, with respect to a Licensed Product that has received Regulatory Approval in a country in the Territory and is being marketed and sold by Clementia or any of its Affiliates or Sublicensees in such country, any pharmaceutical product that: (a) is sold in such country by a Third Party that is not a Sublicensee of Clementia or its Affiliates and did not purchase or acquire such product in a chain of distribution that included Clementia or any of its Affiliates or Sublicensees; and (b) has received Regulatory Approval in such country, for at least one of the same Indications as such Licensed Product, as a "generic medicinal product," "biosimilar," "bioequivalent," "similar biological medicinal product" or similar designation of interchangeability by the applicable Regulatory Authority in such country, pursuant to an expedited or abbreviated approval process in accordance with the then-current rules and regulations in such country, where (i) such Licensed Product is the "reference medicinal product," "reference listed product" or similar designation in such country, and (ii) such approval referred to or relied on (A) the approved MAA for such Licensed Product held by Blueprint or its Affiliate, Clementia or its Affiliate or Sublicensee in such country or (B) Regulatory Data contained or incorporated by reference in such approved MAA for such Licensed Product.

1.86 "**Governmental Authority**" means any multinational, federal, national, state, provincial, local or other entity, office, commission, bureau, agency, political subdivision, instrumentality, branch, department, authority, board, court, arbitral or other tribunal, official or officer, exercising executive,

judicial, legislative, police, regulatory, administrative or taxing authority or functions of any nature pertaining to government, including a Regulatory Authority.

1.87 "**Guarantor**" means Ipsen Pharma SAS, a French corporation with principal offices located at 65 quai Georges Gorse, 92100 Boulogne-Billancourt, France.

1.88 "**ICH**" means the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use.

1.89 "**IND**" means an application submitted to a Regulatory Authority for authorization to commence Clinical Studies, including (a) an Investigational New Drug Application as defined in 21 C.F.R. Part 312 or any successor application or procedure submitted to the FDA, (b) any equivalent of a United States IND in other countries, or regulatory jurisdictions, including a Clinical Trial Application ("**CTA**") and (c) all supplements, amendments, variations, extensions and renewals thereof that may be submitted with respect to the foregoing.

1.90 "**Indemnified Party**" means a Person entitled to indemnification under Article 9.

1.91 "**Indemnifying Party**" means a Party from whom indemnification is sought under Article 9.

1.92 "**Indication**" means a [***]. For clarity, [***].

1.93 "**Infringement Claim**" has the meaning set forth in Section 6.6.

1.94 "**Initiation**" or "**Initiates**" means with respect to a Clinical Study of a product, the administration of the first dose of such product to the first patient or subject in such Clinical Study.

1.95 "**In Process Manufacturing Inventory**" has the meaning set forth in Section 3.2.2(b).

1.96 "**Insolvent Party**" has the meaning set forth in Section 2.5.

1.97 "**Joint Know-How**" means any Know-How conceived, discovered, developed, invented or created jointly by one or more employees of Clementia, its Affiliate, a Sublicensee or a Third Party acting under authority of one of the foregoing, on the one hand, and one or more employees of Blueprint or its Affiliate or a Third Party acting under authority of Blueprint or its Affiliate, on the other hand, in the course of performing activities under or in connection with this Agreement, including the Development Plan or Transition Plan.

1.98 "**Joint Patents**" means all Joint Platform Patents and Joint Product-Specific Patents. Notwithstanding anything to the contrary in this Agreement, Joint Patents shall not be deemed to include any Patents listed on Exhibit C-1 or Exhibit C-2 of this Agreement.

1.99 "**Joint Platform Patents**" has the meaning set forth in Section 1.24.

1.100 "**Joint Product-Specific Patents**" has the meaning set forth in Section 1.27.

1.101 "**Joint Technology**" means, collectively, the Joint Know-How and the Joint Patents.

1.102 "**Know-How**" means any data, results, creative expressions and information of any type whatsoever, in any tangible or intangible form, including know-how, trade secrets, practices, techniques, methods, processes, discoveries and claims, including synthesis, preparation, recovery and purification

processes and techniques, control methods and assays, inventions, works of authorship, developments, specifications, formulations, formulae, materials (including biological or chemical) or compositions of matter of any type or kind, software, source code, object code, user interfaces, application programming interfaces, databases, database schema, algorithms, graphics or images, marketing reports, clinical and non-clinical study reports, regulatory submission documents and summaries, expertise, stability, technology, test data including pharmacological, biological, chemical, biochemical, toxicological, and clinical test data, analytical and quality control data, stability data, studies and procedures; in each case, whether or not patentable or copyrightable, but which are not in the public domain.

1.103 "**Law**" or "**Laws**" means all laws, statutes, rules, codes, regulations, orders, decrees, judgments or ordinances of any Governmental Authority, or any license, permit or similar right granted under any of the foregoing, or any similar provision having the force or effect of law.

1.104 "**Licensed Know-How**" means Blueprint Platform Know-How and Blueprint Product-Specific Know-How.

1.105 "**Licensed Patents**" means Blueprint Platform Patents and Blueprint Product-Specific Patents.

1.106 "**Licensed Product**" means any pharmaceutical product comprised of a Blueprint Compound, [***], including a Combination Product.

1.107 "**Licensed Technology**" means, collectively, the Licensed Patents and the Licensed Know-How.

1.108 "**Loss of Market Exclusivity**" means a condition where, with respect to a particular Licensed Product in a particular country in the Territory, one or more Generic Products are being marketed or sold in such country by a Third Party.

1.109 "**Losses**" means damages, losses, liabilities, costs (including costs of investigation, defense), fines, penalties, taxes, expenses, or amounts paid in settlement (in each case, including reasonable attorneys' and experts' fees and expenses), in each case resulting from an Action by a Third Party.

1.110 "**Major European Market**" means any of the following countries: [***].

1.111 "**Major Market**" means any of the following: [***].

1.112 "**Manufacture**" or "**Manufacturing**" means to engage in activities related to production, manufacture, synthesis, processing, filling, finishing, packaging, labeling, shipping and holding of product or any intermediate thereof, including process development, process qualification and validation, scale-up, commercial manufacture and analytic development, product characterization, stability testing, quality assurance and quality control. When used as a noun, "Manufacturing" means any of the foregoing activities. "Manufacturing" refers to both nonclinical and clinical Manufacturing for Research and Development, and Manufacturing for Commercialization.

1.113 **"Manufacturing Documents"** has the meaning set forth in Section 3.2.2(c).

1.114 "**Marketing Authorization**" means the grant of all necessary permits, registrations, authorizations, licenses and approvals (or waivers) required for the Manufacture and Commercialization of a Licensed Product for use in the Field and in the Territory, including any Regulatory Approval for sale or marketing, and, where required, Pricing and Reimbursement Approvals.

1.115 "**Marketing Authorization Application**" or "**MAA**" means an application to the appropriate Regulatory Authority for approval to market for commercial sale a Licensed Product in a country, including (a) an NDA, (b) a BLA, or (c) an equivalent application for regulatory approval required before commercial sale and use of a Licensed Product submitted to a Regulatory Authority in a country other than the U.S.

1.116 "**Metabolites**" has the meaning set forth in Section 1.19.

1.117 "**MHRA**" means the Medicines and Healthcare products Regulatory Agency in the United Kingdom an any successor agency thereto.

1.118 "**MO**" means multiple osteochondroma.

1.119 "**NDA**" means a new drug application submitted to the FDA pursuant to Section 505(b) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 355(b).

1.120 "**Net Sales**" means, with respect to a Licensed Product, the gross amount invoiced by Clementia, its Affiliates or its Sublicensees on sales or other dispositions for value of Licensed Products to a Third Party, less the following deductions, in each case, related specifically to the Licensed Products and actually incurred, paid or accrued by Clementia, its Affiliates or Sublicensees or specifically allocated in Clementia's, its Affiliates' or Sublicensees' financial statements, as applicable, and calculated in accordance with the applicable Accounting Standards as consistently applied:

(a) discounts (including trade, cash, price and quantity discounts) [***] granted to any Third Party (including to Governmental Authorities, purchasers, reimbursers, customers, distributors, wholesalers, and group purchasing and managed care organizations or entities (and other similar entities and institutions));

(b) tariffs, duties, excises, taxes (including import, export, excise, consumption, sales, value added, or use taxes, other than income taxes) or other governmental charges or fees imposed upon and paid directly with respect to the production, sale, delivery or use of the Licensed Product (excluding taxes based on the income or profits of the selling party);

(c) amounts repaid or credited by reason of rejections, defects, recalls or returns or because of chargebacks, refunds, rebates or retroactive price reductions;

(d) amounts written off as uncollectible, if and when actually written off or allowed, after commercially reasonable debt collection efforts have been exhausted (not to exceed [***] of Net Sales in the aggregate in any period); provided that any such amounts will be added back to Net Sales if and when collected;

(e) price concessions mandated by or negotiated with commercial or governmental payers; and

(f) freight, insurance and other transportation charges incurred and separately invoiced in shipping a Licensed Product to Third Parties.

For the avoidance of doubt, if a single item falls into more than one of the categories set forth in clauses (a)-(f) above, then such item may not be deducted more than once.

In the case of any sale or other disposition of Licensed Products for consideration other than cash (whether such non-cash consideration is payment in kind, exchange or other form), Net Sales shall include an amount calculated based on the on average price charged for the applicable Licensed Product(s) in the applicable country during the preceding royalty period.

Notwithstanding anything to the contrary in the foregoing:

(A) Net Sales will not include [***].

(B) Net Sales will include [***].

In the event that a Licensed Product is sold as a Combination Product, for the purposes of determining royalty payments on the Combination Product, Net Sales will mean the gross amount collected for the Combination Product less the deductions set forth in clauses (a)-(f) above, multiplied by a proration factor that is determined as follows:

(i) If the Blueprint Compound and the Other Components of the Combination Product were sold separately during the same or immediately preceding Calendar Quarter in the same dosages contained in the Combination Product, the proration factor will be determined by the formula [A / (A+B)], where A is the average gross sales price of Licensed Product containing only the Blueprint Compound as its active pharmaceutical ingredient in the same dosage during such period when sold separately from the Other Component(s), and B is the average gross sales price of the Other Component(s) in the same dosage(s) during such period when sold separately from the Licensed Product components (as applicable);

(ii) If a Licensed Product containing only the Blueprint Compound as its active pharmaceutical ingredient was sold separately during the same or immediately preceding Calendar Quarter in the same dosage contained in the Combination Product, but the Other Component(s) of the Combination Product were not sold separately in the same dosage(s) contained in the Combination Product during the same or immediately preceding calendar quarter, the proration factor will be determined by the formula [A/C], where A is the average gross sales price of Licensed Product containing only the Blueprint Compound as its active pharmaceutical ingredient in the same dosage during such period when sold separately from the Other Component(s), and C is the average gross sales price of Combination Product during such period;

(iii) If a Licensed Product containing only the Blueprint Compound as its active pharmaceutical ingredient was not sold separately during the same or immediately preceding Calendar Quarter, but the Other Component(s) of the Combination Product were sold separately in the same dosage(s) contained in the Combination Product during the same or immediately preceding Calendar Quarter, the proration factor will be determined by the formula [1-B/C], where B is the average gross sales price of the Other Components in the same dosage(s) during such period when sold separately from the Licensed Product component, and C is the average gross sales price of Combination Product during such period; or

(iv) If all active pharmaceutical ingredient(s) of the Combination Product were not sold or provided separately during the same or immediately preceding Calendar Quarter, the proration factor will be determined by the Parties in good faith negotiations based on the relative value contributed by each component.

Clementia will not, and will cause its Affiliates and Sublicensees not to, use any Licensed Product as a loss leader or otherwise unfairly or inappropriately discount the gross invoiced sales price of a Licensed

Product in a manner that is intended to benefit, or provide an incentive to enhance sales of, any other pharmaceutical product sold by Clementia or any of its Affiliates or Sublicensees.

1.121 "**New Metabolite**" has the meaning set forth in Section 4.4.1.

1.122 "**Non-Breaching Party**" has the meaning set forth in Section 11.3.

1.123 "**Non-Competitive Infringement**" has the meaning set forth in Section 6.5.2(c).

1.124 "**Non-Exclusive Reversion License**" has the meaning set forth in Section 11.6.4(a)(ii).

1.125 "**Other Components**" has the meaning set forth in Section 1.45.

1.126 "**Party**" or "**Parties**" has the meaning set forth in the introductory paragraph of this Agreement.

1.127 "**Patent**" means (a) a U.S. or foreign patent or a patent application, (b) any additions, priority applications, divisions, continuations, and continuations-in-part of any of the foregoing and (c) all patents issuing on any of the foregoing patent applications, together with all invention certificates, substitutions, reissues, reexaminations, registrations, supplementary protection certificates, confirmations, renewals and extensions of any of clauses (a), (b) or (c), and U.S. or foreign counterparts of any of the foregoing.

1.128 "**Patent Challenge**" has the meaning set forth in Section 11.4.

1.129 **"Payee"** has the meaning set forth in Section 5.8.2.

1.130 **"Payor"** has the meaning set forth in Section 5.8.2.

1.131 "**Person**" means any natural person, corporation, general partnership, limited partnership, joint venture, proprietorship or other business organization or a Governmental Authority.

1.132 "**Phase I Clinical Study**" means a human clinical trial of a product, the principal purpose of which is a preliminary determination of safety in healthy individuals or patients, as described in 21 C.F.R. 312.21(a) (as amended or any replacement thereof), or a similar clinical trial prescribed by the Regulatory Authority in a country other than the United States.

1.133 "**Phase I NHV Study**" has the meaning set forth in Section 3.1.4.

1.134 "**Phase II Clinical Study**" means a human clinical trial of a product, the principal purpose of which is a determination of safety and efficacy in the target patient population, as described in 21 C.F.R. 312.21(b) (as amended or any replacement thereof), or a similar clinical trial prescribed by the Regulatory Authority in a country other than the United States.

1.135 "**Phase III Clinical Study**" means a human clinical trial of a product, the design of which is acknowledged by the FDA to be sufficient for such clinical trial to satisfy the requirements of 21 C.F.R. 312.21(c) (as amended or any replacement thereof), or a similar human clinical trial prescribed by the Regulatory Authority in a country other than the United States, the design of which is acknowledged by such Regulatory Authority to be sufficient for such clinical trial to satisfy the requirements of a pivotal efficacy and safety clinical trial.

1.136 "**Pivotal Study**" means: (a) a Phase III Clinical Study; or (b) [***].

1.137 "**Pricing and Reimbursement Approval**" means, with respect to a Licensed Product, the governmental or relevant health insurance organization's approval, determination or decision establishing the price or level of reimbursement for such Licensed Product, in a given jurisdiction and the written agreement of such price by the Marketing Authorization holder in the Territory enabling the sale and payment of such Licensed Product in such jurisdiction in the Territory.

1.138 "**Prior CDA**" means that certain Confidentiality Agreement, by and between Blueprint and Ipsen Bioscience, Inc., dated as of [***].

1.139 "**Product-Specific Reversion Technology**" has the meaning set forth in Section 11.6.4(a)(i).

1.140 "**Program Liaison**" has the meaning set forth in Section 2.8.

1.141 "**Prosecution and Maintenance**" means, with regard to a particular Patent, the preparation, filing, prosecution, and maintenance (including payment of any patent annuity or maintenance fees) of such Patent, as well as re-examinations, reissues, appeals, post grant reviews, and inter partes reviews or their equivalents with respect to such Patent, together with the initiation or defense of interferences, oppositions and other similar proceedings with respect to the particular Patent.

1.142 "**QP**" means a qualified person as defined under Directive 2001/83/EC of the European Parliament and of the Council.

1.143 "**Receiving Party**" means the Party to whom Confidential Information is disclosed or delivered, including to such Party's Representatives.

1.144 "**Recruiting Party**" has the meaning set forth in Section 13.2.

1.145 "**Regulatory Approval**" means the approval, license, registration or authorization of the applicable Regulatory Authority necessary for the marketing and sale of a Licensed Product in the Field in a country or jurisdiction, but excluding separate Pricing and Reimbursement Approval that may be required. Regulatory Approvals include approvals by Regulatory Authorities of MAAs, or NDAs.

1.146 "**Regulatory Authority**" means any multinational, federal, national, state, provincial or local regulatory agency, department, bureau or other governmental entity with authority over the clinical development, manufacture, marketing or sale of a Licensed Product in a country or region, including the FDA in the United States, the EMA in Europe and the MHRA in the UK.

1.147 "**Regulatory Data**" means any and all Research data, pharmacology data, CMC Data, Safety Data, nonclinical data, clinical data and all other documentation submitted, or required to be submitted, to Regulatory Authorities in association with Regulatory Filings and Regulatory Approvals for the Licensed Products (including any applicable DMFs or similar documentation).

1.148 "**Regulatory Exclusivity Period**" means, with respect to each Licensed Product in any country in the Territory, a period of exclusivity (other than Patent exclusivity) granted or afforded by applicable Law or by a Regulatory Authority in such country that confers exclusive marketing rights with respect to such Licensed Product in such country or prevents another Person from using or otherwise relying on any data supporting Regulatory Approval of such Licensed Product without the prior written consent of the holder of the MAA, such as new chemical entity exclusivity, new use or indication exclusivity, new formulation exclusivity, orphan drug exclusivity, non-patent related pediatric exclusivity, reference product exclusivity or any other applicable marketing or data exclusivity.

1.149 "**Regulatory Filing**" means any documentation comprising or relating to or supporting any submission or application with any Regulatory Authority with respect to a Licensed Product or its use or potential use in humans, including any documents submitted to any Regulatory Authority and all supporting data, including INDs, NDAs, MAAs, and all correspondence with any Regulatory Authority with respect to any Licensed Product (including minutes of any meetings, telephone conferences or discussions with any Regulatory Authority).

1.150 "**Representatives**" means a Party's Affiliates and such Party's or its Affiliate's employees, directors, officers, permitted subcontractors, permitted sublicensees and agents, and advisors (including attorneys, accountants, consultants, bankers and financial advisors).

1.151 "**Research**" to conduct activities related to the synthesis, discovery, identification, screening, optimization, design, profiling and characterization of compounds. When used as a noun, "Research" means any activities involved in conducting Research. "Research" excludes (a) Development, (b) Commercialization and (c) Manufacturing.

1.152 "**Reversion Licenses**" has the meaning set forth in Section 11.6.4(a)(ii).

1.153 "**Reversion Patents**" has the meaning set forth in Section 11.6.4(d)(ii)

1.154 "**Reversion Products**" has the meaning set forth in Section 11.6.4(a)(i).

1.155 "**Reversion Royalty**" has the meaning set forth in Section 11.6.4(n)(i).

1.156 "**Reversion Technology**" means any Clementia Technology, and Clementia's interest in any jointly owned technology, including Joint Technology, that is necessary for Blueprint to Exploit (including, continued Development in accordance with the then current Development Plan) any Reversion Product, as such Reversion Product exists as of the date of the notice of termination that results in termination, including, without limitation, [***].

1.157 "**Reversion Transition Period**" has the meaning set forth in Section 11.6.4(g).

1.158 "**Reverted Licensed Patents**" shall have the meaning set forth in Section 11.6.4(d)(i).

1.159 "**Royalty Payment**" has the meaning set forth in Section 5.5.2.

1.160 "**Royalty Reduction Trigger**" has the meaning set forth in Section 5.6.3.

1.161 "**Royalty Term**" has the meaning set forth in Section 5.4.2.

1.162 "**Safety Data**" means any Adverse Event information and similar data related to the actual or anticipated use of a Blueprint Compound or Licensed Product in humans, including data from Clinical Studies, all results from nonclinical safety studies and data from post-Regulatory Approval use, including toxicology and carcinogenicity data (if any), required by one (1) or more Regulatory Authorities to be collected or to be reported to such Regulatory Authorities under applicable Laws, but excluding any information related to the efficacy of the Licensed Product.

1.163 "**Sales Milestone Event**" has the meaning set forth in Section 5.3.1.

1.164 "**Sales Milestone Payment**" has the meaning set forth in Section 5.3.1.

1.165 "**Severed Clause**" has the meaning set forth in Section 13.4.

1.166 "**Sublicense**" means a grant of rights from Clementia to an Affiliate or permitted Third Party under any of the rights licensed to Clementia by Blueprint under Section 2.1 with respect to the Exploitation of any Licensed Product, including, for the avoidance of doubt, Third Party distributors.

1.167 "**Sublicensee**" means any Affiliate or permitted Third Party granted a Sublicense.

1.168 "**Term**" has the meaning set forth in Section 11.1.

1.169 "**Territory**" means worldwide.

1.170 "**Third Party**" means any Person other than a Party or any of its Affiliates.

1.171 "**Third Party Agreements**" means any [***] agreement between Blueprint (or any of its Affiliates) and any Third Party (a) related to the Research, Development, Manufacture or Commercialization of any Blueprint Compound or Licensed Product, or (b) [***].

1.172 "**Third Party Claim**" has the meaning set forth in Section 9.3.1.

1.173 "**Trademark**" means any trademark, trade name, service mark, service name, brand, domain name, trade dress, logo, slogan or other indicia of origin or ownership, including the goodwill and activities associated with each of the foregoing.

1.174 "**Transition Coordinator**" has the meaning set forth in Section 3.1.1(a).

1.175 "**Transition Period**" has the meaning set forth in Section 3.3.

1.176 "**Transition Plan**" means the plan attached hereto as Exhibit D.

1.177 "**United States**," "**U.S.**" or "**US**" means the United States of America and its territories and possessions.

1.178 "**Valid Claim**" means, with respect to a particular country, a claim [***] of (a) an issued and unexpired patent (or a supplementary protection certificate thereof) that has not (i) irretrievably lapsed or been abandoned, permanently revoked, dedicated to the public or disclaimed or (ii) been held invalid, unenforceable or not patentable by a court, governmental agency, national or regional patent office or other appropriate body that has competent jurisdiction, which holding, finding or decision is final and unappealable or unappealed within the time allowed for appeal or (b) a pending patent application, which claim has not been abandoned or finally disallowed without the possibility of appeal; provided, that, if a pending patent application has been pending for longer than [***] from the date of filing [***], then such corresponding claim in such pending patent application will not be deemed to be a Valid Claim; provided that, if a claim ceases to be a Valid Claim by reason of the foregoing subclause (b), then such claim will again be deemed a Valid Claim in the event such claim subsequently issues prior to the end of the Royalty Term in such country.

ARTICLE 2
LICENSE GRANTS AND EXCLUSIVITY

2.1 License Grants to Clementia.

2.1.1 Exclusive License to Blueprint Product-Specific Technology. Subject to the terms and conditions of this Agreement (including Section 2.1.4), Blueprint hereby grants to Clementia an

exclusive (even with respect to Blueprint and its Affiliates), royalty-bearing, with the right to sublicense and subcontract (subject to Section 2.3), non-transferable (except as provided in Section 13.1) license under the Blueprint Product-Specific Technology to Exploit Blueprint Compounds or Licensed Products in the Field in the Territory during the Term; provided, however, that Blueprint hereby retains, on behalf of itself (and its Affiliates, licensees, and sublicensees) the rights under the Blueprint Product-Specific Technology to perform either itself, or have performed by Third Parties, [***].

2.1.2 [***] License to Blueprint Future Technology. Subject to the terms and conditions of this Agreement (including Section 2.1.4), Blueprint hereby grants to Clementia a [***] (subject to Section 2.3), [***] (except as provided in Section 13.1) license under the Blueprint Future Technology to Exploit Blueprint Compounds or Licensed Products in the Field in the Territory during the Term.

2.1.3 Non-Exclusive License to Blueprint Platform Technology. Subject to the terms and conditions of this Agreement (including Section 2.1.4), Blueprint hereby grants to Clementia a non-exclusive, with the right to sublicense and subcontract (subject to Section 2.3), non-transferable (except as provided in Section 13.1) license under the Blueprint Platform Technology to Exploit Blueprint Compounds or Licensed Products in the Field in the Territory during the Term. For clarity, this license under this Section 2.1.3 will not grant or create (by implication, estoppel or otherwise) any license or right under the Blueprint Platform Technology to Exploit any compound or product that is not a Blueprint Compound or Licensed Product.

2.1.4 Limitations of Licenses. Each of the foregoing licenses to Clementia under Sections 2.1.1, 2.1.2 and 2.1.3 is subject to the limitations in this Section 2.1.4. Under the licenses granted under Sections 2.1.1, 2.1.2, and 2.1.3, Clementia may only make modifications to the Blueprint Compounds to the extent necessary to generate other compounds that are Blueprint Compounds (as set forth in Section 1.19).

2.2 License Grant to Blueprint. Clementia hereby grants to Blueprint a non-exclusive, royalty-free, fully paid-up, transferrable, sublicensable (through multiple tiers) license under the Clementia Technology to perform, either itself or through its Affiliates or subcontractors, its obligations under this Agreement, including under the Transition Plan.

2.3 Sublicensing and Subcontracting.

2.3.1 Clementia Right to Sublicense. Clementia will have the right to grant Sublicenses of any and all rights granted to Clementia by Blueprint pursuant to Section 2.1 to its Affiliates and to Third Parties, in each case, with or without the right to grant further Sublicenses; provided that, prior to [***], Clementia will not be permitted to grant to Third Parties any Sublicenses [***] without Blueprint's prior written consent (such consent not to be unreasonably withheld, conditioned or delayed). After [***], Clementia will not be permitted to grant to Third Parties any Sublicenses [***] without Blueprint's prior written consent (such consent not to be unreasonably withheld, conditioned or delayed).

2.3.2 Clementia Right to Subcontract. Clementia, its Affiliates and its Sublicensees will be permitted to engage and utilize Third Party service providers to provide services to Clementia, its Affiliates and Sublicensees, as applicable, with respect to the Exploitation of the Licensed Products hereunder.

2.3.3 Performance by Clementia Affiliates and Sublicensees. Each Sublicense and subcontract under this Article 2 will be in writing. Clementia will promptly provide Blueprint with a copy of each fully executed Sublicense granted to a Third Party hereunder, which may be redacted solely to

remove information that is not necessary to monitor Clementia's compliance with this Agreement, including information involving products other than the Licensed Product. Any such Sublicense or subcontract entered into by Clementia or its Affiliate will (a) be subject and subordinate to, and consistent with, the terms and conditions of this Agreement; and (b) require the applicable Sublicensee or subcontractor to comply with all applicable terms of this Agreement (except for the payment obligations, for which Clementia will remain responsible), including (i) a requirement that such Sublicensee or subcontractor submit applicable sales or other reports to Clementia (or its Affiliate) to the extent necessary or relevant to the reports required to be made or records required to be maintained under this Agreement; (ii) audit requirements consistent with that set forth in Sections 4.3 and 5.7, as applicable; (iii) a requirement that such Sublicensee or subcontractor comply with confidentiality and non-use provisions of Confidential Information no less stringent than those contained in Article 7 with respect to Blueprint's Confidential Information; and (iv) a requirement that such Sublicensee or subcontractor support or enable Clementia's obligations upon and after termination consistent with Section 11.6. No Sublicense or subcontract will diminish, reduce or eliminate any obligation of Clementia under this Agreement, and Clementia will remain responsible for its obligations under this Agreement and will be responsible for the performance of the relevant Sublicensee or subcontractor as if such Sublicensee or subcontractor, as applicable, were "Clementia" hereunder.

2.4 Reservation of Rights. No rights, other than those expressly set forth in this Agreement, are granted to either Party under this Agreement, and no additional rights will be deemed granted to either Party by implication, estoppel or otherwise, with respect to any intellectual property rights. All rights not expressly granted by either Party or its Affiliates to the other under this Agreement are reserved.

2.5 Bankruptcy Code § 365(n) Election. All rights and licenses now or hereafter granted under or pursuant to this Agreement, are rights to "intellectual property" (as defined in Section 101(35A) of Title 11 of the United States Code (such Title 11, the "**Bankruptcy Code**")). Each Party, as licensee of such rights under this Agreement, will retain and may fully exercise all of its rights and elections under the United States Bankruptcy Code. In the event of the commencement of a bankruptcy proceeding by or against a Party under the Bankruptcy Code (the "**Insolvent Party**"), the other Party will be entitled to a complete duplicate of (or complete access to, as appropriate) any intellectual property licensed to it under this Agreement and all embodiments of such intellectual property (including all information related to such intellectual property and rights of reference with respect to Regulatory Filings and Regulatory Approvals), and same, if not already in its possession, will be promptly delivered to it (a) upon any such commencement of a bankruptcy proceeding upon its written request therefore, unless the Insolvent Party continues to perform all of its obligations under this Agreement, or (b) if not delivered or granted under (a) above, upon rejection of this Agreement by or on behalf of the Insolvent Party upon written request therefore by the other Party. The Insolvent Party (in any capacity, including debtor-in-possession) and its successors and assigns (including any trustee) agrees not to interfere with the exercise by other Party or its Affiliates of its rights and licenses to such intellectual property and such embodiments of intellectual property in accordance with this Agreement, and agrees to assist the other Party and its Affiliates in obtaining such intellectual property and such embodiments of intellectual property in the possession or control of Third Parties as reasonably necessary or desirable for the other Party to exercise such rights and licenses in accordance with this Agreement. The Parties hereto acknowledge and agree that all payments by Clementia to Blueprint under this Agreement, other than royalty payments pursuant to Section 5.4, do not constitute royalties within the meaning of Bankruptcy Code § 365(n) or relate to licenses of intellectual property under this Agreement. The foregoing provisions are without prejudice to any rights the Parties may have arising under the Bankruptcy Code or other applicable Laws.

2.6 Third Party Agreements. With respect to the Third Party Agreements set forth on Exhibit F, subject to any confidentiality obligations under such Third Party Agreements or to such Third Party, Blueprint will [***] assist Clementia in [***]. For the avoidance of doubt, Blueprint's efforts will

not include the expenditure of funds or payments to such Third Party or, except to the extent agreed to by such Third Party, the assignment by Blueprint to Clementia of such Third Party Agreements.

2.7 Exclusivity.

2.7.1 Except for activities performed by or on behalf of Blueprint or its Affiliates pursuant to the Transition Plan, Blueprint will not, directly or with or through any of its Affiliates or a Third Party, (a) Exploit any compound that is Covered by the Licensed Patents for the treatment [***] of FOP or MO during the Term, nor (b) with respect to any small molecule compound that is not Covered by the Licensed Patents, (i) Research, Develop or Manufacture such a compound for the treatment, [***] of FOP or MO for a period of five (5) years from the Effective Date, or (ii) Commercialize such a compound for the treatment, [***] of FOP or MO for a period of seven (7) years from the Effective Date, in each case, other than as specifically permitted under this Agreement.

2.7.2 Notwithstanding Section 2.7.1, if a Change of Control of Blueprint occurs, and a Third Party becomes or has become an Affiliate of Blueprint as a result of such Change of Control (or any of such Third Party's Affiliates or any successors or assigns of such Third Party or such Third Party's Affiliates, other than Blueprint and its Affiliates as of such Change of Control, collectively with such Third Party, an "**Acquiring Party**") already has a program (whether pre-clinical, clinical or commercial stage) that existed prior to such Change of Control, that would otherwise violate any of Section 2.7.1 (a "**Blueprint Change of Control Program**"), then (a) Section 2.7.1 will not apply with respect to such Blueprint Change of Control Program, and (b) such Acquiring Party will be permitted to continue such Blueprint Change of Control Program after such Change of Control and such initiation, pursuit and continuation will not constitute a violation of Section 2.7.1; provided that (i) none of the Licensed Technology, Clementia Technology, or Clementia Development Technology hereunder will be used in such Blueprint Change of Control Program, (ii) the Development activities required under this Agreement will be conducted separately from any Research or Development activities directed to such Blueprint Change of Control Program, including the maintenance of separate lab notebooks and records and separate personnel working on each of the activities under this Agreement and the activities covered under such Blueprint Change of Control Program and (iii) Blueprint will not, and it will cause its Representatives not to, disclose any of Clementia's Confidential Information, Licensed Technology, Clementia Technology, or Clementia Development Technology to, such Acquiring Party or Representative of such Acquiring Party, as applicable. [***]

2.8 Program Liaison. Each Party shall appoint a person(s) (each, a "**Program Liaison**") who shall be the primary point of contact between the Parties, to facilitate communications and the sharing of information related to the Blueprint Compounds and Licensed Products and shall have such other responsibilities as the Parties may agree in writing after the Effective Date, it being understood that any communications between the Program Liaisons, including written communications, shall not constitute a notice or report under Section 13.3. Each Party may replace its Program Liaison at any time by written notice to the other Party.

ARTICLE 3
TECHNOLOGY TRANSFER OF LICENSED KNOW-HOW

3.1 Documents and Filings Technology Transfer.

3.1.1 Transition Coordinator.

(a) Each Party shall appoint one transition coordinator in accordance with the Transition Plan (each, a "**Transition Coordinator**") who shall serve as the principal contact for Clementia

and Blueprint for matters relating to the implementation of the Transition Plan solely during the Transition Period. Each Party may replace its Transition Coordinator at any time upon written notice to the other Party. The initial Transition Coordinators designated by the Parties are set forth on Schedule 1 to the Transition Plan. Other personnel from a Party may assist such Party's Transition Coordinator with the foregoing, including by attending and participating in any meetings (whether by phone or in person) with respect thereto.

(b) The Transition Coordinators shall be responsible solely during the Transition Period for (i) coordinating Transition Plan activities between the Parties, (ii) reviewing the progress being made under the Transition Plan, (iii) modifying the Transition Plan as necessary or desired (provided that any such modification shall be in writing and mutually agreed to by the Transition Coordinators), and (iv) implementing the Transition Plan.

3.1.2 Documents and Filings. Within [***] after the Effective Date and to the extent necessary during the [***] following the Effective Date, as may be reasonably requested by Clementia, Blueprint will transfer electronic copies and assign ownership to Clementia or its Affiliates of all Regulatory Data, Regulatory Filings, Regulatory Approvals and other documents to or from Regulatory Authorities and other Third Parties, relating to the Blueprint Compounds and Licensed Products in the Territory (collectively, "**Documents and Filings**"), as identified on Schedule 2 to the Transition Plan. During the Transition Period, (i) [***] or (ii) [***], Blueprint will provide such documents to Clementia reasonably promptly after becoming aware of such documents or Clementia's request, as applicable. [***] In addition, at Clementia's request, to the extent permitted by the applicable Regulatory Authorities, Blueprint will appoint Clementia as Blueprint's agent (or cause its Representative to appoint Clementia as its agent) for all matters solely related to Licensed Product-related matters in the Territory involving such Regulatory Authorities until all Regulatory Data, Regulatory Approvals and Regulatory Filings in the Territory have been assigned to Clementia or its designee, with it being understood and agreed that Clementia shall promptly take any and all actions as may be required by the relevant Regulatory Authority to permit or finalize the aforementioned assignments to Clementia or its designee.

3.1.3 Right of Reference. Blueprint hereby grants to Clementia and its Affiliates and Sublicensees a "Right of reference or use," as that term is defined in 21 C.F.R. § 314.3(b) (or any successor rule or analogous law recognized outside of the U.S.) to all DMFs Controlled by Blueprint that pertain to the Blueprint Compounds. To the extent Blueprint does not Control such DMFs, Blueprint will reasonably assist Clementia and its Affiliates and Sublicensees in obtaining a Right of reference or use from the Third Party holder of such DMFs.

3.1.4 Ongoing Clinical Study. With respect to Blueprint's Phase 1 Clinical Study for BLU-782 in normal healthy volunteers (the "**Phase I NHV Study**"), Blueprint will, and will cause such Persons conducting such Phase I NHV Study on its behalf to, complete activities necessary for database lock for the Phase I NHV Study.

3.1.5 Phase II Clinical Study Meetings. Blueprint will accommodate Clementia's reasonable requests to participate in communications with FDA regarding the first Phase II Clinical Study of Licensed Product, including attending meetings and reviewing minutes of any meetings, material telephone conferences or material discussions with FDA, in each case solely with respect to Licensed Product and to the extent permitted by FDA.

3.1.6 Blueprint Trademarks and Copyrights. Blueprint will promptly transfer and assign to Clementia, at no cost, all of Blueprint and its Affiliates' rights, title, and interests in and to any Trademarks and copyrights Controlled by Blueprint and exclusively used in connection with the Licensed

Products (but not any Blueprint house marks or any Trademark containing the words "Blueprint," "Blueprint Medicines" or "Blueprint Medicines Corporation").

3.1.7 Patent Information. Upon request by Clementia, Blueprint will provide (a) any and all material correspondence with the relevant patent office(s) pertaining to the Prosecution and Maintenance of the Licensed Patents prior to the Effective Date, (b) a Patent docket report detailing the status of all Licensed Patents with upcoming deadlines for the [***] period following the Effective Date, and (c) [***] the following: (1) [***], (2) [***] and (3) [***] in connection with the Prosecution and Maintenance of the Licensed Patents prior to the Effective Date.

3.1.8 Data Room Transfer. Within [***] of the Effective Date, Blueprint shall provide Clementia with complete, unabridged and unrestricted (including with ability to print and download) electronic copies of all documents and materials that had been placed in the data room established prior to the Effective Date for Clementia's and its Affiliates' diligence of the Blueprint Compounds and Licensed Products.

3.2 Manufacturing Technology Transfer.

3.2.1 Technology Transfer. Within [***] after the Effective Date, [***] Blueprint will transfer to Clementia or its designated CMO an electronic copy of Manufacturing technology related to the Manufacture of BLU-782, as identified on Schedule 3 to the Transition Plan. At Clementia's request, Blueprint will [***]. For the avoidance of doubt, Blueprint's efforts will not include the expenditure of funds or payments to such Blueprint CMO or the assignment by Blueprint to Clementia of any of Blueprint's master service agreements or similar agreements with any such Blueprint CMO.

3.2.2 Manufacturing Inventory.

(a) Existing Manufacturing Inventory. [***] after the Effective Date, the Parties will enter into a bill of sale in the form set forth in Exhibit 3.2.2, and Blueprint will sell to Clementia, and Clementia will purchase, the quantities of BLU-782 and the Licensed Product containing BLU-782 (in bulk form or finished dosage product form) or works-in-progress of each of the foregoing Controlled by Blueprint, identified on and upon the terms and conditions set forth in Schedule 3.2.2(a) ("**Existing Manufacturing Inventory**"), at an amount equal to (i) the aggregate Fully Burdened Costs for such Manufacturing Inventory set forth in Schedule 3.2.2(a), multiplied by (ii) [***]. Title to and risk of loss of such Existing Manufacturing Inventory will pass to Clementia at the time of sale, and such Existing Manufacturing Inventory shall be sold "as is" to Clementia.

(b) In Process Manufacturing Inventory. [***], for the quantities of BLU-782 and the Licensed Product containing BLU-782 (in bulk form or finished dosage product form) and all raw materials or works-in-progress of each of the foregoing Controlled by Blueprint, identified on Schedule 3.2.2(b) ("**In Process Manufacturing Inventory**"), the Parties will enter into a bill of sale in the form set forth in Exhibit 3.2.2, and Blueprint will sell to Clementia, and Clementia will purchase, the In Process Manufacturing Inventory upon the terms and conditions set forth in Schedule 3.2.2(b), at an amount equal to (i) the aggregate Fully Burdened Costs for such In Process Manufacturing Inventory set forth in Schedule 3.2.2(b), multiplied by (ii) [***]. Title to and risk of loss of such In Process Manufacturing Inventory will pass to Clementia at the time of sale, and such In Process Manufacturing Inventory shall be sold "as is" to Clementia.

(c) Manufacturing Documents. Within [***] after the Effective Date (with respect to such Existing Manufacturing Inventory) and within [***] after such sale (with respect to such In Process Manufacturing Inventory), Blueprint will also transfer (or cause to be transferred) to Clementia

copies of Blueprint's Manufacturing records relating to such supply, including copies of the applicable batch records, in-process and release test results, and certificates of analysis and, to the extent applicable, release with respect thereto (the "**Manufacturing Documents**"); provided, however, that in no event shall Blueprint be required to transfer any of its CMO's confidential or proprietary information.

3.3 Assistance by Blueprint. Blueprint will provide reasonable assistance to Clementia in accordance with the Transition Plan for up [***] hours at no cost to Clementia (other than external costs and expenses incurred by Blueprint in connection therewith, for which Blueprint will invoice Clementia); provided that, [***]. For any assistance by Blueprint to Clementia in excess of [***] hours, Blueprint will invoice Clementia for FTEs at the FTE Rate for any FTE hours and external costs and expenses incurred by Blueprint in connection with providing such assistance for a period not to exceed [***] to facilitate (a) the transition of the Licensed Technology and Documents and Filings to Clementia and (b) the transfer of the Manufacturing Documents to Clementia (such period, the "**Transition Period**"). Clementia will pay such invoices within [***] of receipt of each invoice from Blueprint in accordance with Section 5.9. For the avoidance of doubt, Blueprint shall not be required to provide assistance to Clementia pursuant to this Section 3.3 beyond such [***] period, subject to Section 3.4.

3.4 Follow-up Period. If no later than [***], either Party discovers or learns of any material, non-duplicative documents or materials that should have been included in the Documents and Filings or any Know-How that should have been included in the Licensed Technology, such Party shall provide written notice to the other Party, and Blueprint shall [***] provide Clementia with such Documents and Filings or such Licensed Know-How in accordance with the manner specified on Schedule 2 to the Transition Plan.

ARTICLE 4
RESEARCH, DEVELOPMENT, REGULATORY, MANUFACTURING AND COMMERCIALIZATION

4.1 General. Without limiting Clementia's obligations pursuant to Section 4.2, as between the Parties, Clementia will have sole authority and responsibility, at its sole expense, to Develop, Manufacture (subject to Blueprint's obligations pursuant to Section 3.2) and Commercialize Licensed Products in the Field in the Territory. Without limiting the generality of the foregoing, subject to Clementia's obligations pursuant to Section 4.2, as between the Parties, Clementia will be solely responsible and have sole authority for preparing, and submitting all required Regulatory Filings in connection with obtaining and maintaining Regulatory Approvals with respect to Blueprint Compounds and Licensed Products in the Field, including all INDs and NDAs, at Clementia's sole expense. All such submissions and Regulatory Filings relating to Blueprint Compounds and Licensed Products will be submitted in the name of, and owned by, Clementia.

4.2 Diligence.

4.2.1 Research and Development Diligence. During the period commencing with the Effective Date and ending with the date of FDA approval of the first NDA for a Licensed Product, Clementia (directly, or through its Affiliates, Sublicensees and permitted subcontractors) will use Commercially Reasonable Efforts to Research, Develop and obtain Regulatory Approval of [***] Licensed Product for use in humans in the Field in [***] for the treatment [***] of FOP in patients. Without limiting the foregoing sentence, Clementia will (a) use Commercially Reasonable Efforts to implement the initial Development Plan attached hereto as Exhibit B and (b) Initiate a Phase II Clinical Study or Pivotal Study of a Licensed Product for the treatment [***] of FOP in patients by no later than [***] 2020.

4.2.2 Commercialization Diligence. Clementia (directly, or through its Affiliates, Sublicensees and permitted subcontractors) will be responsible for and use Commercially Reasonable

Efforts to Commercialize [***] Licensed Product(s) during the Term following Regulatory Approval for such Licensed Product(s) for use in humans in the Field in [***]

4.2.3 Notification of Inability to Exploit; Resumption of Performance. Notwithstanding the foregoing, Clementia shall not be in breach of this Section 4.2 in the event and to the extent its failure to perform its obligations under this Section 4.2 arises from or is a result of a Delay or Suspension. Clementia will promptly notify Blueprint in writing (and in any event, within [***]) upon it obtaining knowledge of the occurrence of a Delay or Suspension. Such notice shall state the nature of the event or condition, and its anticipated duration (to the extent such anticipated duration can reasonably be estimated). Clementia will promptly respond to Blueprint's reasonable questions or requests for additional information relating to such cause for Delay or Suspension and resumption of Development or Commercialization obligations. Clementia will use Commercially Reasonable Efforts to resolve the cause for such Delay or Suspension and resume performance of its obligations pursuant to Sections 4.2.1 and/or 4.2.2, as applicable.

4.3 Manner of Performance; Records. Clementia will (a) perform, and will cause its Affiliates and Sublicensees to perform, all Research, Development, Manufacturing and Commercialization activities and obligations under this Agreement in good scientific manner and in compliance with all applicable Laws (including with respect to each such activity that will or would reasonably be expected to be submitted to a Regulatory Authority in support of a Regulatory Filing or NDA, then-current Good Laboratory Practices, Good Clinical Practices and Good Manufacturing Practices) and (b) maintain, or cause to be maintained, complete and accurate records of all such activities conducted by or on behalf of Clementia, its Affiliates and Sublicensees, including all results, data, inventions and developments, at a level of detail appropriate for patent and regulatory purposes. In the event Blueprint has a reasonable basis to believe Clementia is not in compliance with applicable Law, Blueprint may appoint an independent third party reasonably acceptable to Clementia to review any such records of Clementia and its Affiliates and Sublicensees, as applicable, in the location(s) where such records are maintained by Clementia and its Affiliates and Sublicensees, upon reasonable prior written notice, during regular business hours and under obligations of confidentiality reasonably satisfactory to Clementia, for the sole purpose of verifying Clementia's and its Affiliates' and Sublicensees' compliance with applicable Law.

4.4 Notice of Metabolites; Reports.

4.4.1 Notice of Metabolites. At any time during the Term, Clementia shall provide Blueprint with written notice of any Metabolite(s) not identified in Exhibit A-2, which notice shall include the chemical structure of such metabolite (such metabolite, a "**New Metabolite**"). Effective upon receipt by Blueprint of such written notice, (a) such New Metabolite shall become a Blueprint Compound and (b) Blueprint hereby grants to Clementia the licenses specified under Sections 2.1.1, 2.1.2, and 2.1.3 with respect to such New Metabolite as a Blueprint Compound; provided that in each case (clauses (a) and (b)) if Blueprint does not, as of the date of such written notice, Control the (i) Blueprint Product-Specific Technology, (ii) Blueprint Future Technology, or (iii) Blueprint Platform Technology, in each case (clauses (i), (ii) and (iii)), respectively, that Covers (with respect to Licensed Patents) or relates to (with respect to Licensed Know-How) the New Metabolite, then (A) such New Metabolite shall not become a Blueprint Compound and (B) Blueprint will not grant to Clementia any license under Section 2.1 with respect to such New Metabolite. Clementia covenants that it will not Develop or Commercialize any Metabolite unless and until such Metabolite becomes a Blueprint Compound; provided, however, that nothing in this Section 4.4.1 will be interpreted to prevent Clementia from continuing to Develop and Commercialize then-existing Blueprint Compounds as contemplated by this Agreement.

4.4.2 Development and Commercialization Reports. During the period commencing with the Effective Date [***], Clementia will provide to Blueprint a written report (in English) at least [***]

describing in reasonable detail Clementia's and its Affiliates' and Sublicensees' activities and progress, including through its Affiliates and Sublicensees, related to the Research, Development, Manufacturing and Commercialization of the Licensed Products in the Territory including with respect to Development, on a Licensed Product-by-Licensed Product and Indication-by-Indication basis and country-by-country basis: (a) [***], (b) [***], (c) [***], (d) [***], (e) [***], (f) [***], and (g) [***] (each such report, a "**Development Report**"). Concurrently with such Development Report, Clementia will provide any updates and amendments to the Development Plan. Beginning after the [***], Clementia will provide such report [***], including a brief overview of (i) any of the foregoing activities ((a) through (g)) related to (A) [***], and (B) [***] and (ii) [***] (each such report, a "**Commercialization Report**"). Clementia will promptly respond to Blueprint's reasonable questions or requests for additional information relating to reported activities and progress in such Development Reports or Commercialization Reports, as applicable. For avoidance of doubt, each Development Report and Commercialization Report shall be Clementia's Confidential Information.

ARTICLE 5
FINANCIAL TERMS

5.1 **Upfront Payment.** Clementia will pay Blueprint an irrevocable, non-refundable, non-creditable payment in the amount of Twenty Five Million Dollars ($25,000,000) within [***] after the Effective Date.

5.2 **Development Milestone Payments.**

5.2.1 **Development Milestones and Development Payments.** In partial consideration of the licenses and rights granted to Clementia hereunder, Clementia will make each of the irrevocable, non-refundable, non-creditable, one-time milestone payments set forth below in Table 5.2.1 (each, a "**Development Milestone Payment**") to Blueprint within [***] after the first achievement by Clementia or any of its Affiliates or Sublicensees of the corresponding milestone event set forth below in such table with respect to a Licensed Product (each, a "**Development Milestone Event**").

Table 5.2.1 – Development Milestones

	Development Milestone Event	**Development Milestone Payments**
1	[***]	$20,000,000 (Twenty Million Dollars)
2	[***]	[***]
3	[***]	[***]
4	[***]	[***]
5	[***]	[***]
6	[***]	[***]
7	[***]	[***]
8	[***]	[***]
9	[***]	[***]
10	[***]	[***]

5.2.2 [***]

(a) [***].

(b) [***].

5.2.3 **One-Time Payments.** For clarity, each Development Milestone Payment in Table 5.2.1 will be due and payable one time only with respect to the first achievement of each Development Milestone Event by the first Licensed Product to achieve such Development Milestone Event (regardless of the number of Licensed Products to achieve such Development Milestone Event), such that the maximum total amount payable under this Section will not exceed [***].

5.2.4 **Milestone Event Notice.** Within [***] after Clementia becomes aware that a Development Milestone Event was achieved, Clementia will notify Blueprint thereof in writing, including identifying the event and the date of its achievement.

5.3 **Sales Milestone Payments.**

5.3.1 **Sales Milestones and Sales Milestone Payments.** Clementia will pay to Blueprint the following irrevocable, non-refundable, non-creditable one-time sales milestone payments (each, a "**Sales Milestone Payment**") within [***] following the end of the first Calendar Year during the Royalty Term in which the aggregate Net Sales of Licensed Products by Clementia, its Affiliates and Sublicensees in the Territory achieves the sales threshold (set forth in the table below) corresponding to such Sales Milestone Payment (each a "**Sales Milestone Event**"):

Table 5.3.1 – Sales Milestones

	Sales Milestone Event	**Sales Milestone Payments**
1	[***]	[***]
2	[***]	[***]
3	[***]	[***]
4	[***]	[***]

Each Sales Milestone Payment will be payable only one-time and only upon the first achievement of the applicable Sales Milestone Event for aggregate Net Sales of Licensed Products in the Territory, and no amounts would be due for subsequent or repeated achievements. For clarity, more than one (1) Sales Milestone Event may occur in a single Calendar Year. For example, [***]. The maximum total amount payable under this Section will not exceed [***].

5.3.2 **Milestone Event Notice.** Within [***] after Clementia becomes aware that a Sales Milestone Event was achieved, Clementia will notify Blueprint thereof in writing, including identifying the event and the date of its achievement.

5.4 **Royalties.**

5.4.1 **Royalty Rate.** Subject to the applicable adjustments in accordance with Section 5.6, during the applicable Royalty Term, Clementia will pay to Blueprint royalties based on the

aggregated Net Sales of all Licensed Products (whether by Clementia, its Affiliates or Sublicensees) in the Territory at the rates set forth in the table below.

Table 5.4.1 – Royalty Rates for Net Sales of Licensed Products	
Worldwide Aggregate Annual Net Sales of Licensed Products	**Royalty Rate (as a percentage of Net Sales)**
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

5.4.2 **Royalty Term.** Royalties will be due under this Section 5.4.2 on a country-by-country and Licensed Product-by-Licensed Product basis during the period commencing on the First Commercial Sale of such Licensed Product in such country and ending upon the latest of (a) the expiration of the last Valid Claim within the Licensed Patents Covering such Licensed Product in such country, (b) upon the expiration of the Regulatory Exclusivity Period for such Licensed Product in such country or (c) the [***] anniversary of the First Commercial Sale of such Licensed Product in such country (such period for such Licensed Product in such country, the "**Royalty Term**").

5.5 **Royalty Payments and Reports.**

5.5.1 [***] **Flash Reports.** Beginning after the first sale of a Licensed Product, (i) as part of the reports described in Section 4.4.2, Clementia will provide a forecast of estimated quarterly and annual Net Sales and (ii) [***], Clementia will provide Blueprint with a flash report providing a good-faith estimate of the amount of Net Sales and the royalties payable to Blueprint on such Net Sales on a Licensed Product-by-Licensed Product and country-by-country basis in the Territory during such [***] (including such amounts expressed in local currency and as converted to Dollars). Notwithstanding the foregoing, Clementia will provide final reports for each Calendar Quarter as set forth in Section 5.5.2, and it is understood that for purposes of calculating the royalty owed under Section 5.4.1 or Section 5.6, as applicable, final reported Net Sales (as reported pursuant to Section 5.5.2) may vary from the flash report for the [***].

5.5.2 **Quarterly Royalty Payments and Final Reports.** Within [***] after the end of each of the Calendar Quarters ended March 31, June 30 and September 30 of each Calendar Year and within [***] after the end of the Calendar Quarter ended December 31 of each Calendar Year, Clementia (i) will pay to Blueprint any amounts due pursuant to Section 5.4.1 ("**Royalty Payments**"), and (ii) will provide to Blueprint concurrently with such payment a statement (in English) setting forth (a) the amount of Net Sales on a Licensed Product-by-Licensed Product and country-by-country basis in the Territory during such Calendar Quarter (including such amounts expressed in local currency and as converted to Dollars); (b) the type and amount of permitted deductions from gross sales to determine Net Sales and the total amount of such deductions; (c) the applicable royalty rates for each Licensed Product in each country in the Territory after applying any permitted deductions in accordance with Section 5.6; and (d) a calculation of the royalties due to Blueprint for such Calendar Quarter.

5.6 **Payment Reductions.**

5.6.1 Blocking Third Party Patent(s). Subject to Section 5.6.5, Clementia will be entitled to deduct from Royalty Payments under Section 5.4 otherwise payable to Blueprint on Net Sales of a Licensed Product in a specific country or countries, [***] of any Blocking Third Party Patent Payments actually paid by Clementia or any of its Affiliates or Sublicensees under a license to Blocking Third Party Payments applicable to such Licensed Product in such country or countries, up to a maximum reduction under this Section 5.6.1 of [***] of the royalties otherwise owed to Blueprint hereunder for the applicable Calendar Quarter for such Licensed Product in such country.

5.6.2 No Exclusivity. Subject to Section 5.6.5 if at any time during the Royalty Term a Licensed Product is sold in a country in the Territory by Clementia or an Affiliate or Sublicensee and such Licensed Product, at the time of such sale:

(a) is not Covered by a Valid Claim within the Licensed Patents Covering such Licensed Product in such country, but is within any applicable Regulatory Exclusivity Period, then, the applicable royalty in effect with respect to such sale of such Licensed Product in such country as specified in Section 5.4.1 will be reduced by [***]; or

(b) is not Covered by a Valid Claim within the Licensed Patents Covering such Licensed Product in such country and is not within any applicable Regulatory Exclusivity Period, then, the applicable royalty in effect with respect to such sale of such Licensed Product in such country as specified in Section 5.4.1 will be reduced by [***].

5.6.3 Generic Competition. Subject to Section 5.6.5, on a Licensed Product-by-Licensed Product and country-by-country basis, if during any Calendar Quarter, there is Loss of Market Exclusivity for such Licensed Product in such country and the aggregate Net Sales of such Licensed Product in such country during any [***] following the Generic Launch Quarter are at least [***] lower than the aggregate Net Sales of such Licensed Product in such country during the [***] immediately prior to the Generic Launch Quarter, then the royalty rate applicable to Net Sales of such Licensed Product in such country in such Calendar Quarter will be reduced by [***] of the applicable royalty rate that would otherwise be owed on such Net Sales of such Licensed Product in such country under Section 5.4.1; provided, that if the aggregate Net Sales of such Licensed Product in that country during any [***] following the Generic Launch Quarter are at least [***] lower than the aggregate Net Sales of such Licensed Product in such country during [***] immediately prior to the Generic Launch Quarter, then the royalty rate applicable to Net Sales of such Licensed Product in such country in such Calendar Quarter will be reduced by [***] of the applicable royalty rate that would otherwise be owed on such Net Sales of such Licensed Product in such country under Section 5.4.1 (each, a "**Royalty Reduction Trigger**"); provided, however, if the aggregate Net Sales of such Licensed Product in a country during any [***] subsequently become equal to or exceed the aggregate Net Sales of such Licensed Product in such country during the last [***] immediately prior to the Generic Launch Quarter, then the applicable royalty rate reduction will cease with respect to such Licensed Product in such country, unless and until a Royalty Reduction Trigger occurs again with respect to such Licensed Product in such country. In the event a royalty rate reduction under this Section 5.6.3 is applied with respect to a Licensed Product in a country during a Calendar Quarter following a Generic Launch Quarter, any royalty reduction previously applied under Section 5.6.2 shall no longer apply with respect to such Licensed Product in such country as of such Calendar Quarter. Clementia will promptly notify Blueprint of the occurrence of Loss of Market Exclusivity, which notice will specify the applicable Generic Products, Indication, and country in the Territory.

5.6.4 Compulsory License. If a Compulsory License is granted to a Third Party with respect to any Licensed Product in any country in the Territory with a royalty rate lower than the applicable royalty rate set forth in this Section 5.6.4, and such Third Party actually sells such Licensed Product in such

country under such Compulsory License, then the royalty rate to be paid by Clementia on Net Sales in that country under this Section 5.6.4 will be reduced to the rate paid by the compulsory licensee.

5.6.5 Maximum Aggregate Reduction. The maximum aggregate of all reductions under Sections 5.6.1 through Section 5.6.3 will reduce the amount of royalties owed to Blueprint hereunder in any given Calendar Quarter by no more than [***] from the amounts otherwise due to Blueprint hereunder in such Calendar Quarter in the absence of any such reductions. Clementia may carry forward to subsequent Calendar Quarters any amounts that it was not able to credit under this Section 5.6.5 on account of such maximum aggregate royalty reduction, subject to the maximum aggregate royalty reduction for all subsequent Calendar Quarters.

5.7 Financial Audits.

5.7.1 Record Keeping. Clementia and its Affiliates and Sublicensees will keep, and will require each of its Sublicensees to keep, complete and accurate records in accordance with the applicable Accounting Standards of the activities and payments underlying (a) the Development Milestone Payments, (b) the Sales Milestone Payments, (c) Net Sales, including the Net Sales and proration factor applied for Combination Products and the deductions from gross revenue to determine Net Sales, (d) Royalty Payments, including reductions taken in accordance with Section 5.6, if any, and (e) any other payments under this Agreement. Blueprint will have the right not more than [***] during the Term and [***] thereafter, at its sole expense, to have an independent, certified public accountant, selected by Blueprint and reasonably acceptable to Clementia, review any such records of Clementia and its Affiliates and Sublicensees, as applicable, in the location(s) where such records are maintained by Clementia and its Affiliates and Sublicensees, as applicable, upon reasonable prior written notice, during regular business hours and under obligations of confidentiality, for the sole purpose of verifying the basis and accuracy of payments made under this Agreement, within the prior [***] period. The records for any Calendar Year may be audited no more than once absent fraud or intentional misconduct that directly inhibited Blueprint's ability to conduct a complete and accurate audit.

5.7.2 Audit Report. The report prepared by the independent certified public accounting firm pursuant to Section 5.7.1, a copy of which report (which will be in English) will be sent or otherwise provided to each Party by such independent public accountant at the same time, will contain the conclusions of such accounting firm regarding the audit and will specify that the amounts paid pursuant thereto were correct or, if incorrect, the amount of any underpayment or overpayment, and the specific details regarding any discrepancies. No other information will be provided to Blueprint without the prior consent of Clementia unless disclosure is required by Law, regulation or judicial order, and if so determined by Blueprint, it will, if permitted, give Clementia prior notice thereof reasonably sufficient for Clementia to seek a protective order against or limiting such disclosure. If such report shows any underpayment, then Clementia will remit to Blueprint, within [***] after receipt of such report, (a) the amount of such underpayment and (b) if such underpayment exceeds [***] of the total amount owed for the period then being audited, the reasonable out-of-pocket costs incurred by Blueprint in conducting such audit. If such report shows any overpayment, then any overpayments will, at Clementia's election, be refunded by Blueprint to Clementia within [***] of receipt of the audit report or deducted from future payments owed to Blueprint. The Parties mutually agree that all information of Clementia, its Affiliates and Sublicensees that is subject to review under this Section is Confidential Information of Clementia and that Blueprint will retain and cause the accountant to retain all such information in confidence in accordance with Article 7.

5.7.3 Audit Period. Upon the expiration of [***] following the end of any Calendar Year, the audit rights set forth in this Section 5.7 will no longer apply to such Calendar Year and the calculation of amounts payable with respect to such Calendar Year will be binding and conclusive absent a showing of fraud or intentional misconduct in the calculation of such amounts.

5.8 Taxes.

5.8.1 VAT. It is understood and agreed between the Parties that any payments made under this Agreement are exclusive of any value added or similar tax ("**VAT**"), which will be added thereon as applicable.

5.8.2 Withholding Taxes. Subject to Section 5.8.5, if a Party is required to make a payment under this Agreement (the "Payor") to the other Party (the "Payee") and such payment is subject to a deduction of tax or withholding tax, then (a) if such withholding or deduction obligation arises as a result of any failure on the part of Payor to comply with applicable tax laws or filing or record retention requirements, that has the effect of modifying the tax treatment of either of the Parties, then the sum payable by Payor (in respect of which such deduction or withholding is required to be made) will be increased to the extent necessary to ensure that Payee receives a sum equal to the sum which it would have received had no such action or failure to act occurred and (b) otherwise, the sum payable by Payor (in respect of which such deduction or withholding is required to be made) will be made to Payee after deduction of the amount required to be so deducted or withheld, which deducted or withheld amount will be remitted in accordance with applicable Law. In addition, in the event of any changes in applicable Law that result (or may result) in any withholding taxes, the Parties shall reasonably cooperate to minimize the amount of any taxes withheld.

5.8.3 Tax Cooperation. To the extent the Payor is required by applicable Law to deduct and withhold taxes on any payments to the Payee, the Payor will pay the amounts of such taxes to the proper Governmental Authority in a timely manner and promptly transmit to the Payee an official tax certificate or other evidence of such withholding sufficient to enable the Payee to claim such payments of taxes. If Payor fails to perform its obligations as set forth in the foregoing sentence, Payor shall reimburse the Payee for any and all interest, penalties, costs and expenses incurred by the Payee arising from such failure. Payee will timely provide to the Payor any tax forms or reports that may be reasonably necessary in order for Payor not to withhold tax or to withhold tax at a reduced rate under an applicable bilateral income tax treaty. Each Party will provide the other with timely and reasonable assistance to enable the recovery, as permitted by applicable Law, of withholding taxes, VAT, or similar obligations resulting from payments made under this Agreement, such recovery to be for the benefit of the Party effectively bearing such withholding tax or VAT. If the sum payable by Payor (in respect of which a deduction or withholding was required to be made) has been increased to the extent necessary to ensure that Payee would receive a sum equal to the sum which it would have received had no such deduction or withholding been required by applicable Law, and if Payee subsequently obtains a tax credit or deduction on account of any such withholding tax, VAT or similar payment obligation paid by Payor (or any fraction thereof), Payee shall promptly refund in cash to Payor an amount equal to such withholding taxes, VAT, or similar payment obligations remitted by Payor to the proper Governmental Authority, to the extent of such tax credit or deduction obtained by Payee; provided that such refund shall only become due and payable if, as and when Payee (i) receives such tax credit as a cash refund from the applicable taxing authority or (ii) is able to apply such tax credit to, or deduct such tax deduction from, a current amount owed by Payee to such taxing authority.

5.8.4 Tax Forms. The Parties agree to cooperate and produce on a timely basis any tax forms or reports reasonably requested by the other Party in connection with any payment made under this Agreement, including any documents reasonably necessary to determine whether the Payee may, or actually did, obtain a foreign tax credit or refund of any withholding tax due on a payment made under this Agreement.

5.8.5 Assignment. If either Party assigns its rights and obligations hereunder to an Affiliate or Third Party in compliance with Section 13.1 and if such Affiliate or Third Party will be required by applicable Law to withhold any taxes from or in respect of any amount payable under this Agreement

as a result of such assignment, then any such amount payable under this Agreement will be increased to take into account the additional taxes withheld as may be necessary so that, after making all required withholdings, Payee receives an amount equal to the sum it would have received had no such assignment been made. The foregoing sentence will not apply to any assignment to an Affiliate or Third Party in compliance with Section 13.1 where such Affiliate or Third Party is a tax resident of the United States, United Kingdom (or any successor country thereto that encompasses England) or France under applicable Law (provided that the Parties shall reasonably cooperate to minimize any taxes withheld). If either Party assigns its rights and obligations hereunder to an Affiliate or Third Party in compliance with Section 13.1 and the other Party will be required by applicable Law to withhold any taxes from or in respect of any amount payable under this Agreement to such Affiliate or Third Party as a result of such assignment, then the sum payable by Payor (in respect of which such deduction or withholding is required to be made) will be made to Payee after deduction of the amount required to be so deducted or withheld, which deducted or withheld amount will be remitted in accordance with applicable Law.

5.9 Currency of Payments; Payments. All amounts payable and calculations under this Agreement will be in Dollars. With respect to Royalty Payments for Net Sales invoiced in any currency other than Dollars and, if applicable, any Royalty Payment reductions in any currency other than Dollars, such amounts shall be converted into Dollars calculated using (i) the exchange rate corresponding to the average of the daily reference rate published by the European Central Bank for the Dollar against the Euro, multiplied by (ii) the average over the applicable Calendar Quarter of the daily fixing cross rate published by the European Central Bank for the Euro against the currency of the country in which the applicable Net Sales were made or the Royalty Payment reduction applies, in each case, as consistently used by Clementia and its Affiliates for purposes of their group consolidated accounts. All payments due to Blueprint under this Agreement will be paid in Dollars by bank wire transfer of immediately available funds to the following bank account of Blueprint (which account Blueprint may update from time to time by written notice to Clementia):

[***]

For Further Credit to:
[***]

5.10 Interest on Overdue Payments. Interest will be payable on any payments that are not paid on or before [***] after the date such payments are due under this Agreement at a rate per annum equal to the lesser of SOFR USD plus [***] or the highest rate allowed by applicable Law, as applicable and commencing on the date such payments are due and ending when paid. In the event that no rate is available for SOFR USD, the Parties shall agree in good faith to substitute a reasonable alternative rate for purposes of this Section 5.10.

ARTICLE 6
INTELLECTUAL PROPERTY OWNERSHIP, PROTECTION AND RELATED MATTERS

6.1 Ownership of Inventions.

6.1.1 Ownership. Inventorship for patentable Know-How conceived or reduced to practice during the course of the performance of activities pursuant to this Agreement will be determined on a worldwide basis in accordance with United States Patent Laws and, except as expressly set forth herein, ownership of any such patentable Know-How will be determined by inventorship under applicable Law.

(a) Pre-existing Patents and Know-How. Subject only to the rights expressly granted to the other Party under this Agreement, each Party will and does own all rights, title, and interest in and to any Patents and Know-How that are Controlled by such Party prior to the Effective Date or that such Party creates or obtains outside the scope of this Agreement.

(b) Clementia Development Technology. Subject only to the rights expressly granted to Blueprint under this Agreement, Clementia will and does own all rights, title, and interest in and to all Clementia Development Technology.

(c) Blueprint Development Know-How and Blueprint Future Technology. Subject only to the rights expressly granted to Clementia under this Agreement, Blueprint will and does own all rights, title, and interest in and to any Blueprint Development Know-How and Blueprint Future Technology.

(d) Joint Technology. Subject only to the rights expressly granted to the Parties under this Agreement, the Parties will and do jointly own the Joint Technology, with each Party having an equal, undivided interest therein. Each Party will promptly disclose to the other Party in writing and will cause its Affiliates, and its and their licensees and sublicensees to so disclose, the making of any Joint Technology. Subject to the licenses granted hereunder and the other terms and conditions of this Agreement, including Section 2.1, each Party may exercise its ownership rights in and to such Joint Technology, including the right to license and sublicense or otherwise to exploit, transfer or encumber its ownership interest, throughout the world, without an accounting or obligation (including paying royalties) to, or consent required from, the other Party. At the reasonable written request of a Party, the other Party will in writing grant such consents and confirm that no such accounting is required to effect the foregoing regarding such Joint Technology.

6.2 Prosecution and Maintenance of Licensed Patents.

6.2.1 Clementia Development Patents. Clementia will have the sole right to control the Prosecution and Maintenance of all Clementia Development Patents, at its sole expense.

6.2.2 Blueprint Future Technology. Blueprint will have the sole right to control the Prosecution and Maintenance of all Patents within the Blueprint Future Technology, at its sole expense.

6.2.3 Licensed Patents and Joint Patents in the Territory. During the Term, Clementia will be responsible (subject to Section 6.2.4), at its sole cost and expense, to Prosecute and Maintain the (a) Licensed Patents (except Joint Patents) in the name of Blueprint in all countries in the Territory and (b) Joint Patents in the name of Blueprint and Clementia in all countries in the Territory, in each case (clauses (a) and (b)) using qualified outside patent counsel and foreign patent associates selected by Clementia; provided that Clementia identifies such counsel and foreign patent associates for Blueprint in advance and Blueprint consents to such counsel and foreign patent associates (such consent not to be unreasonably withheld, conditioned or delayed). Clementia will keep Blueprint informed of all steps with regard to and the status of such Prosecution and Maintenance of such Licensed Patents, including by providing Blueprint with (i) copies of all correspondence and material communications Clementia or its designee sends to or receives from any patent office or agency in the Territory relating to the Licensed Patents, (ii) a draft copy of all applications sufficiently in advance (and no less than [***] in advance) of filing to permit reasonable review and comment by Blueprint, and (iii) a copy of applications as filed, together with notice of its filing date and serial number. During the Term, upon Blueprint's request and not more than [***], Clementia's and Blueprint's patent counsel (and other personnel, as necessary) will meet, in-person or telephonically at a mutually agreeable time and location, to discuss the status and strategy regarding the Prosecution and Maintenance of the Licensed Patents (including Joint Patents). Before

Clementia submits any material filing, including a new patent application, or response to patent authorities with respect to the Licensed Patents, Clementia will provide Blueprint with the opportunity to review and comment on such filing or response (and no less than [***] in advance, to the extent reasonably practicable) and will consider in good faith Blueprint's requests and suggestions regarding the Prosecution and Maintenance of the Licensed Patents under this Section 6.2.3. Upon Blueprint's request, Clementia will file continuing or divisional Patent applications with respect to the Licensed Patents [***] ("**Continuing Applications**"). [***].

6.2.4 Step-In Right. If Clementia elects not to Prosecute and Maintain or not to continue to Prosecute and Maintain a given Patent within the Licensed Patents (such patent, a "**Declined Patent**") in the Territory pursuant to Sections 6.2.3, then Clementia will give Blueprint written notice thereof within a reasonable period (but not less than [***]) prior to allowing such Declined Patent to lapse or become abandoned or unenforceable.

(a) If Blueprint agrees that such Declined Patent should be allowed to lapse or become abandoned or unenforceable, Blueprint will provide written notice to Clementia of such agreement. [***].

(b) If Blueprint desires to maintain the Prosecution and Maintenance of such Declined Patent, Blueprint will provide written notice to Clementia, and will have the following rights with respect to such Declined Patent:

(i) If such Declined Patent is a Blueprint Product-Specific Patent in a country, Blueprint will have the right to require Clementia to continue to Prosecute and Maintain such Declined Patent in such country, and Clementia and Blueprint will equally share the costs and expenses directly related to such Prosecution and Maintenance of such Declined Patent. As of the date of Clementia's notice to Blueprint in accordance with this Section 6.2.4 with respect to a Declined Patent under this Section 6.2.4(b)(i), any exclusive license Clementia may have in such Declined Patent in such country will convert to a non-exclusive license. Before Clementia submits any material filing, including a new patent application, or response to patent authorities with respect to such Declined Patent under this Section 6.2.4(b)(i), Clementia will provide Blueprint with the opportunity to review and comment on such filing or response (and no less than [***] in advance, to the extent reasonably practicable) and will consider in good faith Blueprint's requests and suggestions regarding the Prosecution and Maintenance of such Declined Patent.

(ii) If such Declined Patent is a Blueprint Platform Patent in a country, Blueprint will have the right, but not the obligation to assume responsibility or designate such responsibility to a Third Party for continuing the Prosecution and Maintenance of such Declined Patent in such country, at Blueprint's sole expense, through patent counsel or agents of Blueprint's choice. Reasonably promptly after receipt of Blueprint's notice under this Section 6.2.4 with respect to a Declined Patent under this Section 6.2.4(b)(ii), Clementia will transfer responsibility for the Prosecution and Maintenance of the applicable Declined Patent to Blueprint and Clementia will take all actions and execute all documents reasonably necessary for Blueprint to assume such Prosecution and Maintenance, at no cost to Blueprint. As of the date of Clementia's notice to Blueprint in accordance with this Section 6.2.4, the term "Licensed Patents" will automatically exclude such Declined Patent. For the avoidance of doubt, Section 6.1.1(d) shall apply with respect to any such Declined Patent under this Section 6.2.4(b)(ii) that is a Joint Patent.

6.2.5 Cooperation. With respect to all Prosecution and Maintenance of the Licensed Patents and Continuing Applications, each Party will: (a) execute any instruments to document their respective ownership consistent with this Agreement as reasonably requested by the other Party; (b) make its employees, agents and consultants reasonably available to the other Party (or to the other Party's

authorized attorneys, agents or representatives), to the extent reasonably necessary to enable the appropriate Party hereunder to undertake its Prosecution and Maintenance responsibilities; (c) cooperate, if necessary, with the other Party in gaining Patent term extensions; and (d) act in good faith to coordinate its efforts under this Agreement with the other Party to minimize or avoid interference with such Prosecution and Maintenance by the other Party.

6.3 Patent Extensions and Orange Book Listings. If elections with respect to obtaining patent term extensions or supplemental protection certificates or their equivalents in any country arising from the Exploitation of a Licensed Product, Clementia will have the sole and exclusive right in good faith to make any such elections with respect to a Blueprint Product-Specific Patent. With respect to Regulatory Exclusivity Periods, such as those periods listed in the FDA's Orange Book (including any available pediatric extensions) or periods under national implementations of Article 10.1(a)(iii) of Directive 2001/EC/83 or orphan exclusivity periods, and all equivalents in any country, Clementia will have the sole and exclusive right in good faith to seek and maintain all such Regulatory Exclusivity Periods available for the Licensed Products.

6.4 Marking. To the extent required by applicable Law, Clementia will, and will cause its Affiliates and all Sublicensees to, mark all Licensed Products made, used or sold, or their containers, with the number of each issued Licensed Patent that applies to such Licensed Product.

6.5 Third Party Infringement.

6.5.1 Notice. Each Party will promptly notify the other in writing of any (a) apparent, threatened or actual infringement by a Third Party of any Licensed Patent in the Territory, or (b) unauthorized use or misappropriation of any Licensed Know-How in the Territory by a Third Party of which it becomes aware, and, in each case, will provide the other Party with all evidence in such Party's possession or control supporting such infringement or unauthorized use or misappropriation (each, an "**Infringement**").

6.5.2 Enforcement of Patents in the Territory.

(a) Clementia will have the first right, but not the obligation, using qualified outside counsel of its choosing, provided that Clementia identifies such counsel for Blueprint in advance and Blueprint consents to such counsel (such consent not to be unreasonably withheld, conditioned or delayed), and at Clementia's sole expense, to institute any Action alleging Infringement of any Licensed Patent on account of a Third Party's manufacture, use, offer to sell or sale of any compound or product that competes with a Licensed Product for the treatment, [***] of FOP (each such Infringement, a "**Competitive Infringement**"). Prior to commencing any such Action, Clementia will consult with Blueprint and will consider Blueprint requests and recommendations regarding such proposed Action. Clementia will give Blueprint timely notice of any proposed settlement of any such Action and Clementia will not settle, stipulate to any facts, or make any admission with respect to such Competitive Infringement without Blueprint's prior written consent (such consent not to be unreasonably withheld, conditioned or delayed) if such settlement, stipulation, or admission would: (i) adversely affect the validity, enforceability, or scope, or admit non-Infringement, of any of the Licensed Patents; (ii) give rise to liability of Blueprint or its Affiliates; (iii) grant to a Third Party a license or covenant not to sue under, or with respect to, any Licensed Technology or Blueprint Future Technology; or (iv) otherwise impair Blueprint's or any of its Affiliates' rights in any Licensed Technology or Blueprint's or any of its Affiliates' rights under this Agreement.

(b) If Clementia (i) does not initiate any Action against such Competitive Infringement in a country in the Territory, including by commencement of a lawsuit against the accused Person if necessary or obtain settlement thereof (in accordance with this Agreement), within [***] after

discovering or receiving notice of such Competitive Infringement of such Licensed Patent or Joint Patent or (ii) if such Action is initiated within such period, ceases to pursue or withdraws from such Action, then in each case (clauses (i) and (ii)) Blueprint will be entitled (but will not be obligated), after taking into reasonable consideration Clementia's reason for not initiating such Action, including any identified risks to the Licensed Patents and the Licensed Products, to take all actions reasonably necessary to abate such violation in such country, including commencement of a lawsuit against such accused Third Party if necessary. If Clementia does not prosecute such an Action against such Third Party in such country, then any sales of Generic Products by such Third Party will not be counted to determine whether the market share of Generic Products in such country has been achieved for purposes of determining the amount of any royalty reduction under Section 5.6.3.

(c) Subject to Section 6.5.2(a), Blueprint will have the first right, but not the obligation, using counsel of its choosing at Blueprint's sole expense, to institute any Action alleging Infringement other than a Competitive Infringement ("**Non-Competitive Infringement**") of the Licensed Patents, (including Joint Patents and Continuing Applications) or Blueprint Future Technology in the Field and in the Territory. Blueprint will notify Clementia in writing prior to initiating such Action for Non-Competitive Infringement. If such Action for Non-Competitive Infringement requires the assertion of one or more Licensed Patents that are Blueprint Product-Specific Patents, Blueprint will obtain Clementia's prior written consent before instituting such Action (such consent not to be unreasonably withheld, conditioned or delayed). If such Action for Non-Competitive Infringement requires [***], the Parties shall discuss in good faith the advisability of such Action for Non-Competitive Infringement and Blueprint shall [***] in view of any identified risks to the Licensed Patents and the Licensed Products. For the avoidance of doubt, if such Action for Non-Competitive Infringement requires the assertion only of Patents Covering Blueprint Future Technology, Blueprint may initiate such Action without consulting with or accounting for Clementia.

6.5.3 Cooperation. In any Action alleging Infringement brought under Section 6.5.2, each Party will, and will cause its Affiliates to, reasonably cooperate with each other, in good faith, relative to the other Party's efforts to protect the Patents or Know-How at issue and will join such suit as a party, if requested by the other Party or if required by applicable Law to bring or maintain such Action, and at the cost of the other Party. Furthermore, the Party initiating any Action alleging Infringement pursuant to Sections 6.5.2 will consider in good faith all reasonable and timely comments from the other Party on any proposed arguments asserted or to be asserted in litigation related to the enforcement or defense of any such Patents or Know-How.

6.5.4 Allocation of Recoveries. If a Party brings any Action alleging Competitive Infringement under Section 6.5.2 (except with respect to Blueprint Future Technology) and recovers any damages or other sums in such action, such damages or other sums recovered will first be applied to all out-of-pocket costs and expenses incurred by the Parties in connection therewith (including attorneys' fees). If such recovery is insufficient to cover all such costs and expenses of both Parties, the controlling Party's costs will be paid in full first before any of the other Party's costs. If after such reimbursement any funds will remain from such damages or other sums recovered, such funds will be retained by the Party that controlled the action or proceeding under Section 6.5.2; provided, however, that (a) if Clementia is the Party that controlled such action or proceeding, [***] and (b) if Blueprint is the Party that controlled such action or proceeding, [***].

6.6 Claimed Infringement. Each Party will promptly notify the other Party if a Third Party brings any Action alleging patent infringement by Clementia or any of its Affiliates or Sublicensees or by Blueprint or its Affiliates, in each case with respect to the Exploitation of any Licensed Product under this Agreement (any such Action, an "**Infringement Claim**"). In the case of any Infringement Claim, Clementia will have the right, but not the obligation, to control the defense and response to any such

Infringement Claim in the Territory against Clementia, its Affiliates or Sublicensees. Upon the request of Clementia with respect to any Infringement Claim, Blueprint will reasonably cooperate with Clementia, at its sole cost and expense, in the reasonable defense of such Infringement Claim. Blueprint will have the right to consult with Clementia concerning any Infringement Claim and to participate in and be represented by independent counsel in any associated litigation. If the Infringement Claim is brought against both Parties (or their Affiliates), then each Party will have the right to defend against the Infringement Claim. The Party defending an Infringement Claim under this Section 6.6 will (a) consult with the other Party as to the strategy for the prosecution of such defense, (b) consider in good faith any comments from the other Party with respect thereto and (c) keep the other Party reasonably informed of any material steps taken and provide copies of all material documents filed, in connection with such defense. The Party controlling the defense against an Infringement Claim will have the right to settle such Infringement Claim on terms deemed reasonably appropriate by such Party, provided, that, unless any such settlement includes a full and unconditional release from all liability of the other Party and does not adversely affect the rights of the other Party, any such settlement will be subject to the other Party's prior written consent.

ARTICLE 7
CONFIDENTIALITY AND PUBLICITY

7.1 Confidential Information.

7.1.1 Confidentiality Obligation. During the Term and for a period of [***] after any termination or expiration of this Agreement, the Receiving Party agrees to, and will cause its Affiliates and its and their respective Representatives to, (a) keep in confidence and not to disclose to any Third Party or (b) use for any purpose other than performing its obligations or exercising its rights under this Agreement, any Confidential Information of the Disclosing Party. The Receiving Party will treat all Confidential Information provided by the Disclosing Party with the same degree of care as the Receiving Party uses for its own similar information, but in no event less than a reasonable degree of care. The Receiving Party will promptly notify the Disclosing Party of any misuse or unauthorized disclosure of the Receiving Party's Confidential Information, and the Receiving Party will be responsible for any breach of this Article 7 by any Third Party or any of its Representatives to whom the Disclosing Party's Confidential Information is disclosed by or on behalf of the Receiving Party, and agrees, at its sole expense, to take all reasonable measures (including to court proceedings) to restrain such Third Parties and its Representatives from any prohibited or unauthorized use or disclosure of the Disclosing Party's Confidential Information.

7.1.2 Permitted Disclosures. Notwithstanding Section 7.1.1, each Party may use or disclose Confidential Information of the other Party to the extent reasonably necessary in the following situations:

(a) to the Receiving Party's Affiliates and Representatives on a need-to-know basis to the extent reasonably necessary for purposes of performing its obligations or exercising its rights under this Agreement this Agreement; provided, however, that all such Persons are subject to obligations of confidentiality and non-use at least as stringent as those set forth in this Article 7 or otherwise customary for such type and scope of disclosure (which, for the avoidance of doubt, may include professional ethical obligations) and any such disclosure is limited to the maximum extent practicable for the particular context in which it is being disclosed;

(b) with respect to the terms of this Agreement only, to any bona fide actual or prospective (i) investors, underwriters, lenders or other financing sources or (ii) acquirers, collaborators, licensors, licensees or Sublicensees, or strategic or commercial partners (including in connection with any royalty factoring transaction) and their respective Representatives, who reasonably require such Confidential Information in connection with the evaluation of or due diligence for any actual or potential

investment, debt or other financing transaction, acquisition, license or sublicense, or partnership or collaboration; provided that, in each such case, such Persons are bound by obligations of confidentiality and non-use at least as stringent as those set forth in this Article 7 or otherwise customary for such type and scope of disclosure (which, for the avoidance of doubt, may include professional ethical obligations) and any such disclosure is limited to the maximum extent practicable for the particular context in which it is being disclosed;

(c) to the extent such use or disclosure is consistent with this Agreement and is reasonably necessary for Prosecution and Maintenance of the Licensed Patents, in each case, as contemplated by this Agreement; or (ii) regulatory filings and other filings with Governmental Authorities (including Regulatory Authorities), as necessary for the Exploitation of Licensed Product;

(d) to the extent required to comply with applicable Law (including the rules and regulations of the U.S. Securities and Exchange Commission or equivalent foreign regulatory agency) or judicial or administrative process (including any such disclosures as are required by a Regulatory Authority in connection with seeking Regulatory Approval for any Licensed Product in the Territory); provided that, for the avoidance of doubt, information regarding the achievement of any milestone event and/or the payment of royalties under this Agreement (including the nature, probability, amount, payment and timing of any such milestone event or royalty) shall be disclosable by a Party pursuant to this Section 7.1.2(d). If reasonably practicable, such Party shall provide written notice to the other Party together with a copy of such disclosure prior to such disclosure (which, in the case of Blueprint, such notice may be via e-mail to [***] and, in the case of Clementia, such notice may be via e-mail to [***] for purposes of this Section 7.1.2(d)), and in any event shall provide such notice as soon as is reasonably practicable after such disclosure; or

(e) any disclosure that is permitted pursuant to Section 7.2.

7.1.3 Confidential Treatment. Notwithstanding anything to the contrary set forth in this Agreement, if a Party is required or permitted to make a disclosure of the other Party's Confidential Information pursuant to Section 7.1.2, then it will, to the extent not prohibited by applicable Law or judicial or administrative process, except where impracticable, provide prompt notice to the non-disclosing Party of such disclosure (together with a copy of the proposed text of such disclosure), will consider in good faith any timely comments provided by the non-disclosing Party (provided that the disclosing Party may or may not accept such comments in its sole discretion) and will take (or causes to be taken) all reasonable and lawful actions to seek to avoid and minimize the extent of such disclosure.

7.2 Publicity.

7.2.1 Press Releases. Promptly following the Effective Date, the Parties will issue a mutually agreed upon joint press release in the form attached hereto as Exhibit E. However, the Parties agree that after (a) a disclosure pursuant to Section 7.2 or Section 7.1.2 or (b) the issuance of a press release (including any initial press release) or other public announcement pursuant to this Section 7.2.1 that has been reviewed and approved by the other Party, the Disclosing Party may make subsequent public disclosures reiterating such information without having to obtain the other Party's prior consent and approval so long as the information in such press release or other public announcement remains true, correct, and the most current information with respect to the subject matters set forth therein. Similarly, after a publication has been made available to the public, each Party may post such publication or a link to it on its corporate web site (or any website managed by such Party in connection with a Clinical Study for a Licensed Product, as appropriate) without the prior written consent of the other Party, so long as the information in such publication remains true, correct, and the most current information with respect to the subject matters set forth therein.

7.2.2 Further Publicity; Publications.

(a) Publicity. Except as set forth in Section 7.2.1, neither Party will issue any press release or public announcement relating to this Agreement without the prior written approval of the other Party (such approval not to be unreasonably withheld, conditioned or delayed), except that a Party may (i) once a press release or other public statement is approved in writing by both Parties, make subsequent public disclosure of the information contained in such press release or other written statement without the further approval of the other Party (so long as such information remains true and correct), and (ii) issue a press release or public announcement as required by applicable Law, including by the rules or regulations of the U.S. Securities and Exchange Commission or equivalent foreign regulatory agency or of any stock exchange or listing entity, provided that the Party issuing such press release gives reasonable prior notice to the other Party of and the opportunity to comment on the press release or public announcement, and otherwise complies with this Article 7.

(b) Publications.

(i) By Clementia. Clementia may publish or present the results of Research and Development of a Licensed Product, subject to the prior review and approval by Blueprint for protection of Blueprint's Confidential Information as provided in this Section 7.2.2(b). Clementia will provide to Blueprint the opportunity to review any proposed abstracts, manuscripts or summaries of presentations that cover the results of Research and Development of a Licensed Product (each, a "**Publication**"). Blueprint will designate a person or persons who will be responsible for reviewing such Publications. Such designated person will respond in writing promptly and in no event later than [***] after receipt of the proposed material (or [***] in the case of an abstract) with either approval of the proposed material, or a request to remove Blueprint's Confidential Information from such Publication, and upon such request Clementia shall so remove Blueprint's Confidential Information; provided that, Clementia shall not be required to remove Blueprint's Confidential Information to the extent disclosure is permitted pursuant to this Article 7. In the event of concern, Clementia agrees not to submit or present such proposed Publication until Blueprint is given a reasonable period of time (not to exceed [***]) to seek patent protection for any material in such proposed Publication or presentation that it believes is patentable or to resolve any other issues. Clementia will comply with standard academic practice regarding authorship of scientific publications and recognition of contribution of other parties in any publication.

(ii) By Blueprint. Blueprint may publish or present, without Clementia's prior approval, the academic, scientific or medical abstracts, articles, papers, presentations or other type of public disclosures described on Schedule 7.2.2(b)(ii); provided that, Blueprint shall provide a copy of any such disclosure to Clementia; and provided further that Clementia provides any comments with respect to such disclosure in writing promptly and in no event later than [***] after receipt of the proposed material (or [***] in the case of an abstract), then Blueprint will consider in good faith any such timely comments provided by Clementia.

(iii) Jointly by the Parties. The Parties will jointly present the presentations described on Schedule 7.2.2(b)(iii). The Parties will cooperate in preparing the content and materials for, and in presenting, such presentation.

7.2.3 Use of Names. Following the issuance of the press release attached hereto as Exhibit E, each Party will have the right to use the other Party's name and logo in presentations, its website, collateral materials, investor and analyst presentations and corporate overviews to describe the collaboration relationship, as well as in taglines of press releases issued pursuant to this Section 7.2.3; provided that neither Party will use the other Party's corporate name in such manner that the distinctiveness, reputation, and validity of any Trademarks and corporate or trade names of such other Party will not be

impaired, and consistent with best practices used by such other Party for its other collaborators. Except as permitted under this Section 7.2.3 or with the prior express written permission of the other Party, neither Party will use the name, trademark, trade name, or logo of the other Party or its Affiliates or their respective employees in any publicity, promotion, news release, or disclosure relating to this Agreement or its subject matter except as may be required by applicable Law. Each Party will use the other Party's corporate name in all publicity relating to this Agreement, including the initial press release and all subsequent press releases.

7.3 Tax Treatment. Nothing in Section 7.1 will limit either Party in any way from disclosing to any Third Party such Party's U.S. or foreign income tax treatment and the U.S. or foreign income tax structure of the transactions relating to such Party that are based on or derived from this Agreement, or materials of any kind (including opinions or other tax analyses) relating to such tax treatment or tax structure to the extent that nondisclosure of such matters is reasonably necessary in order to comply with applicable securities laws.

7.4 Attorney-Client Privilege. Neither Party is waiving, nor will be deemed to have waived or diminished, any of its attorney work product protections, attorney-client privileges or similar protections and privileges or the like as a result of disclosing information pursuant to this Agreement, or any of its Confidential Information (including Confidential Information related to pending or threatened litigation) to the Receiving Party, regardless of whether the Disclosing Party has asserted, such privileges and protections. The Parties: (a) share a common legal and commercial interest in such disclosure that is subject to such privileges and protections; (b) are or may become joint defendants in proceedings to which the information covered by such protections and privileges relates; (c) intend that such privileges and protections remain intact should either Party become subject to any actual or threatened proceeding to which the Disclosing Party's Confidential Information covered by such protections and privileges relates; and (d) intend that after the Effective Date both the Receiving Party and the Disclosing Party will have the right to assert such protections and privileges. Notwithstanding the foregoing, nothing in this Section 7.4 will apply with respect to a Dispute between the Parties (including their respective Affiliates).

ARTICLE 8
REPRESENTATIONS AND WARRANTIES; CERTAIN COVENANTS

8.1 Mutual Representations and Warranties. Each Party represents and warrants to the other Party that, as of the Effective Date:

8.1.1 Organization. It is a corporation duly organized, validly existing, and in good standing under the laws of the jurisdiction of its organization, and has all requisite power and authority, corporate or otherwise, to execute, deliver, and perform this Agreement.

8.1.2 Authority. It has full right, power and authority to enter into this Agreement and to perform its respective obligations under this Agreement, it has the right to grant to the other the licenses and sublicenses granted pursuant to this Agreement, and this Agreement and the performance by such Party of this Agreement do not violate such Party's charter documents, bylaws or other organizational documents.

8.1.3 Consents. Except for any Marketing Authorizations, Regulatory Filings, manufacturing approvals or similar approvals necessary for the Research, Development, Manufacture or Commercialization of Licensed Products, all necessary consents, approvals and authorizations of all Governmental Authorities and other Persons required to be obtained by it in connection with the execution, delivery and performance of this Agreement have been obtained.

8.1.4 No Conflict. It is not under any obligation, contractual or otherwise, to any Person that would adversely affect the diligent and complete fulfillment of obligations under this Agreement and the execution and delivery of this Agreement by such Party, and the performance of such Party's obligations under this Agreement (as contemplated as of the Effective Date) and the licenses and sublicenses to be granted by such Party pursuant to this Agreement (a) do not conflict with or violate any requirement of Laws applicable to such Party, (b) do not conflict with or violate any order, writ, judgment, injunction, decree, determination, or award of any court or governmental agency presently in effect applicable to such Party, and (c) do not conflict with, violate, breach or constitute a default under any contractual obligations of such Party or any of its Affiliates.

8.1.5 Enforceability. This Agreement is a legal and valid obligation binding upon it and is enforceable against it in accordance with its terms, subject to the general principles of equity and subject to bankruptcy, insolvency, moratorium, judicial principles affecting the availability of specific performance and other similar Laws affecting the enforcement of creditors' rights generally.

8.2 Additional Representations and Warranties of Blueprint. Blueprint represents and warrants to Clementia that, as of the Effective Date, except as set forth on Schedule 8.2:

8.2.1 Licensed Technology. Blueprint solely Controls the Licensed Technology existing as of the Effective Date, free and clear of any claims, liens, charges or encumbrances.

8.2.2 Licensed Patents. None of the issued Licensed Patents existing as of the Effective Date has been adjudged, in a final and non-appealable decision, invalid, unenforceable or unpatentable by any Governmental Authority of competent jurisdiction, and, to the knowledge of Blueprint, all such issued Licensed Patents existing as of the Effective Date are valid and enforceable.

8.2.3 Third Party Challenges. There are no claims, judgments, or settlements against, or amounts with respect thereto, made against Blueprint or any of its Affiliates relating to the Licensed Technology. No claim or litigation has been brought or, to Blueprint's knowledge, threatened by any Person (a) alleging that the Licensed Patents are invalid or unenforceable, (b) asserting the misuse, or non-infringement of any of the Licensed Patents, (c) regarding inventorship of or challenging Blueprint's Control of the Licensed Patents or (d) alleging misappropriation of the Know-How used in the Development or Manufacture of Licensed Products by or on behalf of Blueprint prior to the Effective Date.

8.2.4 Non-Infringement by Third Parties. To Blueprint's knowledge, no Third Party has infringed, misappropriated or otherwise violated any Licensed Technology.

8.2.5 Blueprint Product-Specific Patents. Exhibit C-1 is, to Blueprint's knowledge, a complete and accurate list of all Blueprint Product-Specific Patents as of the Effective Date, including, where relevant and reasonably available, all application numbers and filing dates, patent numbers, issue dates and jurisdictions.

8.2.6 Scientific and Technical Information. Blueprint has disclosed to Clementia (i) [***], (ii) [***] and (iii) [***]. [***].

8.2.7 Regulatory. All INDs, other regulatory approval applications, and foreign equivalents relating to the Blueprint Compounds are in the name of Blueprint or its Affiliates.

8.2.8 Governmental Authorities; Compliance with Laws. Neither Blueprint or its Affiliates has received written notice from any Governmental Authority terminating or refusing to renew any material governmental licenses, permits, registrations, concessions, franchises and authorizations

relating to the Blueprint Compound or Licensed Products; Blueprint and its Affiliates have complied in all material respects with all applicable Laws in connection with the preparation and submission to all Governmental Authorities and Regulatory Authorities of any IND, or foreign equivalents thereto relating to the Blueprint Compounds; and Blueprint and its Affiliates have not received any notice, and to Blueprint's knowledge, there are no facts, which have, or reasonably should have, led Blueprint or its Affiliates to believe that any such IND, or foreign equivalent is not, or will not be, in good standing with the relevant Governmental Authority or Regulatory Authority or is or will be withdrawn.

8.2.9 Third Party Agreements. Blueprint has disclosed to Clementia [***]. In addition, Blueprint has disclosed to Clementia [***]. All agreements described under this Section 8.2.9 are set forth in Exhibit F.

8.2.10 Non-Infringement of Third Party Rights. To Blueprint's knowledge, neither the Development, Manufacture and Commercialization of Licensed Products in the Field as conducted on or prior to the Effective Date, nor the Development, Manufacture and Commercialization of Licensed Products (as currently constituted) in the Field as described in the Development Plan as of the Effective Date does or would infringe, interfere with or result in the misappropriation of any intellectual property rights of any Third Party existing as of the Effective Date.

8.2.11 Alexion Termination. Alexion has no right, title or interest in Blueprint Compounds, Licensed Products and Blueprint Technology. Blueprint does not and will not have any obligations to Alexion with respect to Blueprint Compounds, Licensed Products and Blueprint Technology that conflicts or will conflict with, interferes or will interfere with or diminishes or will diminish the rights granted to Clementia under this Agreement.

8.3 No Debarment. Each Party represents and warrants that, to its knowledge, neither it nor any of its or its Affiliates' employees or agents performing under this Agreement, or in the case of Blueprint, no employee or agent engaged by Blueprint or its Affiliates in the development of any of the Blueprint Compound or Licensed Product prior to the Effective Date, has ever been, or is currently: (a) debarred under 21 U.S.C. § 335a or its equivalents in the Territory; (b) excluded, debarred, suspended, or otherwise ineligible to participate in federal health care programs or in federal procurement or non-procurement programs; (c) listed in the FDA's Clinical Investigators – Disqualification Proceedings Database, including for restrictions; or (d) convicted of a criminal offense that falls within the scope of 42 U.S.C. § 1320a-7(a) or its equivalents in the Territory, but has not yet been excluded, debarred, suspended, or otherwise declared ineligible. Each Party further covenants that if, during the Term of this Agreement, it becomes aware that it or any of its or its Affiliates' employees or agents performing under this Agreement is the subject of any investigation or proceeding that could lead to that Party becoming a debarred entity or individual, an excluded entity or individual or a convicted entity or individual, such Party will immediately notify the other Party. This provision will survive termination or expiration of this Agreement.

8.4 Additional Covenants.

8.4.1 Clementia represents and warrants to Blueprint that, as of the Effective Date:

(a) Neither Clementia nor any of its Affiliates (or any of their respective Sublicensees, employees and contractors) will, in connection with the exercise of Clementia's rights or performance of its obligations under this Agreement, directly or indirectly through Third Parties, pay, promise or offer to pay, or authorize the payment of, any money or give any promise or offer to give, or authorize the giving of anything of value to a public official or entity or other Person for purpose of obtaining or retaining business for or with, or directing business to, any Person, including Clementia and its Affiliates, nor will Clementia or any of its Affiliates directly or indirectly promise, offer or provide any

corrupt payment, gratuity, emolument, bribe, kickback, illicit gift or hospitality or other illegal or unethical benefit to a public official or entity or any other Person in connection with the exercise of Clementia's rights or performance of Clementia's obligations under this Agreement; and

(b) Neither Clementia nor any of its Affiliates (or any of their respective Sublicensees, employees and contractors), in connection with the exercise of Clementia's rights or performance of Clementia's obligations under this Agreement, will knowingly cause Blueprint to be in violation of Anti-Corruption Laws or Export Control Laws.

8.4.2 Additional Covenants of Blueprint.

(a) Blueprint will not, and shall cause its Affiliates not to (i) license, sell, assign or otherwise transfer to any Person (other than Clementia or its Affiliates or Sublicensees pursuant to the terms of this Agreement) any Licensed Technology (or agree to do any of the foregoing) or (ii) incur or permit to exist, with respect to any Licensed Technology, any lien, encumbrance, charge, security interest, mortgage, liability, assignment, grant of license, in each case (clauses (i) and (ii)) in a manner that is or would be inconsistent with the licenses and other rights granted to Clementia or its Affiliates under this Agreement.

(b) Blueprint will not, and shall cause its Affiliates not to, take any action that diminishes the rights under the Licensed Technology granted to Clementia or Clementia's Affiliates under this Agreement.

8.4.3 Blueprint will, and shall cause its Affiliates to, (a) not enter into any agreement or arrangement that adversely affects (i) the rights granted to Clementia, Clementia's Affiliates or Sublicensees or (ii) Blueprint's ability to fully perform its obligations hereunder; (b) not amend or otherwise modify any Third Party Agreements in any manner that (i) materially and adversely affects the rights granted to Clementia or Clementia's Affiliates or Sublicensees or (ii) Clementia's ability to fully perform its obligations hereunder; (c) promptly furnish Clementia with true and complete copies of all amendments, modifications, consents and waivers to Third Party Agreements to the extent related to either Party's performance of its obligations or exercise of its rights hereunder (subject to any confidentiality obligations to such Third Party); (d) remain, and cause its Affiliates to remain, in compliance in all material respects with Third Party Agreements and (e) furnish Clementia with copies of all notices received by Blueprint or its Affiliates relating to any alleged breach or default by Blueprint or its Affiliates under any Third Party Agreements specifically related to a Licensed Product within [***] after receipt thereof.

8.5 No Other Representations or Warranties.

8.5.1 EXCEPT AS EXPRESSLY STATED IN THIS ARTICLE 8, NO REPRESENTATIONS OR WARRANTIES WHATSOEVER, WHETHER EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, NON-INFRINGEMENT, OR NON-MISAPPROPRIATION OF THIRD PARTY INTELLECTUAL PROPERTY RIGHTS, IS MADE OR GIVEN BY OR ON BEHALF OF A PARTY. EXCEPT AS EXPRESSLY STATED IN THIS AGREEMENT, ALL REPRESENTATIONS AND WARRANTIES, WHETHER ARISING BY OPERATION OF LAW OR OTHERWISE, ARE HEREBY EXPRESSLY EXCLUDED.

8.5.2 THE MATERIALS AND INFORMATION PROVIDED BY BLUEPRINT (OR ITS AFFILIATES) TO CLEMENTIA ARE PROVIDED TO CLEMENTIA "AS IS" WITHOUT ANY REPRESENTATIONS OR WARRANTIES WHATSOEVER, WHETHER EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE,

NON-INFRINGEMENT, OR NON-MISAPPROPRIATION OF THIRD PARTY INTELLECTUAL PROPERTY RIGHTS. REGARDING THE MATERIALS AND THE INFORMATION PROVIDED BY BLUEPRINT (OR ITS AFFILIATES) TO CLEMENTIA, BLUEPRINT (AND ITS AFFILIATES) WILL NOT BE LIABLE FOR ANY USE OF SUCH MATERIALS AND INFORMATION BY CLEMENTIA OR ANY OTHER RECIPIENTS, OR FOR ANY LIABILITIES, LOSSES, COSTS, DAMAGES, FEES, EXPENSES OR OTHER AMOUNTS THAT MAY BE SUFFERED BY CLEMENTIA OR ANY OTHER RECIPIENTS FROM OR IN CONNECTION WITH THIS AGREEMENT OR FROM THE USE, HANDLING OR STORAGE OF SUCH MATERIALS, OR THE USE OF, OR RELIANCE PLACED ON SUCH INFORMATION, OR ANY OTHER ACT OR OMISSION, OF CLEMENTIA OR ANY OTHER RECIPIENTS REGARDING SUCH MATERIALS OR INFORMATION.

ARTICLE 9
INDEMNIFICATION; DAMAGES

9.1 Indemnification by Blueprint. Blueprint will defend, indemnify and hold harmless Clementia, its Affiliates and their respective directors, officers, employees and agents (collectively, the "**Clementia Indemnified Parties**"), from, against and in respect of any and all Losses incurred or suffered by any Clementia Indemnified Party to the extent resulting from: (a) any breach of any obligation, representation, warranty or covenant made by Blueprint in this Agreement; (b) the negligence or intentional misconduct of, or violation of Law by, Blueprint or any of its Affiliates, licensees or sublicensees, or any of their respective directors, officers, employees and agents, in performing Blueprint's obligations or exercising Blueprint's rights under this Agreement or (c) the Exploitation of any Reversion Product under a Reversion License by or on behalf of Blueprint, its Affiliates or sublicensees, including product liability claims relating to a Reversion Product or any actions (or omissions) in the performance of regulatory activities; in each case (clauses (a) through (c)), except to the extent Losses arise from, are based on, or result from any activity or occurrence for which Clementia is obligated to indemnify the Blueprint Indemnified Parties under Section 9.2.

9.2 Indemnification by Clementia. Clementia will defend, indemnify and hold harmless Blueprint, its Affiliates and their respective directors, officers, employees and agents (collectively, the "**Blueprint Indemnified Parties**"), from, against and in respect of any and all Losses incurred or suffered by any Blueprint Indemnified Party to the extent resulting from: (a) any breach of any obligation, representation, warranty or covenant made by Clementia in this Agreement, (b) the negligence or intentional misconduct of, or violation of Law by, Clementia, any of its Affiliates or Sublicensees, or any of their respective directors, officers, employees and agents, in performing Clementia's obligations or exercising Clementia's rights under this Agreement, or (c) the Exploitation of any Blueprint Compound or Licensed Product by or on behalf of Clementia, its Affiliates or Sublicensees, including product liability claims relating to a Licensed Product or any actions (or omissions) in the performance of regulatory activities, in each case (clauses (a) through (c)), except to the extent such Losses arise from, are based on, or result from any activity or occurrence for which Blueprint is obligated to indemnify the Clementia Indemnified Parties under Section 9.1.

9.3 Claims for Indemnification.

9.3.1 Notice. An Indemnified Party entitled to indemnification under Sections 9.1 or 9.2 will give prompt written notification to the Indemnifying Party from whom indemnification is sought of the commencement of any Action by a Third Party for which indemnification may be sought (a "**Third Party Claim**") or, if earlier, upon the assertion of such Third Party Claim by a Third Party; provided, however, that failure by an Indemnified Party to give notice of a Third Party Claim as provided in this Section 9.3.1 will not relieve the Indemnifying Party of its indemnification obligation under this

Agreement, except and only to the extent that such Indemnifying Party is actually prejudiced as a result of such failure to give notice.

9.3.2 Defense. Within [***] after delivery of a notice of any Third Party Claim in accordance with Section 9.3.1, the Indemnifying Party may, upon written notice thereof to the Indemnified Party, assume control of the defense of such Third Party Claim with counsel reasonably satisfactory to the Indemnified Party. If the Indemnifying Party does not assume control of such defense, the Indemnified Party may control such defense. The Party not controlling such defense may participate therein at its sole expense.

9.3.3 Cooperation. The Party controlling the defense of any Third Party Claim will keep the other Party advised of the status of such Third Party Claim and the defense thereof and will reasonably consider recommendations made by the other Party with respect thereto. The other Party will reasonably cooperate with the Party controlling such defense and its Affiliates and agents in defense of the Third Party Claim, with all out-of-pocket costs of such cooperation to be borne by the Party controlling such defense.

9.3.4 Settlement. The Indemnified Party will not agree to any settlement of such Third Party Claim or admit liability with respect to such Third Party Claim without the prior written consent of the Indemnifying Party, which consent will not be unreasonably withheld, conditioned or delayed. The Indemnifying Party will not, without the prior written consent of the Indemnified Party, which will not be unreasonably withheld, conditioned or delayed, agree to any settlement of such Third Party Claim or consent to any judgment in respect thereof that does not include a complete and unconditional release of the Indemnified Party from all liability with respect thereto or that imposes any liability or obligation on the Indemnified Party.

9.4 Insurance. Clementia, at its sole expense, will maintain liability insurance with respect to its activities under this Agreement in an amount consistent with industry standards. Clementia will provide a certificate of insurance (or evidence of self-insurance) evidencing such coverage to the other Party upon request. Without limiting the foregoing, during the Term and for [***] thereafter, each Party will maintain on an ongoing basis comprehensive general liability insurance in the minimum amount of [***]. All of such insurance coverage may be satisfied through one (1) or more policies, including an umbrella policy. Not later than [***] following receipt of written request from a Party, the other Party will provide to the requesting Party a certificate of insurance evidencing such coverage in accordance with this Agreement. Each Party will provide certificates or letters evidencing such insurance coverage without interruption as reasonably requested during the period of time for which such coverage must be maintained. Either Party's failure to maintain adequate insurance will not relieve that Party of its obligations set forth in this Agreement.

ARTICLE 10
LIMITATION OF LIABILITY

10.1 No Consequential or Punitive Damages. EXCEPT AS SET FORTH IN SECTION 10.2, NEITHER PARTY NOR ANY OF ITS AFFILIATES WILL BE LIABLE FOR INDIRECT, INCIDENTAL, CONSEQUENTIAL, SPECIAL, EXEMPLARY, PUNITIVE OR MULTIPLE DAMAGES OR FOR ANY LOST PROFITS ARISING OUT OF THIS AGREEMENT, IN EACH CASE HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, WHETHER IN CONTRACT, TORT, NEGLIGENCE, BREACH OF STATUTORY DUTY OR OTHERWISE, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES.

10.2 Exclusion from Liability Limitation. THE LIMITATIONS AND DISCLAIMER SET FORTH IN SECTION 10.1 WILL NOT APPLY TO A CLAIM (A) FOR GROSS NEGLIGENCE OR WILLFUL MISCONDUCT; (B) FOR A BREACH OF [***]; (C) FOR A BREACH OF [***]; (D) LIABILITY FOR MISAPPROPRIATION OR INFRINGEMENT OF INTELLECTUAL PROPERTY OWNED OR CONTROLLED BY A PARTY, OR (E) FOR INDEMNIFIABLE LOSSES PURSUANT TO SECTION 9.1, OR SECTION 9.2.

ARTICLE 11
TERM AND TERMINATION

11.1 Term. This Agreement will be effective as of the Effective Date and, unless earlier terminated in accordance with this Article 11, will expire on a country-by-country basis and Licensed Product-by-Licensed Product basis at the end of the applicable Royalty Term (such period, the "**Term**"). Following the end of the Term for any such Licensed Product and in such country by expiration (but not termination), the license granted to Clementia under Section 2.1.1, will become exclusive, perpetual, irrevocable, fully paid-up and royalty-free, and the licenses granted to Clementia under Sections 2.1.2 and 2.1.3, will become non-exclusive, perpetual, irrevocable, fully paid-up and royalty-free.

11.2 Termination by Clementia for Convenience. After the second (2nd) anniversary of the Effective Date, Clementia may terminate this Agreement at any time upon at least twelve (12) months' prior written notice to Blueprint. For the avoidance of doubt, Clementia may deliver such notice at any time after the first (1st) anniversary of the Effective Date.

11.3 Termination for Material Breach. Upon (a) any material breach of this Agreement by Blueprint or (b) any material breach of this Agreement by Clementia (the Party so allegedly breaching being the "**Breaching Party**"), the other Party (the "**Non-Breaching Party**") will have the right, but not the obligation, to terminate this Agreement by providing [***] written notice to the Breaching Party in the case of a material breach of a payment obligation, and [***] written notice to the Breaching Party in the case of any other material breach. If the Breaching Party in good faith disputes that it has materially breached this Agreement, the dispute will be resolved in accordance with Article 12, and this Agreement may not be terminated during the pendency of such dispute resolution procedure unless and until such dispute resolution process has been completed. The termination will become effective at the end of the notice period unless the Breaching Party cures such breach during such notice period; provided, however, that the Non-Breaching Party may, by notice to the Breaching Party, designate a later date for such termination in order to facilitate an orderly transition of activities relating to Licensed Products. If, as a result of the application of such dispute resolution procedures, the Breaching Party is determined to be in material breach of this Agreement, then the Non-Breaching Party may terminate this Agreement immediately upon written notice to the Breaching Party as provided in this Section 11.3.

11.4 Termination by Blueprint for Validity Challenge. If during the Term, Clementia or any of its Affiliates or Sublicensees challenges (other than in response to any formal legal proceeding initiated against Clementia, its Affiliates or Sublicensees by Blueprint or its Affiliates, licensees or sublicensees) the validity or enforceability or actively assists any Person in challenging the validity or enforceability of any Licensed Patent before any court, administrative agency, or regulatory body including any patent opposition, re-examination or invalidation proceeding (a "**Patent Challenge**"), then, to the extent permitted by Law, Blueprint will have the right, in its sole discretion, to terminate this Agreement upon [***] prior written notice to Clementia; provided that Blueprint will not have the right to terminate this Agreement if Clementia withdraws or causes to be withdrawn such Patent Challenge within [***] after Clementia's receipt of notice from Blueprint under this Section 11.4. For the avoidance of doubt, a Patent Challenge does not include Clementia or its Affiliates or Sublicensees (a) responding to compulsory discovery,

subpoenas or other requests for information in a judicial or arbitration proceeding or (b) complying with any applicable Law or a court order.

11.5 Termination for Insolvency. If, at any time during the Term (a) a case is commenced by or against either Party under the Bankruptcy Code and, in the event of an involuntary case under the Bankruptcy Code, such case is not dismissed within [***] after the commencement thereof, (b) either Party files for or is subject to the institution of bankruptcy, liquidation or receivership proceedings (other than a case under the Bankruptcy Code), (c) either Party assigns all or a substantial portion of its assets for the benefit of creditors, (d) a receiver or custodian is appointed for either Party's business, or (e) a substantial portion of either Party's business is subject to attachment or similar process; then, in any such case ((a), (b), (c), (d) or (e)), the other Party may terminate this Agreement upon written notice to the extent permitted under applicable Law.

11.6 Effects of Termination.

11.6.1 Effects of Termination Generally. Upon termination of this Agreement in its entirety pursuant to Section 11.2 through 11.5, the Parties' rights and obligations under this Agreement will terminate, and neither Party will have any further rights or obligations under this Agreement from and after the effective date of termination, except as set forth in this Article 11.

11.6.2 Accrued Obligations. Expiration or termination of this Agreement for any reason will not release either Party from any obligation or liability which, on the effective date of such expiration or termination, has already accrued to the other Party or which is attributable to a period prior to such expiration or termination.

11.6.3 Termination of Rights and Licenses. Any rights and licenses with respect to the Licensed Products granted to Clementia under Section 2.1 will immediately terminate, and all such rights will revert back to Blueprint.

11.6.4 Reversion. Upon termination of this Agreement in its entirety by Clementia under [***] or by Blueprint under [***], the following additional provisions will apply:

(a) Reversion Licenses.

(i) Subject to the terms and conditions of this Agreement (including Section 11.6.4(n)(ii)), effective upon the date of termination, Clementia hereby grants (without any further action required on the part of Blueprint) to Blueprint and its Affiliates, a worldwide, irrevocable, perpetual, sublicensable through multiple tiers, exclusive, license under any [***] (collectively, the "**Reversion Products**", and, such license, the "**Exclusive Reversion License**").

(ii) Subject to the terms and conditions of this Agreement (including Section 11.6.4(n)(ii)), effective upon the date of termination, Clementia hereby grants (without any further action required on the part of Blueprint) to Blueprint and its Affiliates, a worldwide, irrevocable, perpetual, sublicensable [***] (such license, the "**Non-Exclusive Reversion License**" and together with the Exclusive Reversion License, the "**Reversion Licenses**").

(b) Regulatory Approvals and Regulatory Filings. Clementia as promptly as practicable, to the extent permitted by applicable Law, will (i) assign to Blueprint or Blueprint's designee possession and ownership of all Regulatory Approvals, Regulatory Filings, and Pricing and Reimbursement Approvals relating exclusively to the Exploitation of the Reversion Products in the Territory (to the extent any of the foregoing is owned by Clementia or held in Clementia's name) and (ii) transfer and assign to

Blueprint or Blueprint's designee copies of all material correspondence and conversation logs with Regulatory Authorities in Clementia's possession or Control related exclusively to the Reversion Products in the Territory and all data, reports, records, and materials, and other sales and marketing related information in Clementia's possession or Control to the extent that such data, reports, records, materials, or other information relate exclusively to the Exploitation of the Reversion Products in the Territory, including all Regulatory Data, and nonclinical and clinical data relating to the Reversion Products and customer lists and customer contact information and all Adverse Event data and Safety Data related to the Reversion Products, in each case, in the Territory and in Clementia's possession or Control. In addition, at Blueprint's request, Clementia will appoint Blueprint or its designee as Clementia's agent (or cause its Representative to appoint Blueprint or its designee as its agent) for all Reversion Product-related matters in the Territory involving Regulatory Authorities until all Regulatory Approvals, Regulatory Filings, and Pricing and Reimbursement Approval in the Territory have been assigned to Blueprint or its designee, with it being understood and agreed that Blueprint shall promptly take any and all actions as may be required by the relevant Regulatory Authority to permit or finalize the aforementioned assignments to Blueprint or its designee.

(c) Clementia Trademarks and Copyrights. Clementia will promptly transfer and assign to Blueprint, at no cost, all of Clementia and its Affiliates' rights, title, and interests in and to any Trademarks and copyrights (and any registrations therefor) Controlled by Clementia and exclusively used in connection with the Reversion Products (but not any Clementia house marks or any Trademark containing the word "Clementia").

(d) Reversion Patent Prosecution and Maintenance.

(i) Clementia's right under Section 6.2.3 to Prosecute and Maintain the Licensed Patents (excluding Joint Patents) shall revert to Blueprint ("**Reverted Licensed Patents**"). For the avoidance of doubt, Blueprint may Prosecute and Maintain such Reverted Licensed Patents without consulting with or accounting for Clementia.

(ii) Prosecution and Maintenance of Patents Covering Product-Specific Reversion Technology ("**Reversion Patents**") shall revert to Blueprint, including Joint Product-Specific Patents. Blueprint will keep Clementia informed of all steps with regard to and the status of such Prosecution and Maintenance of such Reversion Patents, including by providing Clementia with (x) copies of all correspondence and material communications Blueprint or its designee sends to or receives from any patent office or agency in the Territory relating to the Reversion Patents, (y) a draft copy of all applications sufficiently in advance (and no less than [***] in advance, to the extent reasonably practicable) of filing to permit reasonable review and comment by Clementia and (z) a copy of applications as filed, together with notice of its filing date and serial number.

(iii) For the avoidance of doubt, Blueprint's Prosecution and Maintenance of the Reverted Licensed Patents and Reversion Patents under this Section 11.6.4(d) shall be at Blueprint's cost and expense.

(e) Patent Information. Upon request by Blueprint, Clementia will provide any and all (i) documents, files and other materials that Blueprint provided to Clementia under Section 3.1.7 in their current form, including as augmented or supplemented pursuant to Clementia's Prosecution and Maintenance activities under Section 6.2.3 of the Reverted Licensed Patents, (ii) material correspondence with the relevant patent office(s) pertaining to Clementia's Prosecution and Maintenance under Section 6.2.3 of the Reverted Licensed Patents and Reversion Patents to the extent not previously provided to Blueprint during the course of the Agreement, (iii) a Patent docket report detailing the status of all Reverted Licensed Patents and Reversion Patents with upcoming deadlines for the [***] period following the

effective date of termination, and (iv) in a manner to maintain privilege in accordance with Section 7.4, the following: (1) [***], (2) [***] and (3) [***]. For the avoidance of doubt, Blueprint shall be responsible for reasonable costs and expenses related to actions with respect to Reverted Licensed Patents and Reversion Patents under this Section 11.6.4(e).

(f) Appointment as Distributor. If the effective date of termination is after the First Commercial Sale of a Reversion Product, then at Blueprint's request, to the extent permitted by applicable Laws, Clementia or its Affiliates or Sublicensees will use its Commercially Reasonable Efforts to appoint Blueprint or its designee as its exclusive distributor of such Reversion Product in the Territory and grant Blueprint or its designee the right to appoint subdistributors, until such time as all Regulatory Approvals in the Territory have been transferred to Blueprint or its designee.

(g) Transition Assistance. Clementia will, and will cause its Affiliates and Sublicensees, to provide reasonable assistance of up to [***] FTE hours at no cost to Blueprint (other than external costs and expenses incurred by Clementia in connection therewith, for which Clementia will invoice Blueprint). Thereafter, Clementia will invoice Blueprint for FTEs at the FTE Rate for any FTE hours and external costs and expenses incurred by Clementia in connection with providing such assistance, for the purpose of enabling Blueprint or its designee to commence or continue Researching, Developing, Manufacturing or Commercializing Licensed Products in the Territory pursuant to this Section 11.6.4, for a period of no longer than [***] after the effective date of such termination (the "**Reversion Transition Period**"). To the extent Clementia is then performing or having performed such activities, including assigning, transferring or amending as appropriate, upon request of Blueprint, any agreements or arrangements with Third Parties to Research, Develop, Manufacture and Commercialize the Licensed Products in the Territory (including distributors and CMOs) shall be assigned to Blueprint (or its designee) or terminated. At Blueprint's request, Clementia shall assign to Blueprint (or its designee) any Sublicenses that Clementia entered into with Third Parties. To the extent that any such contract between Clementia and a Third Party is not assignable to Blueprint or its designee, then Clementia will reasonably cooperate with Blueprint to arrange to continue to and provide such services from such entity.

(h) Ongoing Clinical Studies. If at the time of such termination, any Clinical Studies for the Licensed Products are being conducted by or on behalf of Clementia, then, at Blueprint's election, subject to patient safety and well-being on a Clinical Study-by-Clinical Study basis: (i) Clementia will, and will cause its Affiliates and Sublicensees to, [***], and (ii) Clementia will, and will cause its Affiliates and Sublicensees to, [***]. Clementia will accommodate Blueprint's reasonable requests to participate in communications with FDA regarding any such Clinical Studies for the Licensed Products, including attending meetings and reviewing minutes of any meetings, material telephone conferences or material discussions with FDA, in each case, solely with respect to applicable Licensed Product and to the extent permitted by FDA.

(i) Inventory. At Blueprint's election, Clementia will (i) transfer to Blueprint or its designee all inventory of the Blueprint Compounds and Licensed Products (including all final Blueprint Compounds, Licensed Products and raw materials and work-in-progress as supplied by Blueprint) and all works in progress of the foregoing then in possession or control of Clementia, its Affiliates or Sublicensees; provided that Blueprint will pay Clementia a price equal to the actual price paid by Clementia for Licensed Products or (ii) (A) have the right to continue to Commercialize all inventory of the Licensed Products then in possession or control of Clementia during the Reversion Transition Period and make the corresponding payments, including any milestone payments or royalties to Blueprint under this Agreement as though this Agreement had not been terminated and (B) after the Reversion Transition Period, transfer to Blueprint or its designee any remaining inventory of the Licensed Products to Blueprint or its designee at a price equal to Clementia's costs for such Licensed Products.

(j) Supply of Reversion Products and Palovarotene. At Blueprint's request, Clementia will supply to Blueprint (or have supplied) such quantities of the Reversion Products (in bulk drug substance, bulk drug product, or finished dosage product form, as requested by Blueprint) as Blueprint reasonably indicates in written forecasts and orders therefor from time to time at Clementia's Manufacturing costs for such supplies, [***], to Manufacture or have Manufactured such Reversion Products until the earlier of (i) [***] and (ii) [***]; provided, that Blueprint shall use Commercially Reasonable Efforts (defined for purposes of this Section 11.6.4(j) to apply to Reversion Products in the same manner as defined hereunder with respect to Blueprint Compounds and Licensed Products) to obtain an alternative supply of Reversion Products as promptly as practicable. [***].

(k) Return of Confidential Information. Except in the case of Blueprint for any Confidential Information that is the subject of its Reversion Licenses, each Party will promptly return to the other Party (or as directed by such other Party destroy and certify to such other Party in writing as to such destruction) all of such other Party's Confidential Information provided by or on behalf of such other Party hereunder that is in the possession or control of such Party (or any of its Affiliates, Sublicensees or subcontractors), except that such Party will have the right to retain one (1) copy of intangible Confidential Information of such other Party for legal purposes.

(l) Cooperation. Each Party will cause its Affiliates and Sublicensees to comply with the obligations in this Section 11.6; provided that the good faith failure by Clementia to provide immaterial information, reports records, correspondence or other materials to Blueprint shall not be a breach of Clementia's obligations under this Section 11.6. Within a reasonable period of time following notice of termination from Clementia to Blueprint, if requested by Blueprint, the Parties will meet to mutually agree upon a transition plan to effect an orderly and timely transition to Blueprint of all Development, Manufacture and Commercialization activities and responsibilities with respect to Reversion Products consistent with this Section 11.6.

(m) Termination of Rights and Obligations. Except as set forth in this Section 11.6 and Sections 11.8 and 11.8(a), as of the effective date of such termination all rights and obligations of the Parties under this Agreement will terminate.

(n) Consideration for Reversion Product License.

(i) Upon termination by Clementia under [***] as partial consideration for the licenses granted under Section 11.6.4(a), Blueprint will pay to Clementia a royalty ("**Reversion Royalty**"), as set forth below Table 11.6.4(n)(i), based on the aggregated net sales (whether by Blueprint, its Affiliates or Sublicensees), calculated on the same basis as Net Sales and using the same terms, mechanics, adjustments and procedures applied to payments by Clementia to Blueprint under Article 5, mutatis mutandis, with respect to such Reversion Products in the Territory. [***]. For the avoidance of doubt, if aggregate Net Sales of Reversion Products meet or exceed the applicable Net Sales Reversion Threshold in a given Calendar Year, Blueprint will pay Clementia the applicable Reversion Royalty (A) [***] and (B) [***]; provided, however, that Blueprint will have no obligation to pay an applicable Reversion Royalty if aggregate payments of Reversion Royalties for Reversion Products equal the amount set forth in Table 11.6.4(n)(i) (the "**Reversion Royalty Cap**").

Table 11.6.4(n)(i) – Consideration for Reversion Product License			
	[***]	[***]	[***]
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]

Table 11.6.4(n)(i) – Consideration for Reversion Product License			
	[***]	[***]	[***]
[***]	[***]	[***]	[***]

(ii) Notwithstanding anything to the contrary in this Section 11.6.4, Clementia will have the right to terminate the licenses granted to Blueprint in Section 11.6.4(a) with respect to Reversion Products in full upon [***] prior written notice to Blueprint in the event of any material breach by Blueprint of its payment obligations under this Section 11.6.4(n). Notwithstanding the foregoing, any such termination under this Section 11.6.4(n) will not be effective if such breach has been cured within [***] after written notice thereof is given by Clementia to Blueprint specifying the nature of the alleged breach.

(o) As partial consideration for the Reversion Licenses, Blueprint would fully and forever release and discharge Clementia and its Affiliates, from any and all claims, demands, liabilities, obligations, responsibilities, suits, actions and causes of action, known or unknown, past, present or future, or otherwise, arising out of or relating to this Agreement or a breach of Clementia's rights and obligations under this Agreement; provided, however, that the foregoing release does not discharge any rights or obligations set forth in Sections 11.6.4(b) through 11.6.4(l), 11.6.4(n), 11.6.4(p) and 11.8 or for payment of any royalties, milestones, or any amounts owed under this Agreement.

(p) **Future Assurances.** Clementia will execute all documents and take, or cause to be taken, all such further actions as may be reasonably requested by Blueprint in order to give effect to the foregoing clauses.

11.6.5 **Other Remedies.** Except as provided in Section 11.6.4(n) or Section 11.8, termination or expiration of this Agreement for any reason will not constitute a waiver or release of, or otherwise be deemed to prejudice or adversely affect, any rights, remedies or claims, whether for damages or otherwise, that a Party may have hereunder or that may arise out of or in connection with such termination or expiration.

11.7 **Termination by Clementia Due to Material Breach.** Notwithstanding anything to the contrary set forth in this Agreement, upon the termination of this Agreement by Clementia pursuant to Section 11.3, all of the provisions of Section 11.6.4 will apply, except that to the extent Clementia is obligated to perform under any of the provisions of Sections 11.6.4(b), 11.6.4(c), 11.6.4(g) and 11.6.4(h), Blueprint will reimburse Clementia for all reasonable and documented committed and non-cancellable costs incurred by Clementia in connection with such performance, including after the effective date of termination, including both its reasonable external costs plus its reasonable internal costs calculated on a reasonable FTE basis.

11.8 **Alternative in Lieu of Termination by Clementia Due to Material Breach.**

(a) Notwithstanding anything to the contrary set forth in this Agreement, if Clementia notifies Blueprint in writing of a material breach by Blueprint such that Clementia would have a right of termination of this Agreement in its entirety by Clementia pursuant to Section 11.3, in lieu of such termination right pursuant to Section 11.3, in the event such material breach remains uncured after [***] such that Clementia would be entitled to terminate this Agreement pursuant to Section 11.3, Clementia may elect, beginning on the date Clementia would be entitled to terminate this Agreement for such uncured material breach, to have this Agreement continue in full force and effect without such termination; provided that Clementia notifies Blueprint within [***] of its election. Upon Blueprint's receipt of such election notice from Clementia, (a) [***], (b) all other rights and obligations of each Party

hereunder with respect to all Licensed Products throughout the Territory shall continue in full force and effect, and (c) Clementia shall fully and forever release and discharge Blueprint and its Affiliates, from any and all claims, demands, liabilities, obligations, responsibilities, suits, actions and causes of action, known or unknown, past, present or future, or otherwise, arising out of or relating to such uncured material breach.

(b) For the avoidance of doubt, (i) [***], or (ii) [***].

11.9 Continuation of Sublicenses. In the event that the licenses granted to Clementia under this Agreement are terminated by Blueprint, any granted Sublicenses by Clementia (or by its Affiliates or Sublicensees) will remain in full force and effect; provided that the Sublicensee is not then in breach of its Sublicense and the Sublicensee as licensee agrees to be bound to Blueprint as a licensor under the terms and conditions of the Sublicense. Blueprint will enter into appropriate agreements or amendments to the Sublicense to substitute itself for Clementia as the licensor under such Sublicense.

11.10 Survival. Any termination of this Agreement shall be without prejudice to the rights of either Party against the other accrued or accruing under this Agreement upon or prior to termination, including without limitation (a) obligations to pay any royalties, license fees, milestone payments or other payments that accrue under this Agreement upon or prior to termination and (b) the obligation to share any costs incurred prior to such termination in accordance with this Agreement, in accordance with the provisions of Article 5. In addition, the following Articles and Sections, as well as, to the extent applicable, any other Sections or defined terms referred to in such Sections or Articles or necessary to give them effect, will survive any expiration or termination of this Agreement in its entirety: Section 2.4 (Reservation of Rights), Section 6.1 (Ownership of IP), Section 6.2 (Prosecution and Maintenance of Licensed Patents) (but, solely with respect to, and to the extent, any Patent is a Joint Patent or Reversion Technology), Section 6.5 (Third Party Infringement) (but, solely with respect to, and to the extent, any Patent is a Joint Patent or Reversion Technology), Section 7.1 (Confidentiality), Section 7.3 (Tax Treatment), Section 7.4 (Attorney-Client Privilege), Section 8.5 (No Other Representations or Warranties), Article 9 (Indemnification), Article 10 (Limitation of Liability), Section 11.1 (Term) (but solely with respect to expiration and not termination), Section 11.6 (Effects of Termination), Section 11.7 (Termination by Clementia Due to Material Breach), Section 11.9 (Survival of Sublicenses), Section 11.10 (Survival), Article 12 (Dispute Resolution), Article 13 (Miscellaneous). Furthermore, any other provisions required to interpret the Parties' rights and obligations under this Agreement, including applicable definitions in Article 1 (Definitions), will survive to the extent required. Except as otherwise expressly provided in this Agreement, all rights and obligations of the Parties under this Agreement, including any licenses granted under this Agreement, will terminate upon expiration or termination of this Agreement in its entirety for any reason.

ARTICLE 12
DISPUTE RESOLUTION

12.1 Disputes. Disputes of any nature arising under, relating to, or in connection with this Agreement ("**Disputes**") will be resolved pursuant to this Article 12.

12.2 Dispute Escalation. In the event of a Dispute between the Parties, the Parties will first attempt to resolve such dispute by negotiation and consultation between themselves. In the event that such dispute is not resolved on an informal basis within twenty (20) days from receipt of the written notice of a Dispute, any Party may, by written notice to the other have such dispute referred to the Executive Officers (or their designee, which designee is required to have decision-making authority on behalf of such Party), who will attempt to resolve such Dispute in good faith by negotiation and consultation for a thirty (30) day period following receipt of such written notice. If the matter is not resolved within such thirty (30) day

period, either Party will thereafter have the right to pursue any and all other remedies available at law or in equity, subject to this Article 12.

12.3 Governing Law. This Agreement will be governed by and interpreted under the laws of the State of New York, other than any principle of conflict or choice of laws that would cause the application of the laws of any other jurisdiction; provided, however, that all questions concerning inventorship, scope, validity, enforceability or infringement of any Patents will be determined in accordance with the laws of the country, region or other jurisdiction in which the particular patent has been filed or granted, as the case may be. The Parties agree to exclude the application to this Agreement of the United Nations Conventions on Contracts for the International Sale of Goods.

12.4 Jurisdiction. For the purposes of this Article 12, the Parties, except as provided in Section 12.6, agree to accept the jurisdiction of any United States District Court located in the State of New York.

12.5 Injunctive Relief. Nothing in this Article 12 will preclude either Party from seeking equitable relief or interim or provisional relief from a court of competent jurisdiction, including a temporary restraining order, preliminary injunction or other interim equitable relief. For the avoidance of doubt, nothing in this Section 12.5 will otherwise limit a breaching Party's opportunity to cure a material breach as permitted in accordance with Section 11.3.

12.6 Patent, Trademark and Copyright Disputes. Notwithstanding Section 12.3 and Section 12.4, any dispute, controversy or claim relating solely to the inventorship, scope, validity, enforceability or infringement of any Patents, Trademarks or copyrights within the Licensed Technology, Blueprint Future Technology or Joint Technology or otherwise Covering the manufacture, use, importation, offer for sale or sale of any Blueprint Compounds or Licensed Products will be submitted to a court of competent jurisdiction in the country in which such Patents, or Trademarks or copyrights were granted or arose.

ARTICLE 13
MISCELLANEOUS

13.1 Assignment. This Agreement and the rights and obligations of each Party under this Agreement cannot be assigned or otherwise transferred by either Party without the prior written consent of the other Party; provided, however, that (i) either Party may assign or transfer this Agreement, without such consent (but with written notice to the other Party promptly following such assignment or transfer), to an Affiliate of such Party, (ii) Blueprint may assign or transfer this Agreement, without such consent (but with written notice to Clementia promptly following such assignment or transfer) to a successor in interest to all or substantially all of the business or assets of Blueprint to which this Agreement relates, whether by merger, consolidation, reorganization, acquisition, sale of stock, sale of assets, royalty factoring or similar transaction or series of transactions, or (iii) beginning on the [***] of the Effective Date, Clementia may assign or transfer this Agreement without such consent (but with written notice to Blueprint promptly following such assignment or transfer) to a successor in interest to all or substantially all of the business or assets of Clementia to which this Agreement relates (including FOP and MO), whether by merger, consolidation, reorganization, acquisition, sale of stock, sale of assets, royalty factoring or similar transaction or series of transactions. For the avoidance of doubt, at no time during the Term shall a Change of Control with respect to Ipsen S.A. or Guarantor be deemed an assignment or transfer requiring the consent of Blueprint pursuant to this Section 13.1. Any permitted assignment of the rights and obligations of a Party under this Agreement will be binding on, and inure to the benefit of and be enforceable by and against, the successors and permitted assigns of the assigning Party. Any permitted assignee or transferee will assume all obligations of its assignor or transferor under this Agreement. Any assignment or attempted

assignment by either Party in violation of the terms of this Section 13.1 will be null, void and of no legal effect.

13.2 Non-Solicitation. During the first [***] after the Effective Date, each Party (each, a "**Recruiting Party**") agrees that neither it nor any of its Affiliates will recruit, solicit, or induce any full-time employee of the other Party (the "**Employing Party**") or any of its Affiliates who has been in contact with the Recruiting Party in connection with this Agreement (whether prior to, on or after the Effective Date) to terminate his or her employment with the Employing Party or any of its Affiliates and become employed by or consult for the Recruiting Party or any of its Affiliates, and whether or not such employment or consulting is pursuant to a written agreement or such employment is at-will. For purposes of the foregoing, "recruit," "solicit," or "induce" will not be deemed to mean (a) circumstances where an employee of an Employing Party or any of its Affiliates (i) initiates contact with the Recruiting Party or any of its Affiliates with regard to possible employment; or (ii) responds to general solicitations of employment not specifically targeted at employees of the Employing Party or any of its Affiliates, including responses to general advertisements or postings, and (b) discussions, interviews, negotiations, offers, or acceptances of employment or similar activities that arise as a result of circumstances described in the foregoing clause (a); provided that the obligations under this Section 13.2 shall terminate upon a Change of Control of the Employing Party.

13.3 Notices. Any notice or report required or permitted to be given or made under this Agreement by one Party to the other will be in writing in English and, unless a right or obligation is triggered by receipt of a notice or report, will be deemed to have been delivered (a) upon personal delivery and (b) on the second (2nd) Business Day (at the place of delivery) next following deposit with a reputable, internationally recognized overnight courier that maintains records of delivery (with a courtesy copy sent by e-mail to the addresses specified below, which will not constitute notice). This Section 13.3 is not intended to govern the day-to-day business communications necessary between the Parties in performing their obligations under the terms of this Agreement.

If to Clementia:

Clementia Pharmaceuticals Inc.
1000 de la Gauchetière Street West, Suite 1200
Montreal, QC H3B 4W5, Canada
Attn: Chief Executive Officer
Email: [***]

With a copy to:

Ipsen Pharma SAS
65 quai Georges Gorse
92100 Boulogne-Billancourt, France
Attn: General Counsel
Email: [***]

With a copy to (which copy will not constitute notice):

Faber Daeufer & Itrato PC
125 Park Avenue, 25th floor
New York, NY 10017
Attn: [***]
Email: [***]

If to Blueprint:

Blueprint Medicines Corporation
45 Sidney Street
Cambridge, Massachusetts 02139 USA

Attention: Chief Executive Officer
Email: [***]

With copies to (which copies will not constitute notice):

Goodwin Procter LLP
100 Northern Avenue
Boston, Massachusetts 02210 USA
Attention: [***]
Email: [***]

Blueprint Medicines Corporation
45 Sidney Street
Cambridge, Massachusetts 02139 USA
Attention: Chief Legal Officer
Email: [***]

13.4 Severability. If, under applicable Law, any provision of this Agreement is invalid or unenforceable, (such invalid or unenforceable provision, a "**Severed Clause**"), it is mutually agreed that (a) this Agreement will endure except for the Severed Clause, (b) this Agreement will be construed and enforced as if such Severed Clause had never comprised a part hereof, (c) the remaining provisions of this Agreement will remain in full force and effect and will not be affected by the Severed Clause or by its severance herefrom, and (d) in lieu of such illegal, invalid, or unenforceable provision, there will be added automatically as a part of this Agreement a legal, valid, and enforceable provision as similar in terms to such illegal, invalid, or unenforceable provision as may be possible and reasonably acceptable to the Parties.

13.5 Integration. This Agreement, together with all schedules and exhibits attached hereto, constitutes the entire agreement between the Parties with respect to the subject matter of this Agreement and supersedes all previous arrangements between the Parties with respect to the subject matter hereof, whether written or oral, including the Prior CDA. In the event of a conflict between any schedules or attachments to this Agreement, on the one hand, and this Agreement, on the other hand, the terms of this Agreement will govern. Each Party confirms that it is not relying on any representations or warranties of the other Party except as specifically set forth in this Agreement.

13.6 Waivers and Amendments. The failure or delay of any Party to assert a right under this Agreement or to insist upon compliance with any term or condition of this Agreement will not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition by the other Party. No waiver will be effective unless it has been given in writing and signed by the Party giving such waiver, and no provision of this Agreement may be amended or modified other than by a written document signed by authorized representatives of each Party.

13.7 Independent Contractors; No Agency. Neither Party will have any responsibility for the hiring, firing or compensation of the other Party's or such other Party's Affiliates' employees or for any employee benefits with respect thereto. No employee or representative of a Party or its Affiliates will have any authority to bind or obligate the other Party for any sum or in any manner whatsoever, or to create or impose any contractual or other liability on such other Party, without such other Party's written approval. For all purposes, and notwithstanding any other provision of this Agreement to the contrary, each Party's legal relationship under this Agreement to the other Party will be that of independent contractor, and the relationship between the two Parties will not constitute a partnership, joint venture, or agency, including for all tax purposes.

13.8 Force Majeure. Neither Party will be responsible to the other for, or be deemed to have defaulted under or breached this Agreement for, any failure or delay in performing any of its obligations under this Agreement or for other nonperformance under this Agreement (excluding, in each case, the obligation to make payments when due) if such delay or nonperformance is caused by or results from events beyond the reasonable control of the non-performing Party, including strike, fire, flood, earthquake, hurricanes, accident, war, acts of war (whether war be declared or not), insurrections, riots, civil commotion, strikes, lockouts, or other labor disturbances (whether involving the workforce of the non-performing Party or of any other Person), act of terrorism, act of God or acts, omissions or delays in acting of the government of any region or of any local government, or by cause unavoidable or beyond the reasonable control of such Party (except to the extent such delay results from the breach by the non-performing Party or any of its Affiliates of any term or condition of this Agreement) (a "**Force Majeure Event**"). In such event, the Party affected will promptly (and, in any event, subject to Section 4.2.3, within thirty (30) days) notify the other Party in writing of such Force Majeure Event, stating the nature of the event, its anticipated duration, and any action being taken to avoid or minimize its effect. The suspension of performance will be of no greater scope and no longer duration than is necessary and the non-performing Party and will use Commercially Reasonable Efforts to resume performance of its obligations.

13.9 No Third Party Beneficiary Rights. This Agreement is not intended to and will not be construed to give any Third Party any interest or rights (including any third party beneficiary rights) with respect to or in connection with any agreement or provision contained herein or contemplated hereby, other than, to the extent provided in Article 9, the Indemnified Parties.

13.10 Non-Exclusive Remedy. Except as expressly provided herein, the rights and remedies provided herein are cumulative and each Party retains all remedies at law or in equity, including the Parties' ability to receive legal damages or equitable relief, with respect to any breach of this Agreement. Neither Party will be required to terminate this Agreement due to a breach of this Agreement by the other Party.

13.11 Interpretation. The captions and headings to this Agreement are for convenience only, and are to be of no force or effect in construing or interpreting any of the provisions of this Agreement. Unless specified to the contrary, references to Articles, Sections or Exhibits mean the particular Articles, Sections or Exhibits to this Agreement and references to this Agreement include all Exhibits hereto. Unless context otherwise clearly requires, whenever used in this Agreement: (a) the words "include" or "including" will be construed as incorporating, also, "but not limited to" or "without limitation;" (b) the word "day" or "year" means a calendar day or year unless otherwise specified; (c) the word "notice" means notice in writing (whether or not specifically stated) and will include notices, consents, approvals and other written communications contemplated under this Agreement; (d) the words "hereof," "herein," "hereby" and derivative or similar words refer to this Agreement (including any Exhibits); (e) the word "or" will be construed as the inclusive meaning identified with the phrase "and/or;" (f) provisions that require that a Party or the Parties hereunder "agree," "consent" or "approve" or the like will require that such agreement, consent or approval be specific and in writing, whether by written agreement, letter or otherwise and that consents not be unreasonably withheld, delayed or conditioned; (g) words of any gender include the other gender; and (h) words using the singular or plural number also include the plural or singular number, respectively. Ambiguities and uncertainties in this Agreement, if any, will not be interpreted against either Party, irrespective of which Party may be deemed to have caused the ambiguity or uncertainty to exist. This Agreement has been prepared in the English language, and the English language will control its interpretation. In addition, all notices required or permitted to be given hereunder, and all written, electronic, oral or other communications between the Parties regarding this Agreement will be in the English language.

13.12 Performance by Affiliates; Guarantee.

13.12.1 Performance by Affiliates. Each of Blueprint and Clementia acknowledge that their obligations under this Agreement may be performed by their respective Affiliates. Notwithstanding any delegation of obligations under this Agreement by a Party to an Affiliate, each Party will remain primarily liable and responsible for the performance of all of its obligations under this Agreement and for causing its Affiliates to act in a manner consistent with this Agreement. Wherever in this Agreement the Parties delegate responsibility to Affiliates or local operating entities, the Parties agree that such entities will not make decisions inconsistent with this Agreement, amend the terms of this Agreement or act contrary to its terms in any way.

13.12.2 Guarantee. Guarantor has agreed to guarantee certain obligations and undertakings of Clementia under or in connection with this Agreement pursuant to the letter agreement, dated as of the Effective Date, between Blueprint and Guarantor.

13.13 Further Assurances. Each Party will duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents, and instruments, as may be necessary or as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes hereof, or to better assure and confirm unto such other Party its rights and remedies under this Agreement.

13.14 Ambiguities; No Presumption. Each of the Parties acknowledges and agrees that this Agreement has been diligently reviewed by and negotiated by and between them, that in such negotiations each of them has been represented by competent counsel and that the final agreement contained herein, including the language whereby it has been expressed, represents the joint efforts of the Parties hereto and their counsel. Accordingly, in interpreting this Agreement or any provision hereof, no presumption will apply against any Party as being responsible for the wording or drafting of this Agreement or any such provision, and ambiguities, if any, in this Agreement will not be construed against any Party, irrespective of which Party may be deemed to have authored the ambiguous provision.

13.15 Execution in Counterparts; Facsimile Signatures. This Agreement may be executed in counterparts, each of which counterparts, when so executed and delivered, will be deemed to be an original, and all of which counterparts, taken together, will constitute one and the same instrument even if both Parties have not executed the same counterpart. Signatures provided by facsimile transmission or in Adobe™ Portable Document Format (PDF) sent by electronic mail will be deemed to be original signatures.

[Remainder of this page intentionally blank.]

IN WITNESS WHEREOF, each Party has caused this Agreement to be duly executed by its authorized representative on the Effective Date.

BLUEPRINT MEDICINES CORPORATION

By: /s/ Jeffrey W. Albers

Name: Jeffrey W. Albers

Title: President and Chief Executive Officer

CLEMENTIA PHARMACEUTICALS, INC.

By: /s/ Clarissa DESJARDINS

Name: Clarissa DESJARDINS

Title: Chief Executive Officer

[Signature Page to License Agreement]

EXHIBIT A-1

BLUEPRINT COMPOUNDS

[***]

EXHIBIT A-2

METABOLITES

[***]

EXHIBIT B

DEVELOPMENT PLAN

[***]

EXHIBIT C-1

BLUEPRINT PRODUCT-SPECIFIC PATENTS

[***]

EXHIBIT C-2

BLUEPRINT PLATFORM PATENTS

Country	Application Number	Filing Date	Patent Number	Issue Date
[***]	[***]	[***]	[***]	[***]

EXHIBIT D

TRANSITION PLAN

[***]

EXHIBIT E

PRESS RELEASE

(omitted intentionally)

EXHIBIT F

THIRD PARTY AGREEMENTS

[***]

EXHIBIT 1.57

[***]

EXHIBIT 3.2.2

BILL OF SALE

[***]

Schedule 1.18

BLUEPRINT CMOS

[***]

Schedule 1.23

CERTAIN BLUEPRINT PLATFORM KNOW-HOW

[***]

Schedule 1.26

CERTAIN BLUEPRINT PRODUCT-SPECIFIC KNOW-HOW

[***]

Schedule 2.1.1

BLUEPRINT PERMITTED ACTIVITIES

Blueprint is permitted to use, or have used by Third Parties, the Blueprint Compounds as follows:

[***]

Schedule 3.2.2(a)

EXISTING MANUFACTURING INVENTORY

[***]

Schedule 3.2.2(b)

IN PROCESS MANUFACTURING INVENTORY

[***]

Schedule 7.2.2(b)(ii)

BLUEPRINT'S PERMITTED PUBLICATIONS

Blueprint plans to publish manuscripts related to the topics set forth below; provided that nothing in this Schedule 7.2.2(b)(ii) shall prevent Blueprint from submitting such manuscripts to a different journal or on a different timing, subject to Blueprint's compliance with Section 7.2.2(b)(ii) of the Agreement.

Planned Topic	Planned Journal	Planned Submission Timing
[***]	**[***]**	**[***]**
[***]	**[***]**	**[***]**
[***]	**[***]**	**[***]**

Schedule 7.2.2(b)(iii)

JOINT PRESENTATIONS

1. IFOPA Drug Development Forum

    a. Abstract Title: An update on BLU-782, a selective ALK2 inhibitor in development for Fibrodysplasia Ossificans Progressiva (FOP)

    b. Dates: November 13-14, 2019

2. IFOPA Drug Development Forum – Family Poster Session

    a. Poster Title: An update on BLU-782, a selective ALK2 inhibitor in development for Fibrodysplasia Ossificans Progressiva (FOP)

    b. Date: November 15, 2019

3. IFOPA Family Conference

    a. Oral Presentation: an update on BLU-782

    b. Dates: November 15-17, 2019

Schedule 8.2

EXCEPTIONS TO BLUEPRINT'S REPRESENTATIONS AND WARRANTIES

[***]

[***] CERTAIN INFORMATION IN THIS DOCUMENT HAS BEEN OMITTED FROM THIS EXHIBIT BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

SIXTH AMENDMENT TO COLLABORATION AND LICENSE AGREEMENT

This Sixth Amendment (this "**Sixth Amendment**"), effective November 1, 2019 ("**Sixth Amendment Effective Date**"), is by and between F. Hoffmann-La Roche Ltd, with an office and place of business at Grenzacherstrasse 124, 4070 Basel, Switzerland and Hoffmann-La Roche Inc., with an office and place of business at 150 Clove Road, Suite 8, Little Falls, New Jersey 07424, U.S.A. (together referred to as "**Roche**"), and Blueprint Medicines Corporation, with a principal place of business at 45 Sidney Street, Cambridge, Massachusetts 02139 U.S.A. ("**BPM**"). Capitalized terms used and not otherwise defined in this Sixth Amendment shall have the meanings set forth in the Agreement (as defined below).

WHEREAS, BPM and Roche entered into a Collaboration and License Agreement, dated March 14, 2016, as amended by an amendment, effective April 15, 2016, a second amendment, effective April 27, 2016, a third amendment, effective August 4, 2016, a fourth amendment, effective February 25, 2019, and a fifth amendment, effective June 28, 2019 (collectively, the "**Agreement**"); and

WHEREAS, the Parties wish to enable the Joint Research Committee to approve alternative funding arrangements for preclinical development activities conducted under Research Plans as set forth herein;

WHEREAS, the Parties wish to be able to conduct preclinical development activities for Collaboration Targets with Roche Clinical Compounds and Roche Marketed Products;

WHEREAS, the Parties wish to terminate [***] as a Collaboration Target under the Agreement;

NOW THEREFORE, Roche and BPM hereby agree as follows:

1. Section 1.108 of the Agreement is hereby amended by adding the following sentence to the end of such section:

> "In the event that the JRC approves an Alternative Funding Arrangement for a Collaboration Target, then the Research Plan for such Collaboration Target shall also specify (i) the budget for the applicable preclinical development activities and (ii) the percentage of the corresponding costs and expenses that each Party (if applicable) will be responsible for funding (e.g., fifty percent-fifty percent cost sharing)."

2. The definition of "Roche Clinical Compounds" in Section 1.110 of the Agreement shall be amended by deleting it in its entirety and replacing it with the following Section 1.110:

> **"1.110 Roche Clinical Compounds**
>
> The term "Roche Clinical Compounds" shall mean clinical-stage compounds controlled by Roche or its Affiliates (but not Products or Licensed Products) and provided for (i) combination preclinical development activities with Library Compounds, Collaboration Compounds, Other Compounds or Products during Lead Nomination or Lead Optimization, or (ii) combination Clinical Studies with Products or Licensed Products."

3. The definition of "Roche Marketed Products" in Section 1.113 of the Agreement shall be amended by deleting it in its entirety and replacing it with the following Section 1.113:

"1.113 Roche Marketed Products

The term "Roche Marketed Products" shall mean marketed products controlled by Roche or its Affiliates (but not Products or Licensed Products) and provided for (i) combination preclinical development activities with Library Compounds, Collaboration Compounds, Other Compounds or Products during Lead Nomination or Lead Optimization, or (ii) combination Clinical Studies with Products or Licensed Products."

4. Section 4.1.3 is hereby amended by adding the following paragraph immediately after the first paragraph of Section 4.1.3:

"If any Research Plan (or any amendment thereto) contemplates the conduct of any preclinical development activities [***] by one or more Third Party(ies) on behalf of BPM, such Research Plan (or an amendment thereto) shall also specify (a) the budget for the applicable preclinical development activities and the percentage of the corresponding costs and expenses that each Party (if applicable) will be responsible for funding (e.g., cost sharing fifty percent (50%) by BPM and fifty percent (50%) by Roche), (b) the specific compounds to be used in such activities (including any Roche Clinical Compounds or Roche Marketed Products), (c) the specific Third Party(ies) that BPM intends to use to conduct such preclinical development activities, and each such Third Party shall be an approved CRO under the Agreement or specified for such activities in the Research Plan, and (d) any costs previously incurred by BPM related to such activities that are to be retroactively shared by the Parties (and the applicable percentage of such costs that each Party (if applicable) will be responsible for funding). Any such Research Plan that contemplates the Parties sharing the costs and expenses of any such preclinical development activities performed by one or more Third Party(ies) on behalf of BPM is referred to herein as an "**Alternative Funding Arrangement**"."

5. Clause (a) of Section 8.4 of the Agreement is hereby deleted in its entirety and replaced by the following new clause (a):

"(a) approve each Research Plan and any revisions thereto, including any Alternative Funding Arrangement and Alternative Funding Costs for such Research Plan;"

6. Notwithstanding anything to the contrary in Section 8.8 of the Agreement, all Alternative Funding Arrangements and Alternative Funding Arrangement Costs must be approved by consensus of both Parties' JRC Members (i.e., neither BPM nor Roche has final decision).

7. Section 12.3 of the Agreement is hereby deleted in its entirety and replaced by the following new Section 12.3:

"**12.3 Costs for Work Conducted under Research Plans**

Except for Alternative Funding Arrangements approved by consensus of the JRC (i.e. neither BPM nor Roche have final decision) pursuant to the JRC's authority under Section 8.4(c) hereof or as otherwise provided in this Agreement, each Party shall be responsible for its own costs incurred in the conduct of its activities under each Research Plan.

Commencing the first Calendar Quarter immediately following BPM incurring costs under an Alternative Funding Arrangement within a Research Plan ("**Alternative Funding Arrangement Costs**") and continuing thereafter so long as BPM incurs costs under such

Alternative Funding Arrangement under this Agreement, within forty-five (45) days following the end of such Calendar Quarter, BPM shall submit to Roche a report setting forth the Alternative Funding Arrangement Costs incurred by BPM in such Calendar Quarter; provided that if there are any Alternative Funding Arrangement Costs incurred in such Calendar Quarter that BPM is unable to timely include in such financial report, then such amount shall be included and reconciled in the financial report in a future Calendar Quarter. Each such report shall specify in reasonable detail the Alternative Funding Arrangement Costs incurred and shall include reasonably detailed supporting information. Within [***] after receipt of each such report, the Finance Officers (as defined in Section 12.5 below) shall confer and agree in writing on whether a reconciliation payment is due from Roche to BPM, and if so, the amount of such reconciliation payment, so that the Parties share Alternative Funding Arrangement Costs in accordance with the allocation specified in the applicable Research Plan for such Alternative Funding Arrangement. Roche shall make such payment to BPM within [***] after the end of each Calendar Quarter; provided, however, that in the event of any disagreement with respect to the calculation of such reconciliation payment, any undisputed portion of such reconciliation payment shall be paid in accordance with the foregoing timetable and the remaining, disputed portion shall be paid within [***] after the date on which the Parties, using good faith efforts, resolve the dispute. Notwithstanding anything to the contrary in this Section 12.3, in the event that the JRC approves an Alternative Funding Arrangement for which the approved budget includes costs and expenses previously incurred by BPM that are to be shared retroactively by the Parties (as specified in the applicable Research Plan), then Roche's portion of such previously incurred costs and expenses shall be included in the first Calendar Quarter report submitted by BPM related to such Alternative Funding Arrangement (or if BPM is unable to timely include such costs and expenses in such financial report, then such amount shall be included and reconciled in the financial report in a future Calendar Quarter)."

8. Section 16.1 of the Agreement is hereby amended by adding the following sentence to the end of such section.

"Any and all Collaboration Compounds and all Other Compounds (including Combination Products) for a given Collaboration Target or other Targets, including their methods of manufacture (other than Roche Process IP) and use, and all Patent Rights and Know-How relating thereto (including Collaboration Compound IP) that are created or conceived in connection with a Research Plan shall be solely owned by BPM as Collaboration Compound IP or Other Compound IP, as applicable, except that all Patent Rights and Know-How that solely relate to Roche Clinical Compounds or Roche Marketed Products, including their methods of manufacture (other than Roche Process IP) and use, shall be solely owned by Roche.

9. [***] is classified as a "Terminated Target" under the Agreement in all countries in the Territory in accordance with Section 21.2.4. Notwithstanding the written notice period set forth in such Section 21.2.4, the effective date of termination of such Terminated Target will be the Sixth Amendment Effective Date. Further, the Parties hereby acknowledge and agree that this Sixth Amendment will be deemed to constitute a "Continuation Election Notice" in accordance with Section 21.3.1, and Roche will comply with its obligations under 21.3.1 and 21.3.4; provided that no payment will be due or payable to Roche under Section 21.3.1(f) or 21.3.4.4. As of the Sixth Amendment Effective Date, (a) the rights and licenses granted by BPM to Roche under the Agreement related to the aforementioned Terminated Target terminate in their entirety in all countries in the Territory, (b) except as set forth herein, the rights and obligations of the Parties under the Agreement terminate with respect to such Terminated Target, (c) Roche's obligations under Section 20.1 survive with respect to such Terminated Target, and (d) BPM solely owns all Collaboration Compounds and Other Compounds for such Terminated Target, including their methods of manufacture and use, and all Patent Rights and Know-How relating thereto. Further, for the avoidance of doubt, it is understood

and agreed that BPM has the right to (i) research, develop, manufacture, commercialize and otherwise exploit compounds and products related to such Terminated Target outside of the Agreement without any financial obligations to Roche, (ii) publish data and other Know-How related to the Terminated Target (including without limitation the name of the target and Collaboration Compounds and Other Compounds for such Terminated Target) generated by or on behalf of the Parties under the Agreement prior to the Sixth Amendment Effective Date or thereafter without obtaining prior review or approval from Roche and (iii) disclose, in its sole discretion, in a manner consistent with BPM's then-current disclosure or publication practices or policies that such data or Know-How was generated under the Agreement and/or the names and affiliations of the individuals involved in the generation of such data or Know-How, if and as applicable.

This Sixth Amendment may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered via facsimile, electronic mail (including pdf or other electronic signature) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

This Sixth Amendment shall be effective as of the Sixth Amendment Effective Date. On and after the Sixth Amendment Effective Date, each reference in the Agreement to "this Agreement," "hereunder," "hereof," "herein" or words of like import, and each similar reference in the other documents entered into in connection with the Agreement, shall mean and be a reference to the Agreement, as amended by this Sixth Amendment. Except as specifically amended above, the Agreement shall remain in full force and effect in accordance with its terms and is hereby ratified and confirmed.

This Sixth Amendment shall be governed by and construed in accordance with the laws of the State of New York, without reference to its conflict of laws principles, and shall not be governed by the United Nations Convention of International Contracts on the Sale of Goods (the Vienna Convention).

[Signature page follows.]

IN WITNESS WHEREOF, the Parties have caused this Sixth Amendment to be executed by their respective duly authorized representatives as of the Sixth Amendment Effective Date.

Blueprint Medicines Corporation

/s/ Jeffrey W. Albers

Name: Jeffrey W. Albers

Title: President and Chief Executive Officer

F. Hoffmann-La Roche Ltd

/s/ Tim Steven

Name: Tim Steven

Title: Global Alliance and Asset Management Director

/s/ Stefan Arnold

Name: Stefan Arnold

Title: Head Legal Pharma

Hoffmann-La Roche Inc.

/s/ John P. Praise

Name: John P. Praise

Title: Authorized Signatory

Exhibit 31.1

CERTIFICATIONS

I, Jeffrey W. Albers, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Blueprint Medicines Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 5, 2019

By: /s/ Jeffrey W. Albers
Jeffrey W. Albers
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Michael Landsittel, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Blueprint Medicines Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 5, 2019

By: /s/ Michael Landsittel
Michael Landsittel
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Blueprint Medicines Corporation (the "Company") for the period ended September 30, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: November 5, 2019

By: /s/ Jeffrey W. Albers
Jeffrey W. Albers
President and Chief Executive Officer
(Principal Executive Officer)

Date: November 5, 2019

By: /s/ Michael Landsittel
Michael Landsittel
Chief Financial Officer
(Principal Financial Officer)