UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): **April 10, 2021**

Blueprint Medicines Corporation
(Exact name of registrant as specified in its charter)

Delaware	**001-37359**	**26-3632015**
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

45 Sidney Street **Cambridge, Massachusetts** (Address of principal executive offices)	**02139** (Zip Code)

Registrant's telephone number, including area code: **(617) 374-7580**

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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. ☐

Securities registered pursuant to Section 12(b) of the Exchange 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

Item 7.01 Regulation FD.

On April 12, 2021, Blueprint Medicines Corporation (the "Company") is hosting an investor conference call and webcast to review data presented at the American Association for Cancer Research ("AACR") Annual Meeting 2021 for multiple research- and clinical-stage programs across its precision oncology and hematology portfolio. A copy of the presentation from the investor conference call and webcast is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On April 10, 2021, the Company issued a press release announcing preclinical data for multiple programs from various poster presentations at the AACR Annual Meeting 2021. A copy of the press release is filed herewith as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference.

On April 11, 2021, the Company issued a press release announcing data from multiple presentations reported at the AACR Annual Meeting 2021 across its systemic mastocytosis program. A copy of the press release is filed herewith as Exhibit 99.3 to this Current Report on Form 8-K and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	**Description**
99.1	Corporate slide presentation of Blueprint Medicines Corporation dated April 12, 2021
99.2	Press release issued by Blueprint Medicines Corporation on April 10, 2021
99.3	Press release issued by Blueprint Medicines Corporation on April 11, 2021
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 101)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

BLUEPRINT MEDICINES CORPORATION

Date: April 12, 2021

By: /s/ Jeffrey W. Albers
Jeffrey W. Albers
Chief Executive Officer


blueprint MEDICINES
ADVANCING SCIENCE
10
CHANGING LIVES
Celebrating our first decade
of innovation in precision medicine
Advancing our next wave of
precision therapies to patients
AACR Annual Meeting 2021
APRIL 12, 2021
© 2021 Blueprint Medicines Corporation

Forward-looking statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. In this presentation, forward-looking statements include, without limitation, statements regarding plans, strategies, timelines and expectations for the current or future approved drugs and drug candidates of Blueprint Medicines Corporation (the "Company"), including timelines for marketing applications and approvals, commercialization activities, the initiation of clinical trials, or results of ongoing and planned clinical trials; the potential benefits of any of the Company's current or future approved drugs or drug candidates in treating patients; and the Company's strategy, goals and anticipated milestones, business plans and focus.

The Company has based these forward-looking statements on management's current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks, uncertainties and other important factors, many of which are beyond the Company's control and may cause actual results, performance or achievements to differ materially from those expressed or implied by any forward-looking statements. These risks and uncertainties include, without limitation, risks and uncertainties related to the impact of the COVID-19 pandemic to the Company's business, operations, strategy, goals and anticipated milestones, including the Company's ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved drugs, and launching, marketing and selling current or future approved drugs; the Company's ability and plans in establishing a commercial infrastructure, and successfully launching, marketing and selling current or future approved products; the Company's ability to successfully expand the approved indications for AYVAKIT™/AYVAKYT® (avapritinib) and GAVRETO® (pralsetinib) or obtain marketing approval for AYVAKIT/AYVAKYT in additional geographies in the future; the delay of any current or planned clinical trials or the development of the Company's drug candidates or the licensed drug candidate; the Company's advancement of multiple early-stage efforts; the Company's ability to successfully demonstrate the efficacy and safety of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; the preclinical and clinical results for the Company's drug candidates, which may not support further development of such drug candidates; actions or decisions of regulatory agencies or authorities, which may affect the initiation, timing and progress of clinical trials or marketing applications; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT, GAVRETO or any drug candidates it is developing; the Company's ability to develop and commercialize companion diagnostic tests for any of the Company's current or future approved drugs or drug candidates; and the success of the Company's current and future collaborations, partnerships and licenses. These and other risks and uncertainties are described in greater detail under "Risk Factors" in the Company's filings with the Securities and Exchange Commission ("SEC"), including its most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q, and any other filings it has made or may make with the SEC in the future. The Company cannot guarantee future results, outcomes, levels of activity, performance, developments, or achievements, and there can be no assurance that its expectations, intentions, anticipations, beliefs, or projections will result or be achieved or accomplished. The forward-looking statements in this presentation are made only as of the date hereof, and except as required by law, the Company undertakes no obligation to update any forward-looking statements contained in this presentation as a result of new information, future events or otherwise.

This presentation also contains estimates, projections and other statistical data made by independent parties and by the Company relating to market size and growth and other data about the Company's industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of the Company's future performance and the future performance of the markets in which the Company operates are necessarily subject to a high degree of uncertainty and risk.

Blueprint Medicines call participants

PREPARED REMARKS

Celebrating 10 years of innovation in precision medicine	**Jeff Albers**, Chief Executive Officer
AACR 2021 review	**Fouad Namouni, MD**, President, R&D
Our plan to transform the treatment of EGFRm NSCLC	
Selective CDK2 inhibition: a promising therapeutic strategy	**Becker Hewes, MD**, Chief Medical Officer
Q&A	**All**

AACR, American Association for Cancer Research; CDK2, cyclin dependent kinase 2; EGFRm, mutant epithelial growth factor receptor; NSCLC, non-small cell lung cancer.

Our first decade of precision therapy innovation

AYVAKIT™ avapritinib | tablets

GAVRETO® pralsetinib | 100mg capsules

- First to achieve FDA approval of two internally discovered medicines within 10 years
- 9 approved or investigational precision therapies[1], plus multiple additional undisclosed research programs
- 5 FDA breakthrough therapy designations
- Global commercial footprint in the U.S. and Europe
- Multiple transformative collaborations
- Strong financial position to further accelerate innovation

COMPANY COMMENCED OPERATIONS IN APRIL 2011

blueprint™ MEDICINES

1. Includes AYVAKIT, GAVRETO, fisogatinib, BLU-263, BLU-701, BLU-945, BLU-852, BLU-222 and BLU-782 (out-licensed to Ipsen). FDA, U.S. Food and Drug Administration.

Extraordinary research productivity

5 DEVELOPMENT CANDIDATES NOMINATED IN LAST ~18 MONTHS

Program	Target	Therapeutic area focus	Trial	Planned initiation
BLU-263	KIT D816V	Non-advanced SM	Phase 2/3	Mid 2021
BLU-945	EGFR triple mutant	EGFRm NSCLC	Phase 1	Q2 2021
BLU-701	EGFR double mutant	EGFRm NSCLC	Phase 1	2H 2021
BLU-222	CDK2	Cyclin E aberrant cancers	Phase 1	1H 2022
BLU-852	MAP4K1	Cancer immunotherapy	Phase 1	2022

MULTIPLE CLINICAL PROOF-OF-CONCEPT DATASETS ANTICIPATED IN 2022

KIT, KIT proto-oncogene receptor kinase; MAP4K1, hematopoietic progenitor kinase 1; SM, systemic mastocytosis.

Increasingly significant opportunities to impact patients across our portfolio

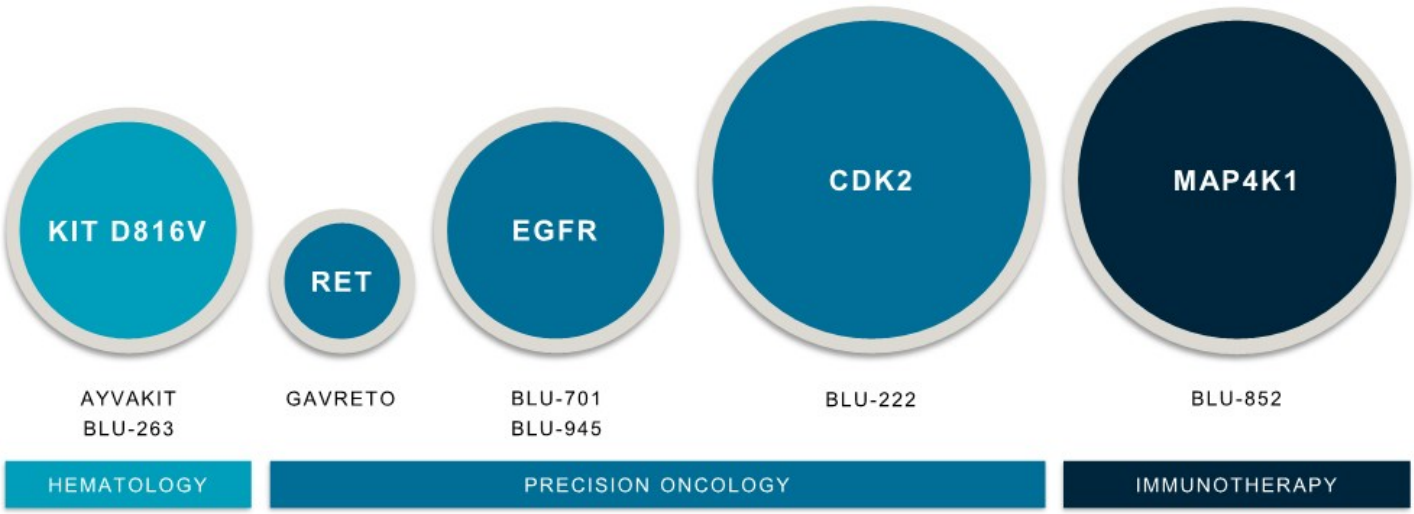


Figure is illustrative.

blueprint MEDICINES

ADVANCING SCIENCE 10 CHANGING LIVES

Celebrating our first decade
of innovation in precision medicine

AACR 2021 review

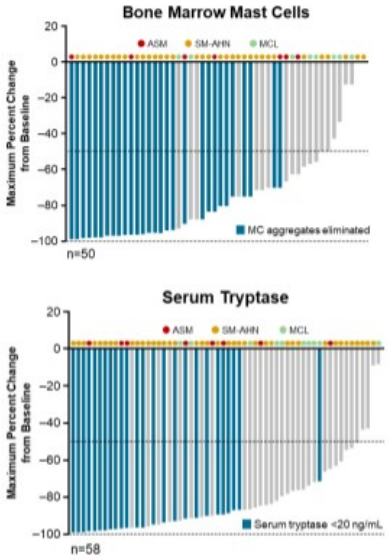
Our plan to transform treatment of EGFRm NSCLC

Fouad Namouni, MD
President, Research & Development

Interim analysis from PATHFINDER trial of AYAVKIT in advanced SM

AYVAKIT
SELECTIVE AND POTENT KIT INHIBITOR

- Interim analysis consistent with prior data
- 75% ORR[1] (95% CI: 57%, 89%) per IWG-MRT-ECNM response criteria
- Robust reductions in mast cell burden and improvements in disease symptoms and patient-reported quality of life
- Generally well-tolerated at 200 mg QD proposed dose, based on the observed benefit-risk profile
- Supplementary marketing applications under review in U.S. and Europe, with FDA PDUFA action date on June 16, 2021



Data presented at AACR 2021 Annual Meeting. Data cut-off: June 23, 2020. 1. ORR defined as complete remission with full or partial recovery of peripheral blood counts, partial remission or clinical improvement. ASM, aggressive SM; CI, confidence interval; IWG-MRT-ECNM, International Working Group-Myeloproliferative Neoplasms Research and Treatment and European Competence Network on Mastocytosis; MC, mast cell; MCL, mast cell leukemia; ng/mL, nanograms per milliliter; ORR, overall response rate; PDUFA, Prescription Drug User Fee Act; QD, once daily; SM-AHN, SM with an associated hematologic neoplasm.

Results from a Phase 1 trial of BLU-263 in healthy volunteers

BLU-263
NEXT-GENERATION KIT INHIBITOR

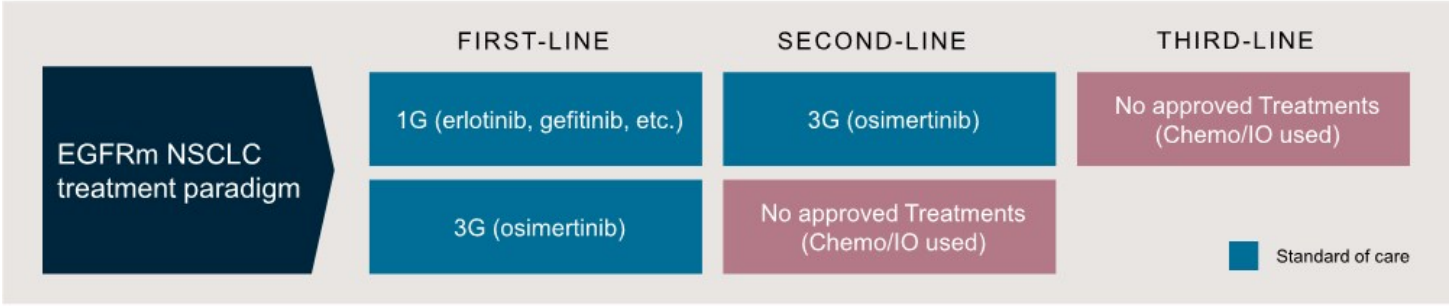
- BLU-263 was generally well-tolerated at all doses tested in healthy volunteers
- Pharmacokinetics were linear and dose-dependent
- Half-life supports once-daily dosing
- Plan to initiate Phase 2/3 HARBOR trial in non-advanced SM, at doses ranging 25-100 mg QD, in mid 2021

Treatment-related AEs, N of subjects	Single ascending dose cohorts	
	All other doses N=24	200 mg N=6
Any TRAE	0	1
Upper abdominal pain	0	1
Decreased appetite	0	1
Somnolence	0	0
Headache	0	0

Treatment-related AEs, N of subjects	Multiple ascending dose cohorts		
	25 mg N=6	50 mg N=6	100 mg N=6
Any TRAE	1	0	0
Upper abdominal pain	1	0	0
Fatigue	1	0	0
Chapped lips	1	0	0
Nausea	1	0	0
Headache	1	0	0

Data presented at AACR 2021 Annual Meeting. Data cut-off: November 9, 2020. AE, adverse event; TRAE, treatment-related AE.

Significant patient needs remain in EGFRm NSCLC across all lines of therapies



- Treatment resistance emerges over time which represents a significant barrier to durable benefit
- Chemotherapy +/- IO are the main treatment options post-osimertinib[1]
- CNS is a common site of metastases in EGFR driven NSCLC that needs to be targeted[2]
- **To improve durability and overall treatment outcome, we need effective, highly tolerated, brain-penetrant treatment options that target the most common on-target mutations early in initial therapy**

1. Piper-Vallillo, et al. Emerging treatment paradigms for EGFR-mutant lung cancers progressing on osimertinib. Journal of Clinical Oncology, 2020. 2. Remon and Besse. Brain metastases in oncogene-addicted NSCLC patients: incidence and treatment. Frontiers in Oncology, 2018. CNS, central nervous system; 1G, first-generation; 3G, third-generation; Chemo/IO, chemotherapy/immunotherapy.

BLU-701: potential best-in-class coverage of activating EGFR mutations, plus C797S osimertinib-resistant mutants

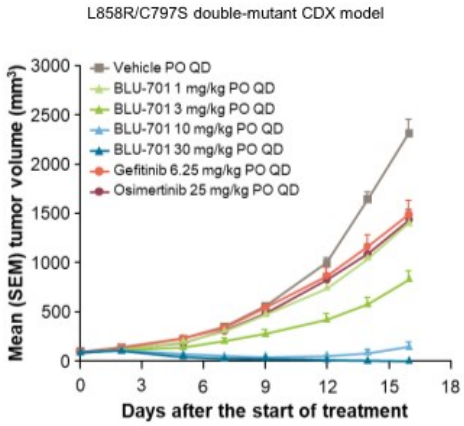
POTENCY ON ACTIVATING & RESISTANCE MUTANTS[1]

	BLU-701	gefitinib	osimertinib
ex19del	**3.3**	4.6	5.0
L858R	**3.3**	4.2	10.3
ex19del/C797S	**1.8**	6.1	>8000
L858R/C797S	**3.3**	3.8	>7000

WILD-TYPE SELECTIVITY[2]

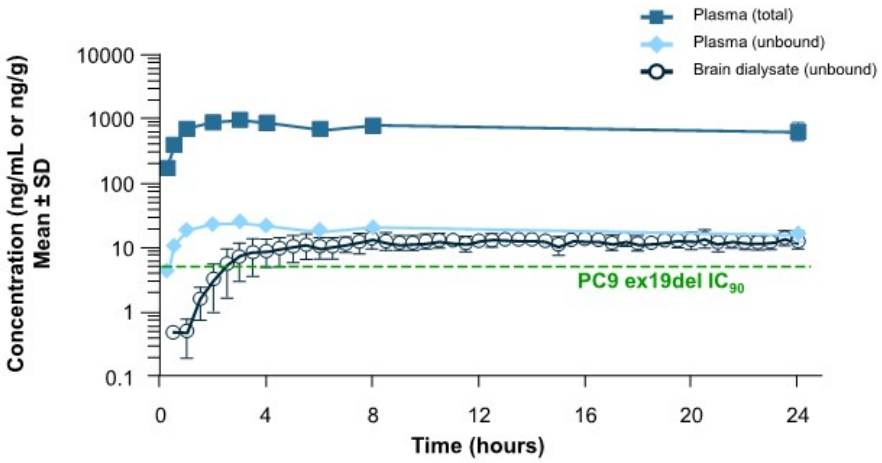
Wild-type EGFR	**107.3**	16.6	113.6

SINGLE AGENT ANTI-TUMOR ACTIVITY



Data presented at AACR 2021 Annual Meeting. 1. Cellular inhibition IC_{50} (nM) in Ba/F3 cell lines. 2. Cellular inhibition IC_{50} in A431 (wild-type EGFR) cell line. Wild-type EGFR selectivity shading: green = >50 nM; yellow = >10 nM, ≤50 nM. PO, oral administration. CDX, cell-line derived xenograft.

BLU-701 plasma and brain concentrations are comparable in preclinical models, suggesting significant brain penetration



Compound	IV infusion $Kp_{u,u}$ (C_{ss})[a]
BLU-701	0.98
Gefitinib	0.11
Osimertinib	0.30

BLU-701 30 MG/KG ACHIEVED CONCENTRATIONS ABOVE IC90 IN PLASMA AND BRAIN DIALYSATE

BLU-945: potential first-in-class triple-mutant EGFR inhibitor, with exceptional wild-type EGFR selectivity to enable combinations

POTENCY ON RESISTANCE MUTANTS[1]

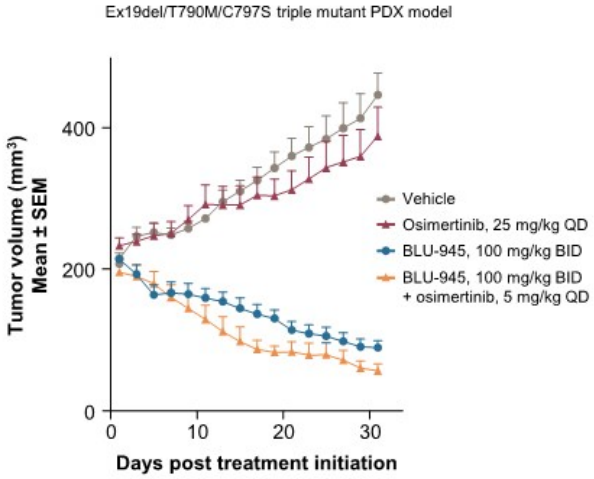
	BLU-945	gefitinib	osimertinib
L858R/T790M	**1.2**	4679.8	4.7
ex19del/T790M/C797S	**4.4**	4864.7	>10000
L858R/T790M/C797S	**2.9**	6707.7	7754.6

WILD-TYPE SELECTIVITY[2]

Wild-type EGFR	**544.4**	16.5	115.9

- BLU-945 demonstrated robust CNS activity in preclinical models

ANTI-TUMOR ACTIVITY ALONE AND IN COMBINATION WITH OSIMERTINIB



Data presented at AACR 2021 Annual Meeting. 1. Cellular inhibition IC_{50} (nM) in NCI-H1975 (EGFR double mutant) and Ba/F3 (EGFR triple mutant) cell lines. 2. Cellular inhibition IC_{50} in A431 (wild-type EGFR) cell line. Wild-type EGFR selectivity shading: green = >50 nM; yellow = >10 nM, ≤50 nM. PDX, patient-derived xenograft.

BLU-701 and BLU-945 provide comprehensive EGFR mutational coverage

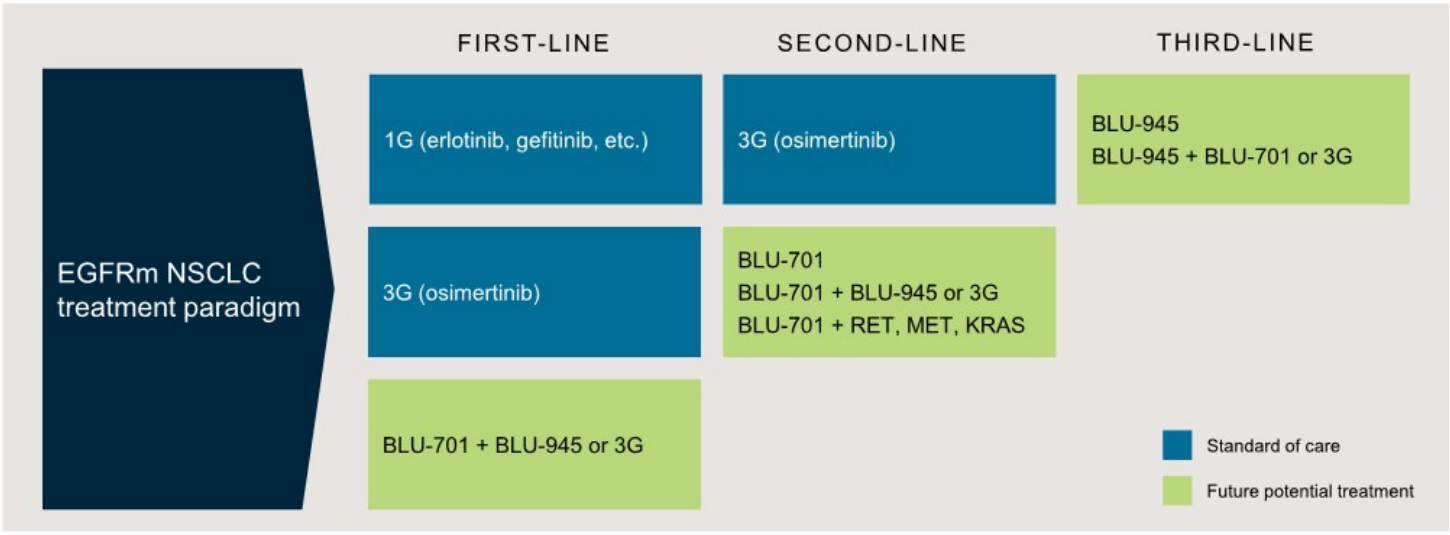
T790M & C797S: MOST COMMON ON-TARGET RESISTANCE TO 1G AND 3G, RESPECTIVELY

		1G	*3G*	*4G*		***Potential Combinations***		
	*EGFR mutational coverage**	*Gefitinib*	*Osimertinib*	*BLU-701*	*BLU-945*	*BLU-701 + osimertinib*	*BLU-945 + osimertinib*	*BLU-701 + BLU-945*
1L	L858R							
1L	ex19del							
2L	L858R or ex19del / T790M							
2L	L858R or ex19del / C797S							
3L	L858R or ex19del / T790M / C797S							

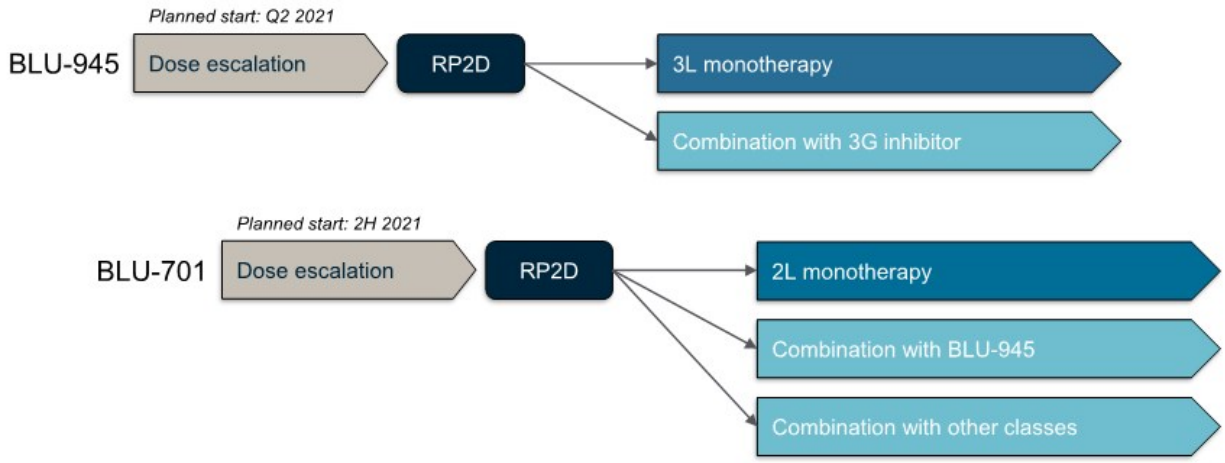
IC_{50} ≤10 nM 10 nM< IC_{50} ≤50 nM IC_{50} >50 nM

* Based on biochemical IC_{50}. 1L, first line; 2L, second line; 3L, third line; 4G, fourth generation.

We aim to transform EGFRm NSCLC treatment with 4G inhibitors that overcome or prevent on-target resistance across treatment lines

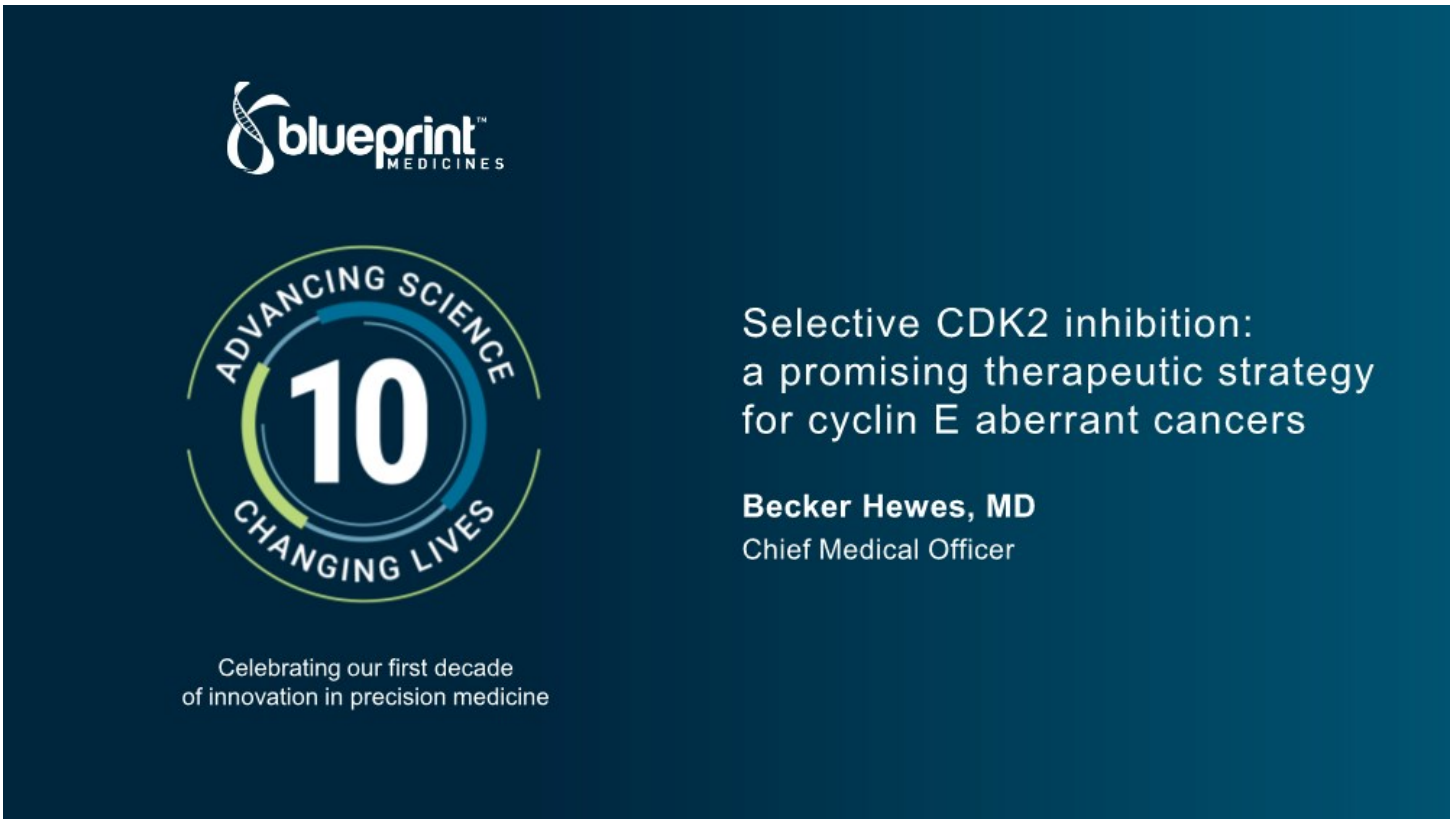


Plan to rapidly develop BLU-945 and BLU-701 monotherapy and combination regimens



BLU-945 IND APPLICATION CLEARED BY U.S. FDA

IND, investigational new drug application; RP2D, recommended Part 2 dose.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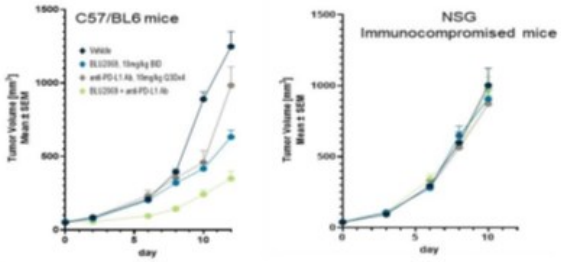
10
CHANGING LIVES
Celebrating our first decade
of innovation in precision medicine
Selective CDK2 inhibition:
a promising therapeutic strategy
for cyclin E aberrant cancers
Becker Hewes, MD
Chief Medical Officer

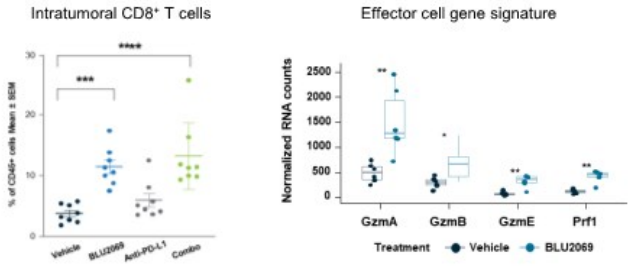
BLU-852, the first development candidate nominated under our cancer immunotherapy collaboration with Roche, has best-in-class potential

Compound	Enzyme activities IC_{50} (nM)			Cell activity IC_{50} or EC_{50} (nM)		Whole Blood activity IC_{50} or EC_{50} (nM)		Selectivity
	MAP4K1	LCK	MAP4K4	pSLP76*	IL-2†	pSLP76*	IL-2†	% kinome >100x
BLU2069	0.17	19	45	29	16	615	517	95%
BLU6348	0.13	78	73	27	11	1033	1194	96%
BLU-852	0.11	502	1196	40	11	851	1240	97%

ANTI-TUMOR ACTIVITY IN AN MCA-205 SARCOMA MODEL



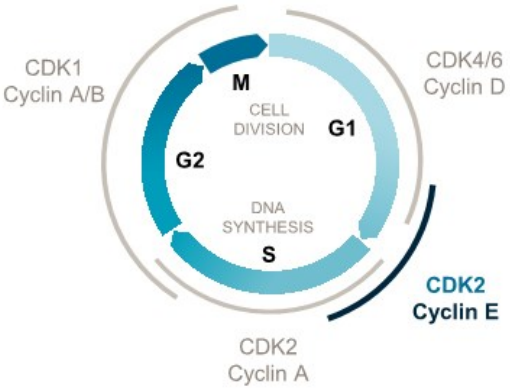
INCREASED CD8 T CELL FREQUENCY & ACTIVATION



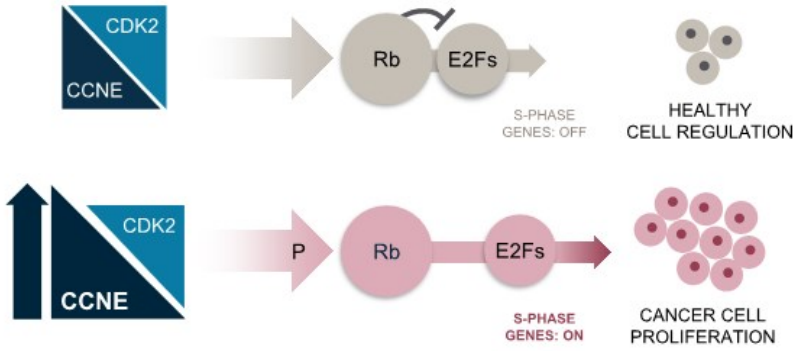
Data presented at AACR 2021 Annual Meeting. * IC_{50} values. † EC_{50} values. EC_{50}, half-maximal effective concentration; IC_{50}, half-maximal inhibitory concentration; nM, nanomolar.

Aberrant cyclin E unleashes cellular proliferation

CDK-CYCLIN COMPLEXES REGULATE THE CELL CYCLE



ABERRANT CYCLIN E (CCNE) DRIVES PROLIFERATION

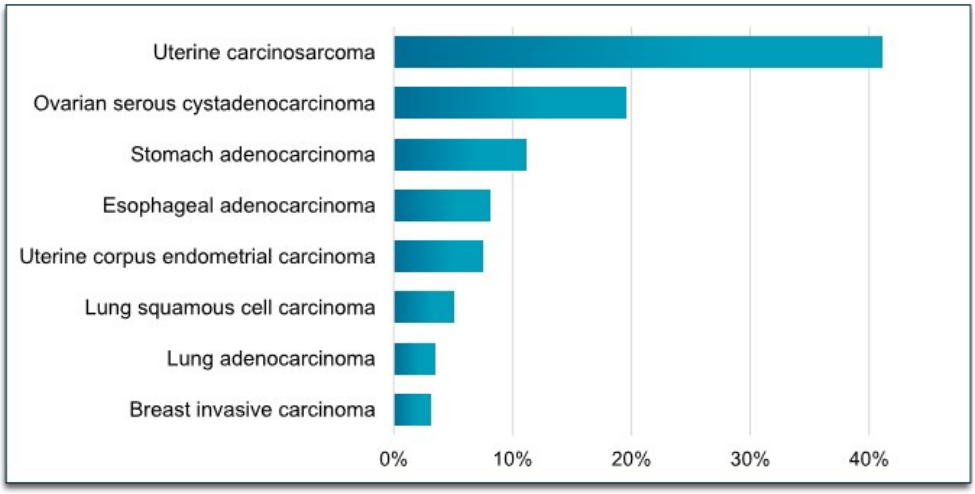


Aberrant CCNE hyperactivates CDK2, dysregulating Rb protein phosphorylation and E2F transcription factor activation of S-phase genes, resulting in cancer cell proliferation

E2F, E2F transcription factor; P, phosphorylation; Rb, retinoblastoma protein.

Aberrant CCNE is a disease driver in multiple cancers

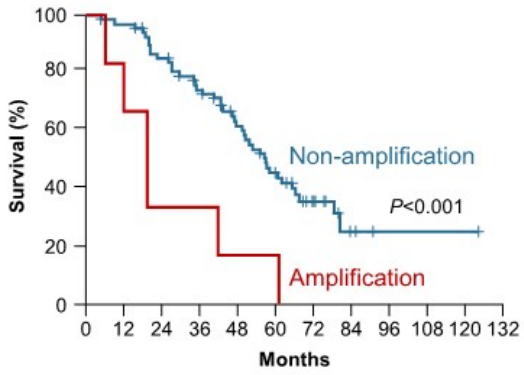
REPRESENTATIVE TUMOR TYPES
BY PERCENT FREQUENCY OF CCNE1 AMPLIFICATION



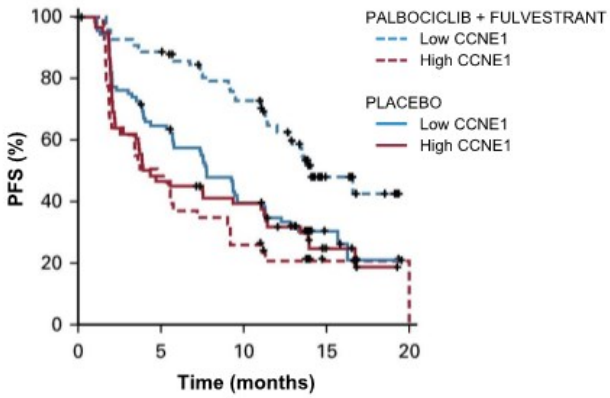
CCNE1 amplification frequency represented as percentage of total patient samples. Data from the National Cancer Institute's The Cancer Genome Atlas Program (www.cancer.gov/tcga).

Aberrant CCNE is associated with poor disease outcomes

CCNE1 AMPLIFICATION CORRELATES WITH POOR SURVIVAL IN OVARIAN CANCER[1]



PALBOCICLIB-TREATED HR+ BREAST CANCER PATIENTS WITH HIGH CCNE1 EXPRESSION HAD LOWER PFS[2]



1. Etemadmoghadam, et al. Amplicon-dependent CCNE1 expression is critical for clonogenic survival after cisplatin treatment and is correlated with 20q11 gain in ovarian cancer. Plos One, 2010. 2. Turner, et al. Cyclin E1 expression and palbociclib efficacy in previously treated hormone receptor-positive metastatic breast cancer. J Clin Oncol, 2019.

Our highly selective and potent CDK2 inhibitors spare CDK anti-targets

KEY ANTI-TARGETS

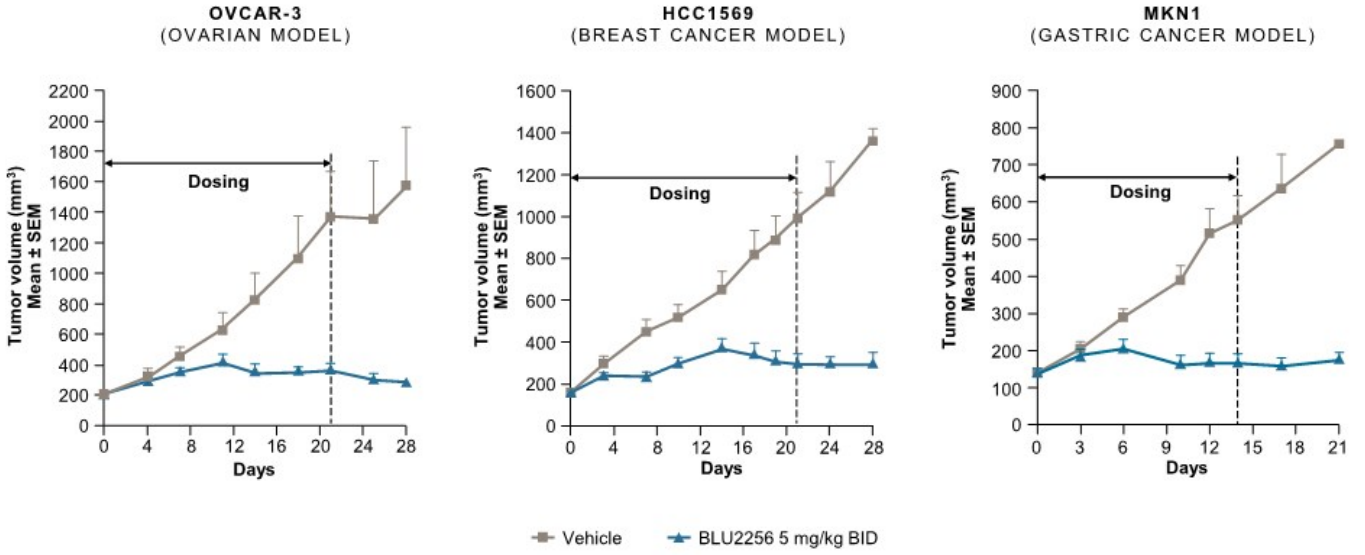
	ENZYME ACTIVITY IC_{50} (NM)						
	Kinome S (10)	CDK2	CDK1	CDK4	CDK6	CDK7	CDK9
BLU0298	0.045	2.6	233.6	377.4	275.2	6941.2	6115.1
BLU1954	0.055	0.2	110.1	114.5	190.6	3928.9	849.1
BLU2256	0.040	0.1	152.9	116.9	393.2	4826.4	9063.2

ASSOCIATED TOXICITIES:	Gastrointestinal	Hematologic

blueprint MEDICINES

Data presented at AACR 2021 Annual Meeting.

Selective CDK2 inhibition leads to sustained anti-tumor activity in CCNE1-amplified *in vivo* models



Data presented at AACR 2021 Annual Meeting. BID, twice daily.

Multiple pipeline programs driving to planned clinical data disclosures in 2022

BLU-263
NEXT-GENERATION KIT INHIBITOR

- Initiate Phase 2/3 HARBOR trial of BLU-263 in non-advanced systemic mastocytosis in mid 2021

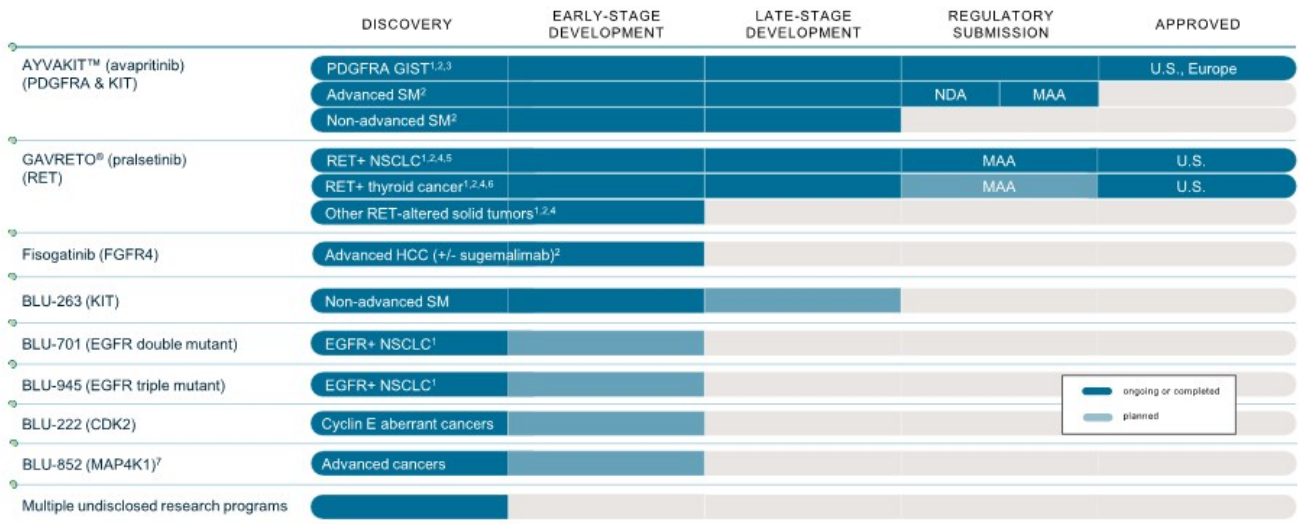
BLU-701 AND BLU-945
POTENTIAL FIRST- AND BEST-IN-CLASS 4G EGFR INHIBITORS

- Initiate Phase 1 trial of BLU-945 in Q2 2021
- Initiate Phase 1 trial of BLU-701 in 2H 2021
- Report preclinical combination data in 2H 2021

BLU-222
POTENTIAL BEST-IN-CLASS CDK2 INHIBITOR

- Initiate IND-enabling studies in Q2 2021
- Report additional preclinical data in 2H 2021
- Initiate Phase 1 trial of BLU-222 in 1H 2022

Rapidly expanding portfolio highlights precision therapy leadership



1. Unresectable or metastatic disease. 2. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan. 3. Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. Received conditional marketing authorization in Europe under the brand name AYVAKYT® for the treatment of adults with unresectable or metastatic GIST harboring the PDGFRA D842V mutation. 4. In collaboration with Roche. Blueprint Medicines and Roche have co-exclusive rights to develop and commercialize pralsetinib in the U.S., and Roche has exclusive rights to develop and commercialize pralsetinib outside the U.S., excluding the CStone territory. 5. Received accelerated approval in the U.S. for the treatment of adults with metastatic RET fusion-positive NSCLC. Continued approval may be contingent on a confirmatory trial. The proposed indication for the MAA is locally advanced or metastatic RET fusion-positive NSCLC previously treated with platinum-based chemotherapy. 6. Received accelerated approval in the U.S. for the treatment of patients with advanced or metastatic RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer. Continued approval may be contingent on confirmatory trials. 7. In collaboration with Roche. Blueprint Medicines and Roche are conducting activities for up to two programs under the collaboration, including the program targeting MAP4K1. For one of the programs, Blueprint Medicines has U.S. commercial rights and Roche has ex-U.S. commercialization rights. For one of the programs, Roche has worldwide commercialization rights. GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; MAA, marketing authorization application; NDA, new drug application; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

Updated as of April 12, 2021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MEDICINES


ADVANCING SCIENCE
10
CHANGING LIVES

Blueprint Medicines Presents Preclinical Data Highlighting Broad Precision Therapy Research Pipeline at AACR Annual Meeting 2021

-- Preclinical data presented at AACR highlight four precision therapies with first- or best-in-class potential --

-- IND application cleared by FDA for BLU-945, a triple-mutant EGFR inhibitor for EGFR-driven lung cancer --

-- Nominated BLU-222, a selective and potent CDK2 inhibitor development candidate, for cyclin E-aberrant cancers --

-- Blueprint Medicines to host investor conference call and webcast on Monday, April 12 at 8:00 a.m. ET --

CAMBRIDGE, Mass., April 10, 2021 – Blueprint Medicines Corporation (NASDAQ: BPMC) today announced data from multiple poster presentations highlighting the breadth of the company's precision therapy pipeline at the virtual American Association for Cancer Research (AACR) Annual Meeting 2021. Collectively, the presentations, including foundational preclinical data for multiple programs, demonstrate the productivity of the company's scientific platform. Additional presentations of clinical data for AYVAKIT™ (avapritinib) and BLU-263 will be reported on Sunday, April 11, 2021.

"Our data presentations at the AACR annual meeting showcase Blueprint Medicines' next wave of precision therapies, which have the potential to impact large global patient populations," said Fouad Namouni, M.D., President, Research & Development at Blueprint Medicines. "Building on the foundation of our approved medicines AYVAKIT and GAVRETO®, these presentations highlight our efforts to address significant patient needs in areas such as EGFR-driven lung cancer, cyclin E-aberrant cancers and cancer immunotherapy. As we celebrate our 10th anniversary as a company, and our rapidly expanding pipeline now includes our ninth development candidate, we look forward to continuing to leverage our productive research platform to advance potent and selective inhibitors that have the potential to enable transformative benefit for patients."

BLU-701 and BLU-945: Double- and triple-mutant inhibitors in EGFR-driven NSCLC

Lung cancer is the leading cause of cancer death globally, and approximately 17 percent of patients with lung adenocarcinoma, the most common form of non-small cell lung cancer (NSCLC), have EGFR-driven disease. While first- and third-generation EGFR inhibitors have improved treatment outcomes for patients with EGFR-driven NSCLC, resistance inevitably emerges, with the T790M and C797S mutations being the most common on-target resistance mechanisms. Together, BLU-701 and BLU-945 are designed to provide comprehensive coverage of the most common activating and on-target resistance mutations, spare wild-type EGFR to limit toxicities driven by wild-type EGFR inhibition and treat or prevent central nervous system (CNS) metastases. Ultimately, with these characteristics, BLU-701 and BLU-945 have the potential to be used either as monotherapy or in combination, together or with other agents, to potentially overcome or prevent on-target resistance across multiple lines of treatment.

BLU-701 is a potential best-in-class, selective, potent, fourth-generation double-mutant EGFR inhibitor with activity against EGFR activating mutations and the C797S osimertinib-resistant mutation. Preclinical data presented at the conference showed strong and durable inhibition of tumor growth at doses that are EGFR wild-type sparing. BLU-701 also indicated significant CNS penetration in preclinical models, with comparable exposure in the plasma and brain, which illustrates its potential to treat or prevent CNS metastases in patients with EGFR-driven tumors. With activity also shown against the activating EGFR mutants, BLU-701 has potential to be used in both first- and second-line settings.

BLU-945 is a potential first- and best-in-class, selective, potent, fourth-generation triple-mutant EGFR inhibitor with activity against the T790M and C797S resistance mutations. BLU-945 is highly selective over wild-type EGFR and off-target kinases, highlighting its potential to enable tolerable combinations with BLU-701 or other therapies. Data presented at the conference demonstrated potent anti-tumor activity in triple-mutant osimertinib-resistant tumor models, as well as activity in a triple-mutant intracranial patient-derived xenograft model. In addition, the combination of BLU-945 with either gefitinib or osimertinib showed enhanced anti-tumor activity when compared with either gefitinib or osimertinib alone.

The preclinical data presented for BLU-701 and BLU-945 support the continued development of both candidates in patients with EGFR-driven NSCLC. An investigational new drug (IND) application for BLU-945 has been cleared by the U.S. Food and Drug Administration (FDA) and an international Phase 1 dose escalation trial is expected to begin this quarter. Future clinical development of BLU-945 in combination with other agents across multiple treatment settings is planned. BLU-701 is expected to enter clinical development later this year.

BLU-222: CDK2 inhibitor in cyclin E-aberrant cancers

Cyclin dependent kinases (CDKs) and their cyclin partners regulate the cell cycle. In subsets of patients across multiple cancer types, aberrant cyclin E (CCNE) hyperactivates CDK2, resulting in cell cycle dysregulation and tumor proliferation. Aberrant CCNE has been observed as a primary driver of disease as well as a mechanism of resistance to CDK4/6 inhibitors and other therapies. In addition, data have shown that ovarian and hormone-receptor-positive breast cancer patients with aberrant CCNE have poor outcomes. Prior drug discovery efforts targeting CDK2 have been hindered by challenges in achieving selectivity over other CDK family members associated with toxicity.

At AACR, preclinical data highlighted a set of potent and selective CDK2 inhibitors designed by Blueprint Medicines. The data showed that selective CDK2 inhibition arrested the cell cycle and blocked tumor proliferation in CCNE-amplified cell lines and demonstrated robust and sustained anti-tumor activity in vivo in models of CCNE-amplified ovarian, breast and gastric cancer. A selective CDK2 inhibitor also showed improved tolerability compared to a pan-CDK inhibitor and chemotherapy, as measured by animal body weight.

Based on this work and further optimization, Blueprint Medicines today announced the nomination of a potentially best-in-class selective and potent CDK2 inhibitor development candidate, BLU-222, which is expected to enter clinical development in the first half of 2022.

BLU-852: MAP4K1 inhibitor

MAP4K1 is a well-characterized immunokinase target involved in the regulation of immune cells; however, prior drug discovery efforts have been hindered by challenges in achieving selectivity over other MAP4K family members associated with toxicity. In January 2021, Blueprint Medicines announced the nomination of a highly selective and potent MAP4K1 inhibitor development candidate, BLU-852, with best-in-class potential.

Data presented at AACR highlighted a set of potent and highly selective MAP4K1 inhibitors designed by Blueprint Medicines, including BLU-852. The inhibitors were shown to enhance intratumoral immune cell activation, overcome T cell suppression, and reduce tumor burden both as a monotherapy and in combination with checkpoint inhibition. The data support the continued development of BLU-852 under the company’s cancer immunotherapy collaboration with Roche, with Phase 1 trial initiation anticipated in 2022.

Copies of Blueprint Medicines data presentations from the AACR annual meeting are available in the “Science—Publications and Presentations” section of the company’s website at www.BlueprintMedicines.com.

Conference Call Information

Blueprint Medicines will host a live webcast on Monday, April 12, 2021 beginning at 8:00 a.m. ET to review data for multiple research- and clinical-stage programs presented at the AACR annual meeting. To access the live call, please dial (855) 728-4793 (domestic) or (503) 343-6666 (international) and refer to conference ID 5548976. A webcast of the conference call will be available under ”Events and Presentations” in the Investors & Media section of Blueprint Medicines’ website at http://ir.blueprintmedicines.com. The archived webcast will be available on Blueprint Medicines’ website approximately two hours after the conference call and will be available for 30 days following the call.

About Blueprint Medicines

Blueprint Medicines is a global precision therapy company that invents life-changing medicines for people with cancer and hematologic disorders. Applying an approach that is both precise and agile, we create therapies that selectively target genetic drivers, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. Today, we are delivering our approved medicines to patients in the United States and Europe, and we are globally advancing multiple programs for genomically defined cancers, systemic mastocytosis, and cancer immunotherapy. For more information, visit www.BlueprintMedicines.com and follow us on Twitter (@BlueprintMeds) and LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding the plans, timing, designs, implementation, enrollment and announcement of results regarding Blueprint Medicines’ ongoing and planned clinical trials for its drug candidates; the potential benefits of Blueprint Medicines’ current and future drug candidates in treating patients; and Blueprint Medicines’ strategy, goals and anticipated milestones, business plans and focus. The words “aim,” “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “target” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management’s current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks and uncertainties related to the impact of the COVID-19 pandemic to Blueprint Medicines’ business, operations, strategy, goals and anticipated milestones, including Blueprint Medicines’ ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products; Blueprint Medicines’ ability and plans in establishing a commercial infrastructure, and successfully launching, marketing and selling current or future approved products, including AYVAKIT™/AYVAKYT® (avapritinib) and GAVRETO® (pralsetinib); Blueprint Medicines’ ability to successfully expand the approved indications for AYVAKIT/AYVAKYT and GAVRETO or obtain marketing approval for AYVAKIT/AYVAKYT and GAVRETO in additional geographies in the

future; the delay of any current or planned clinical trials or the development of Blueprint Medicines' current or future drug candidates; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; the preclinical and clinical results for Blueprint Medicines' drug candidates, which may not support further development of such drug candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for its current and future drug candidates; and the success of Blueprint Medicines' current and future collaborations, partnerships or licensing arrangements. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' filings with the Securities and Exchange Commission (SEC), including Blueprint Medicines' most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q and any other filings that Blueprint Medicines has made or may make with the SEC in the future. Any forward-looking statements contained in this press release represent Blueprint Medicines' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements.

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Media Contact

Andrew Law
617-844-8205
media@blueprintmedicines.com

Investor Relations Contact

Kristin Hodous
617-714-6674
ir@blueprintmedicines.com

Blueprint Medicines Data Highlight Clinical Leadership in Systemic Mastocytosis at AACR Annual Meeting 2021

-- 75% confirmed ORR, with all responses ongoing, in PATHFINDER trial of AYVAKIT in advanced SM --

-- New patient-reported outcomes data from PATHFINDER trial show AYVAKIT significantly reduced disease symptoms and improved quality of life --

-- BLU-263 was well-tolerated across all doses tested in Phase 1 healthy volunteer trial, supporting plans to initiate Phase 2/3 HARBOR trial in non-advanced SM in mid-2021 --

-- Blueprint Medicines to host investor conference call and webcast on Monday, April 12 at 8:00 a.m. ET --

CAMBRIDGE, Mass., April 11, 2021 – Blueprint Medicines Corporation (NASDAQ: BPMC) today announced that multiple presentations across the company's leading systemic mastocytosis (SM) program are being reported at the virtual American Association for Cancer Research (AACR) Annual Meeting 2021. The presentations focus on registrational PATHFINDER trial data of AYVAKIT™ (avapritinib) in advanced SM, PIONEER Part 1 data highlighting the impact of AYVAKIT on skin manifestations of SM, and Phase 1 trial data for BLU-263, a next-generation KIT D816V inhibitor. Blueprint Medicines is developing AYVAKIT for advanced and non-advanced SM, and BLU-263 to further address the range of patient needs in non-advanced SM and other mast cell disorders.

"Data reported at AACR reflect our commitment to transform treatment for patients living with systemic mastocytosis," said Becker Hewes, M.D., Chief Medical Officer at Blueprint Medicines. "In the PATHFINDER trial, AYVAKIT had high response rates consistent with EXPLORER trial data, reinforcing the profound clinical benefits that can be achieved by precisely targeting the underlying driver of disease. For BLU-263, data in healthy volunteers showed a well-tolerated safety profile and support our plans to initiate the Phase 2/3 HARBOR study, which expands our development efforts into a broader population of patients with non-advanced SM. We are currently on the precipice of our first potential approval in advanced SM, and we are committed to working closely with the SM community so we may meet the needs of patients as quickly as possible."

AYVAKIT – Highlights from the Registrational Phase 2 PATHFINDER Trial

In a pre-specified interim analysis from the PATHFINDER trial, 32 patients who primarily received a starting dose of 200 mg once daily were evaluable for response, as of a data cutoff date of June 23, 2020. Combined with Phase 1 EXPLORER trial results, these data support Blueprint Medicines' marketing applications in advanced SM under review in the U.S. and Europe. Overall, 75 percent (95% CI: 57%, 89%) of patients had a confirmed response, which was defined as complete remission with full or partial recovery of peripheral blood counts (CR/CRh), partial remission or clinical improvement. The median time to response was two months, and all responses were ongoing at a median follow-up of 10.4 months. The CRh rate was 19 percent, with a median time to CRh of 5.6 months. These results show that responses deepened over time at a rate consistent with the EXPLORER trial.

AYVAKIT led to robust and durable benefits across a number of additional clinical activity measures. In new patient-reported outcomes data, AYVAKIT showed a statistically significant reduction in total symptom score after 40 weeks ($p<0.001$), as measured by the Advanced Systemic Mastocytosis Symptom Assessment Form. Treatment with AYVAKIT resulted in robust improvements in patient-reported quality of life, based on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire. Across multiple measures of mast cell burden, AYVAKIT showed profound reductions in serum tryptase, bone marrow mast cells, KIT D816V allele burden and spleen volume.

Consistent with previously disclosed data, AYVAKIT was generally well-tolerated in 62 patients enrolled in the PATHFINDER trial, and most adverse events (AEs) were reported as Grade 1 or 2. The most common AEs (≥15 percent) were peripheral edema, periorbital edema, thrombocytopenia, anemia, neutropenia, diarrhea, nausea, vomiting and fatigue. Three patients (5 percent) discontinued AYVAKIT due to treatment-related AEs, and most patients (84 percent) have remained on treatment as of the data cutoff date.

“These data reinforce the potential of avapritinib to improve the standard of care for patients with advanced systemic mastocytosis, a disease characterized by organ damage due to mast cell infiltration,” said Daniel DeAngelo, M.D., Ph.D., Chief of the Division of Leukemia at Dana-Farber Cancer Institute. “I am highly encouraged by the rapid and durable responses shown across multiple measures of mast cell burden, patient-reported symptoms as well as quality of life. Furthermore, avapritinib was generally well-tolerated, with 5 percent of patients discontinuing due to treatment-related adverse events. Since avapritinib is able to selectively target the primary driver of the disease, it has the potential to fundamentally change the outlook for patients with advanced SM.”

AYVAKIT – Statistically Significant Reductions of Aberrant CD30-Positive Mast Cells in Skin Lesions Shown in Phase 2 PIONEER Trial

In non-advanced SM, skin symptoms frequently persist and can severely impact quality of life. To assess the effects of AYVAKIT on mast cell burden in skin lesions, skin biopsies were obtained at baseline and week 12 in Part 1 of the PIONEER trial. Immunohistochemistry tests were performed to determine the proportion of aberrant mast cells in skin tissue, based on expression of CD25, CD30 and other transmembrane receptors observed in SM. Skin lesional tissue at baseline had more CD30-positive than CD25-positive mast cells. Following 12 weeks of treatment, AYVAKIT significantly reduced the proportion of aberrant CD30-positive mast cells in skin lesions compared to placebo (p=0.0082), as of a data cutoff date of December 4, 2020. These data expand on previously reported results showing the impact of AYVAKIT on skin manifestations of SM, and suggest that CD30 may be an important biomarker of aberrant mast cells in SM-related skin lesions.

BLU-263 – Safety and Pharmacokinetics Profile from Phase 1 Trial in Healthy Volunteers

A placebo-controlled, Phase 1 trial evaluated the safety, tolerability and pharmacokinetics of BLU-263 in healthy volunteers. This AACR presentation reported on single ascending dose cohorts (15 to 200 mg doses) and multiple ascending dose cohorts (25 to 100 mg once-daily doses for ten consecutive days), as of a data cutoff date of November 9, 2020. BLU-263 was well-tolerated across all doses studied, and all AEs were reported as Grade 1. Pharmacokinetic data showed dose-dependent increases in systemic exposure of BLU-263, with the half-life of BLU-263 supporting once-daily dosing. Based on these results, the company plans to evaluate BLU-263 at doses ranging from 25 to 100 mg once daily in Part 1 of the Phase 2/3 HARBOR trial in patients with non-advanced SM, which the company plans to initiate in mid-2021.

Copies of Blueprint Medicines data presentations from the AACR annual meeting are available in the “Science—Publications and Presentations” section of the company’s website at www.BlueprintMedicines.com.

Conference Call Information

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About SM

SM is a rare disease driven by the KIT D816V mutation. Uncontrolled proliferation and activation of mast cells result in chronic, severe and often unpredictable symptoms for patients across the spectrum of SM. The vast majority of those affected have non-advanced (indolent or smoldering) SM, with debilitating symptoms that lead to a profound, negative impact on quality of life. A minority of patients have advanced SM, which encompasses a group of high-risk SM subtypes including aggressive SM, SM with an associated hematological neoplasm and mast cell leukemia. In addition to mast cell activation symptoms, advanced SM is associated with organ damage due to mast cell infiltration and poor survival.

Debilitating symptoms, including anaphylaxis, maculopapular rash, pruritis, diarrhea, brain fog, fatigue and bone pain, often persist across all forms of SM despite treatment with a number of symptomatic therapies. Patients often live in fear of severe, unexpected symptoms, have limited ability to work or perform daily activities, and isolate themselves to protect against unpredictable triggers. Currently, there are no approved therapies for the treatment of SM that selectively inhibit D816V mutant KIT.

About AYVAKIT (avapritinib)

AYVAKIT (avapritinib) is a kinase inhibitor approved by the U.S. Food and Drug Administration (FDA) for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumors (GIST) harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. For more information, visit www.AYVAKIT.com. This medicine is approved in Europe under the brand name AYVAKYT® for the treatment of adults with unresectable or metastatic GIST harboring the PDGFRA D842V mutation, and in China for the treatment of adults with unresectable or metastatic PDGFRA exon 18 mutant GIST.

AYVAKIT/AYVAKYT is not approved for the treatment of any other indication, including SM, in the U.S. by the FDA, in Europe by the European Commission or in China by the National Medical Products Administration, or for any indication in any other jurisdiction by any other health authority.

Blueprint Medicines is developing AYVAKIT globally for the treatment of advanced and non-advanced SM. The FDA granted breakthrough therapy designation to AYVAKIT for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematological neoplasm and mast cell leukemia, and for the treatment of moderate to severe indolent SM.

To learn about ongoing or planned clinical trials, contact Blueprint Medicines at medinfo@blueprintmedicines.com or 1-888-BLU-PRNT (1-888-258-7768). Additional information is available at www.pioneertrial.com or www.clinicaltrials.gov.

Blueprint Medicines has an exclusive collaboration and license agreement with CStone Pharmaceuticals for the development and commercialization of AYVAKIT in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains development and commercial rights for AYVAKIT in the rest of the world.

About BLU-263

BLU-263, a next-generation KIT D816V inhibitor, has the potential to expand the reach of KIT D816V-targeted therapy to a broad population of patients with non-advanced SM and related mast cell disorders. BLU-263 was designed to target D816V mutant KIT with similar sub-nanomolar potency as AYVAKIT, enhanced selectivity and minimal central nervous system penetration. BLU-263 was developed based on learnings from the AYVAKIT clinical program. The initial focus of the BLU-263 development program is non-advanced SM.

About Blueprint Medicines

Blueprint Medicines is a global precision therapy company that invents life-changing medicines for people with cancer and hematologic disorders. Applying an approach that is both precise and agile, we create therapies that selectively target genetic drivers, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. Today, we are delivering our approved medicines to patients in the United States and Europe, and we are globally advancing multiple programs for genomically defined cancers, systemic mastocytosis, and cancer immunotherapy. For more information, visit www.BlueprintMedicines.com and follow us on Twitter (@BlueprintMeds) and LinkedIn.

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the future; the delay of any current or planned clinical trials or the development of Blueprint Medicines' current or future drug candidates; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; the preclinical and clinical results for Blueprint Medicines' drug candidates, which may not support further development of such drug candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for its current and future drug candidates; and the success of Blueprint Medicines' current and future collaborations, partnerships or licensing arrangements. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' filings with the Securities and Exchange Commission (SEC), including Blueprint Medicines' most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q and any other filings that Blueprint Medicines has made or may make with the SEC in the future. Any forward-looking statements contained in this press release represent Blueprint Medicines' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements.

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Media Contact

Andrew Law
617-844-8205
media@blueprintmedicines.com

Investor Relations Contact

Kristin Hodous
617-714-6674
ir@blueprintmedicines.com