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): **June 3, 2019**

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**	**02139**
(Address of principal executive offices)	(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:

- o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- o 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 Disclosure.

On June 3, 2019, Blueprint Medicines Corporation hosted an investor call and live webcast to discuss updated data from its Phase 1 ARROW clinical trial evaluating BLU-667 for the treatment of patients with RET-altered non-small cell cancer, medullary thyroid cancer and other advanced solid tumors and from its Phase 1 NAVIGATOR clinical trial evaluating avapritinib for the treatment of patients with advanced gastrointestinal stromal tumors, which were presented at the American Society of Clinical Oncology 2019 Annual Meeting in Chicago, Illinois. A copy of the presentation from the investor call 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, 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 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Presentation by Blueprint Medicines Corporation at investor call on June 3, 2019

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: June 4, 2019

By: /s/ Tracey L. McCain

Tracey L. McCain
Chief Legal Officer

Exhibit 99.1


blueprint MEDICINES
Advances in Precision Oncology:
BLU-667 data review and portfolio update
2019 ASCO Annual Meeting
JUNE 3, 2019
Diane Legg, founder of LUNGSTRONG visits Blueprint Medicines in June 2018

Forward-looking statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. The words "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 about plans and timelines for the development of avapritinib and BLU-667 and the ability of Blueprint Medicines Corporation (the "Company") to implement those development plans; the potential benefits of Blueprint Medicines' current and future drug candidates in treating patients; plans and timelines for marketed products and marketing applications in the United States and Europe, therapeutic candidates in clinical development and research programs; and the Company's strategy, key 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 delay of any current or planned clinical trials or the development of the Company's drug candidates, including avapritinib, BLU-667, BLU-554 and BLU-782; 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; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for any drug candidates it is developing; the Company's ability to develop and commercialize companion diagnostic tests for its current and future drug candidates; and the success of the Company's current and future collaborations, including its cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. and its collaboration with CStone Pharmaceuticals.

These and other risks and uncertainties are described in greater detail under "Risk Factors" in the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2019, as filed with the Securities and Exchange Commission ("SEC") on May 9, 2019, and any other filings the Company 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 the Company's 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.

Agenda

Introduction and portfolio update	**Jeff Albers** Chief Executive Officer
BLU-667 clinical data review	**Benjamin Besse, M.D., Ph.D.** Head of Cancer Medicine Department, Gustave Roussy Cancer Center
BLU-667 program strategy	**Andy Boral, M.D., Ph.D.** Chief Medical Officer
Questions and answers	**All**
Closing remarks	**Jeff Albers** Chief Executive Officer

Precision therapies for people with cancer and rare diseases

A NEW WAY OF LOOKING AT KINASE MEDICINES

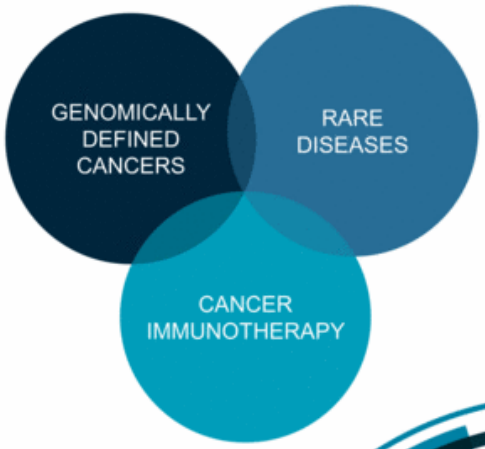
SELECTIVE

avapritinib

NON-SELECTIVE

Rydapt® (midostaurin)

WITH A FOCUS ON CORE AREAS OF EXPERTISE



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Our vision for building the leading precision therapy company

Rapid, reproducible product development

Robust scientific platform to design selective kinase medicines

Disciplined portfolio management focused on therapeutic area leadership

Effective and nimble commercial organization with global reach

Reinvestment of revenue to sustain constant innovation cycle

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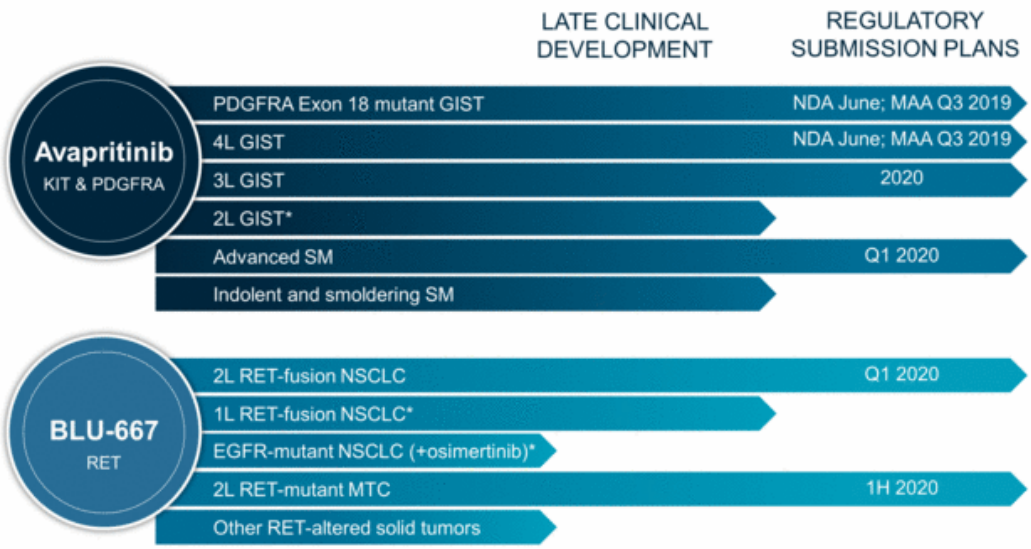
Rapidly advancing pipeline of investigational precision therapies

DRUG CANDIDATE (TARGET)	DISCOVERY	EARLY CLINICAL DEVELOPMENT	LATE CLINICAL DEVELOPMENT	REGULATORY SUBMISSION	APPROVED	COMMERCIAL RIGHTS
Avapritinib (KIT & PDGFRA)	PDGFRA Exon 18 mutant GIST [1]			NDA planned June 2019		
	4L GIST [1]			NDA planned June 2019		
	3L GIST [1]			NDA planned 2020		
	2L GIST [1]		trial planned 2H 2019			
	Advanced SM			NDA planned Q1 2020		
	Indolent and smoldering SM					
BLU-667 (RET)	2L RET-fusion NSCLC [1]			NDA planned Q1 2020		
	1L RET-fusion NSCLC [1] – trial planned 2H 2019					
	EGFR-m NSCLC (+osimertinib) [1] – trial planned 2H 2019					
	2L RET-mutant MTC [1]			NDA planned 1H 2020		
	Other RET-altered solid tumors [1]					
BLU-554 (FGFR4)	Advanced HCC					
	Advanced HCC (+CS-1001) – trial planned 2H 2019					
BLU-782 (ALK2)	FOP [2]					
4 undisclosed targets						
Immunokinase targets	Up to 5 cancer immunotherapy programs; development stage undisclosed					

EGFR-m, EGFR mutant; FOP, fibrodysplasia ossificans progressive; GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; NSCLC, non-small cell lung cancer; MTC, medullary thyroid cancer; SM, systemic mastocytosis. [1] Unresectable or metastatic disease. [2] Phase 1 trial in healthy volunteers ongoing. Phase 2 trial in patients with FOP planned Q4 2019. * CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, BLU-554 and BLU-667 in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains all rights in the rest of the world. ** Blueprint Medicines has U.S. commercial rights for up to two programs. Roche has worldwide commercialization rights for up to three programs and ex-U.S. commercialization rights for up to two programs.

Multiple planned marketing applications to support our rapid evolution into a fully-integrated biopharmaceutical company



Clinical Experience

~1,000

people enrolled across avapritinib and BLU-667 trials

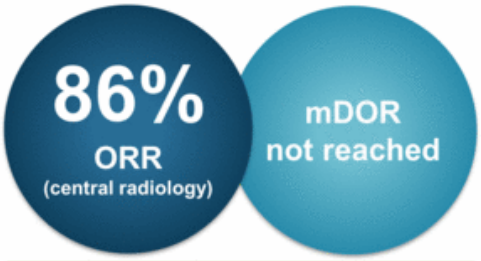
7

ongoing or planned global registration-enabling trials

* Trials planned to initiate 2H 2019.
All target GIST, NSCLC and MTC populations have unresectable or metastatic disease. MAA, marketing authorization application; NDA, new drug application.

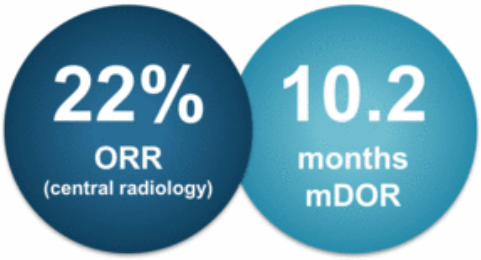
Data presented at ASCO to form the basis of initial planned global marketing applications for avapritinib in advanced GIST

PDGFRA Exon 18 Mutant GIST (n=43)[1]



Breakthrough Therapy Designation[2]

4L GIST (n=111)[1]



Safety Results (N=204):

- Avapritinib was generally well-tolerated and most AEs reported by investigators were Grade 1 or 2
- Grade ≥3 treatment-related AEs included anemia, fatigue, blood bilirubin increased, cognitive effects and diarrhea
- Relative dose intensity was 86% at 300 mg QD, the recommended dose for planned marketing applications
- Across all doses, 8.3% of patients discontinued avapritinib due to treatment-related AEs

Plan to submit NDA for PDGFRA Exon 18 mutant and 4L GIST in June 2019

[1] Patients treated with a starting dose of 300 or 400 mg QD. One response pending confirmation for ORR in PDGFRA Exon 18 mutant GIST and for ORR in 4L GIST.
[2] Avapritinib granted Breakthrough Therapy Designation for the treatment of patients with unresectable or metastatic GIST harboring the PDGFRα D842V mutation.
Data reported at ASCO 2019 Annual Meeting on June 1, 2019. Data cutoff date: November 16, 2018.
AE, adverse events; mDOR, median duration of response; ORR, objective response rate; QD, once daily.

BLU-667 clinical profile aligns with opportunities in RET-altered cancers

Promising emerging BLU-667 clinical profile

- ✓ **High response rates and durable anti-tumor activity** regardless of RET genotype, tumor type or prior therapy
  - Strong activity against brain metastases in NSCLC patients
- ✓ **Favorable safety profile** with low discontinuation rates in advanced cancer populations
- ✓ Regulatory feedback on expedited development and **Breakthrough Therapy Designations for NSCLC and MTC**
- • **Plan to submit NDA** for previously treated NSCLC in Q1 2020 and previously treated MTC in 1H 2020

Significant opportunities to impact patient care

RET fusion+ NSCLC

~1–2% of NSCLC

RET mutation+ MTC

~90% of advanced MTC

Tumor agnostic RET+ cancers

Low variable RET frequency across tumor types

Resistant EGFR mutation+ NSCLC

Growing understanding of RET-driven resistance

Data reported at ASCO 2019 Annual Meeting on June 1 and 3, 2019. Data cutoff date: April 28, 2019.
1. Lipson, et al. *Nat Med* 2012; 2. Takeuchi, et al. *Nat Med 2012*; 3. Romei, et al. *Oncotarget* 2018.
BLU-667 granted Breakthrough Therapy Designation for the treatment of patients with RET-fusion positive NSCLC that has progressed following platinum-based chemotherapy and for the treatment of patients with RET mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments.

BLU-667 clinical data review

Benjamin Besse, M.D., Ph.D.
Gustave Roussy Cancer Center

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Clinical Activity and Tolerability of BLU-667, a Highly Potent and Selective RET Inhibitor, in Patients with Advanced RET-Fusion+ Non-small Cell Lung Cancer (Oral Abstract 9008)

Justin F. Gainor, Dae Ho Lee, Giuseppe Curigliano, Robert C. Doebele, Dong-Wan Kim, Christina S. Baik, Daniel Shao-Weng Tan, Gilberto Lopes, Shirish M. Gadgeel, Philippe Alexandre Cassier, Matthew H. Taylor, Stephen V. Liu, **Benjamin Besse**, Michael Thomas, Viola Weijia Zhu, Hui Zhang, Corinne Clifford, Michael R. Palmer, Christopher D. Turner, Vivek Subbiah

Activity and Tolerability of BLU-667, a Highly Potent and Selective RET Inhibitor, in Patients with Advanced RET-altered Thyroid Cancers (Poster Abstract 6018)

Matthew H. Taylor, Justin F. Gainor, Mimi I-Nan Hu, Viola Weijia Zhu, Gilberto Lopes, Sophie Leboulleux, Marcia S. Brose, Martin H. Schuler, Daniel W. Bowles, Dong-Wan Kim, Christina S. Baik, Elena Garralda, Chia-Chi Lin, Douglas Adkins, Debashis Sarker, Giuseppe Curigliano, Hui Zhang, Corinne Clifford, Michael R. Palmer, Christopher D. Turner, Vivek Subbiah

Disclosures

Benjamin Besse, M.D., Ph.D.

- Research funding: AbbVie, Amgen, AstraZeneca, Biogen, Blueprint Medicines, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Ignyta, Inivata, Lilly, Merck KGaA, MSD Oncology, Nektar, Onxeo, Pfizer, PharmaMar, Sanofi, Spectrum Pharmaceuticals, Takeda, Tiziana Therapeutics

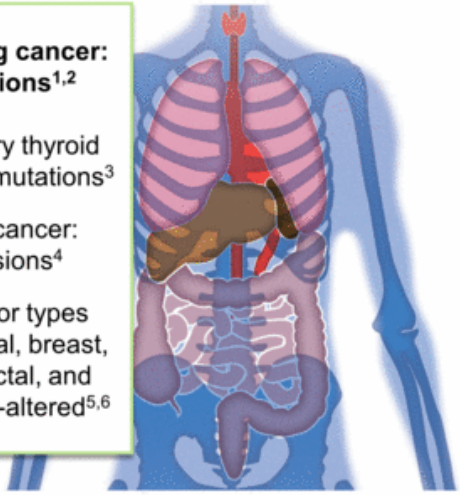
RET Alterations: Diverse Oncogenic Drivers Lacking Targeted Therapeutic Approach

Non-small cell lung cancer: ~1-2% RET fusions[1,2]

Advanced medullary thyroid cancer: ~90% RET mutations[3]

Papillary thyroid cancer: ~20% RET fusions[4]

Multiple other tumor types including esophageal, breast, melanoma, colorectal, and leukemia: <1% RET-altered[5,6]



NSCLC patients with RET fusions have not significantly benefited from existing therapy

- Chemotherapy: nonspecific, low response rates, significant toxicity
- Checkpoint inhibition: Preliminary evidence for lack of benefit in RET-altered NSCLC[7]
- Multikinase inhibitors: ↓ activity, ↑ off-target toxicity[8,9]

No selective RET inhibitors are approved

NSCLC, non-small cell lung cancer; ORR, overall response rate; PFS, progression-free survival. 1. Lipson, et al. *Nat Med* 2012; 2. Takeuchi, et al. *Nat Med* 2012; 3. Romei, et al. *Oncotarget* 2016; 4. Santoro, et al. *J Clin Invest* 1992; 5. Kato, et al. *Clin Cancer Res* 2017; 6. Ballerini, et al. *Leukemia* 2012; 7. Mazieres, et al. *JCO* 2018; 8. Drilon, et al. *Lancet* 2017; 9. Yoh, et al. *Lancet Respir Med* 2017

ARROW: BLU-667 Dose-Escalation and Expansion Study

Part 1: Dose-Escalation (N=62; Complete)[1]

RET-altered advanced solid tumors

BLU-667: 30-600 mg by daily oral administration (QD or BID)

Phase 2 dose determined (400 mg QD)

ARROW is registered with clinicaltrials.gov (NCT03037385)

Part 2: Expansion Cohorts (Ongoing)

BLU-667 400 mg QD

- Unresectable, advanced solid tumor
- RET alteration status by local tumor testing
- No additional driver mutation
- ECOG PS 0-1
- Asymptomatic brain metastases allowed
- Progressive disease or intolerant to SOC therapy, or not a candidate

Primary objectives:

Overall response rate (RECIST 1.1)

Safety

- RET fusion+ NSCLC, prior platinum (n=80)
- RET fusion+ NSCLC, platinum naïve (n=40)
- MTC, prior cabozantinib or vandetanib (n=60)
- MTC, no prior cabozantinib or vandetanib (n=40)
- Other RET fusion+ tumors (n=40)
- Other RET-mutated tumors (n=20)
- RET-altered, prior selective RET inhibitor (n=20)

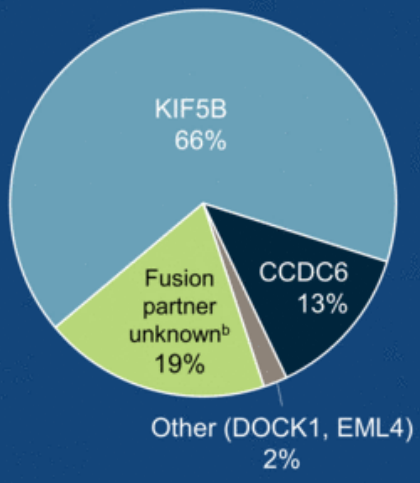
BID, twice daily dosing; ECOG PS, Eastern Cooperative Oncology Group performance status; MTC, medullary thyroid cancer; QD, once daily dosing; RECIST, response evaluation criteria in solid tumors; SOC, standard of care.

1. Subbiah, et al. *Cancer Res* 2018.

Baseline Characteristics
RET Fusion+ Advanced NSCLC Patients

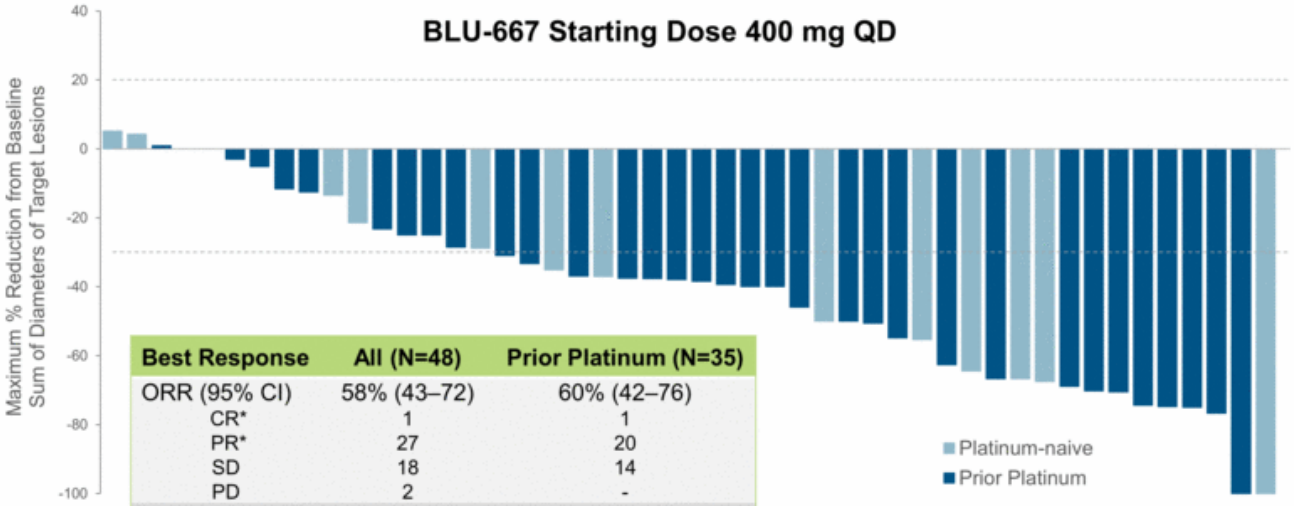
Characteristic	RET-Fusion+ Advanced NSCLC 400 mg QD Starting Dose	
	All (N=120)	Prior Platinum (N=91)
Age (years), median (range)	60 (28-87)	60 (28-85)
Male, n (%)	59 (49)	45 (49)
ECOG PS, n (%)		
0	46 (38)	33 (36)
1-2	74 (62)	58 (64)
Brain metastases, n (%)	48 (40)	36 (40)
Prior systemic regimens, median (range)	2 (0-11)	2 (1-11)
Any prior anticancer treatment	101 (84)	91 (100)
Chemotherapy, n (%)	92 (77)	91(100)
PD-1 or PD-L1 inhibitor, n (%)	47 (39)	41 (45)
Chemotherapy + PD-(L)1 combination, n (%)	41 (34)	41 (45)
Multikinase inhibitor, n (%)	21 (18)	20 (22)
Smoking history[a]		
Current/Prior	41 (34)	33 (36)
Never	78 (65)	57 (63)
Histology		
Adenocarcinoma	114 (95)	87 (96)
Other	6 (5)	4 (4)

RET Fusion Partner



ECOG PS, Eastern Cooperative Oncology Group Performance Status. [a]Smoking history is unknown for one patient. [b]Includes RET fusion+ by fluorescence *in situ* hybridization (FISH); RET fusion partner to be determined via central analysis. Data cut-off date: 28 Apr 2019.

BLU-667 Demonstrates Substantial Antitumor Activity in RET Fusion+ Advanced NSCLC



Best Response	All (N=48)	Prior Platinum (N=35)
ORR (95% CI)	58% (43–72)	60% (42–76)
CR*	1	1
PR*	27	20
SD	18	14
PD	2	-
DCR (95% CI)	96% (86–99)	100% (90–100)

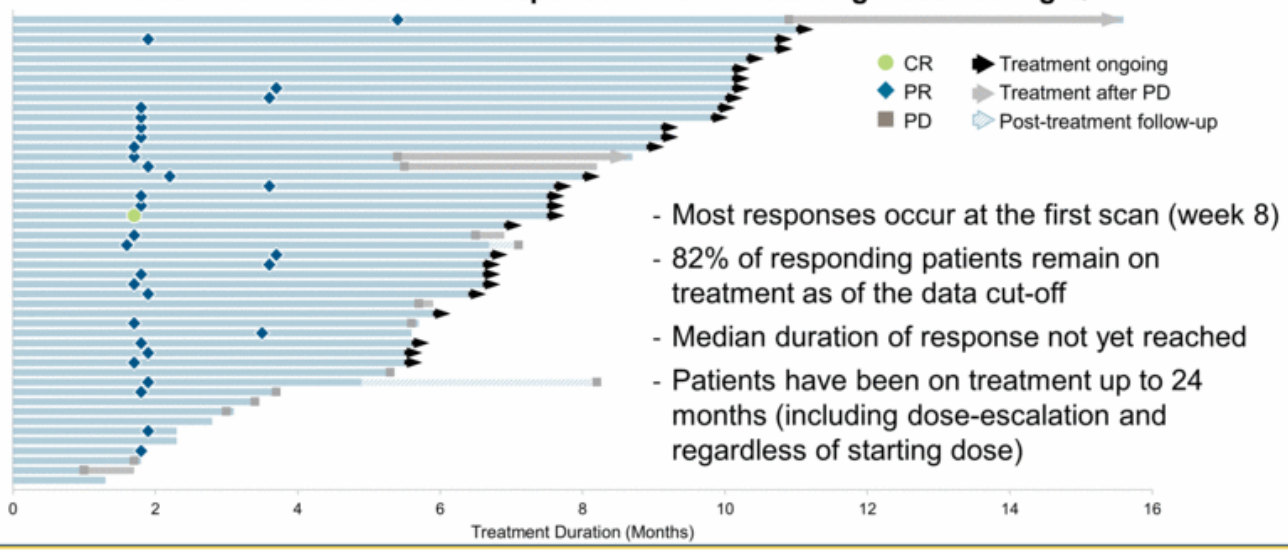
* All responses are confirmed on two consecutive assessments as per RECIST 1.1.

- 5/7 (71%) treatment-naïve patients had confirmed PR

CI, confidence interval; CR, complete response; DCR, disease control rate (best response of SD or better); ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease. Patients enrolled by 14 Nov 18, data cut-off 28 Apr 19. Response-evaluable population includes patients with measurable disease at baseline and ≥1 evaluable post-treatment disease assessment, and excludes 4 patients who previously received >1 cycle of a selective RET inhibitor.

BLU-667 Induces Rapid and Durable Responses in RET Fusion+ Advanced NSCLC

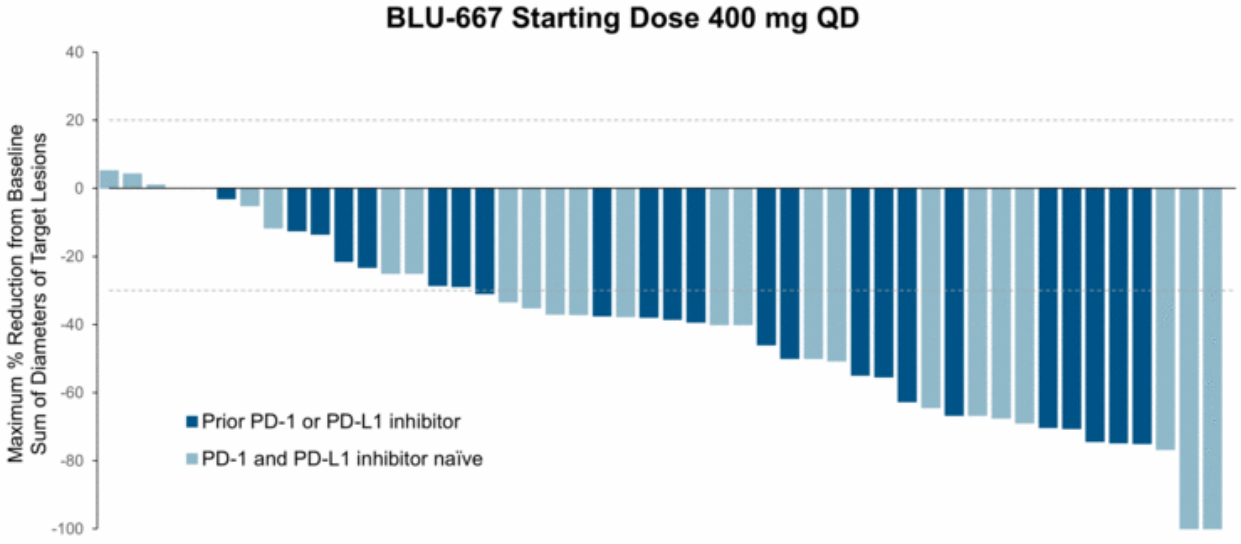
Duration of Treatment and Response: BLU-667 Starting Dose 400 mg QD



- Most responses occur at the first scan (week 8)
- 82% of responding patients remain on treatment as of the data cut-off
- Median duration of response not yet reached
- Patients have been on treatment up to 24 months (including dose-escalation and regardless of starting dose)

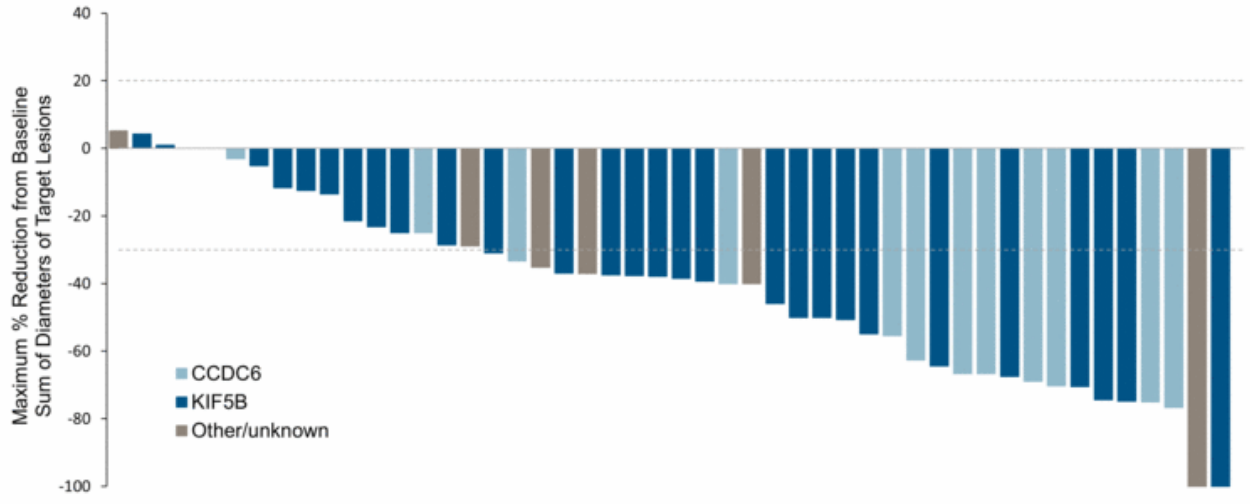
Patients enrolled by 14 Nov 18, data cut-off 28 Apr 19.

BLU-667 is Active Regardless of Prior Checkpoint Treatment



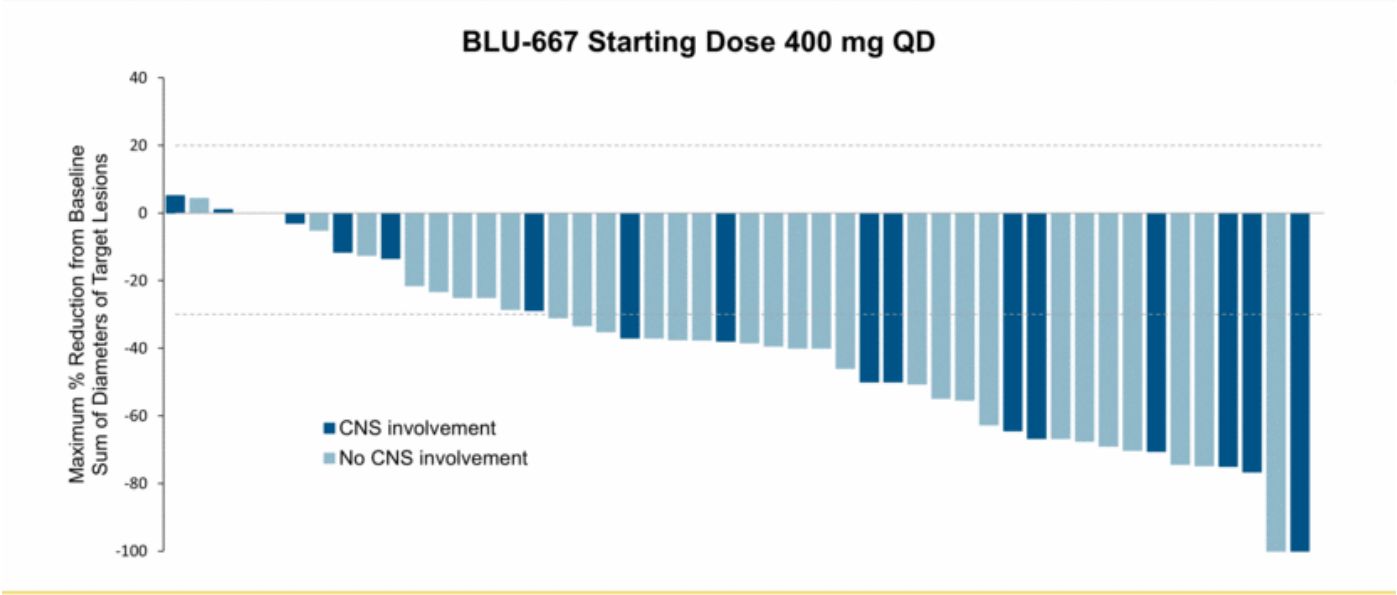
Patients enrolled by 14 Nov 18, data cut-off 28 Apr 19.

BLU-667 is Active Across RET Fusion Genotypes



Patients enrolled by 14 Nov 18, data cut-off 28 Apr 19.

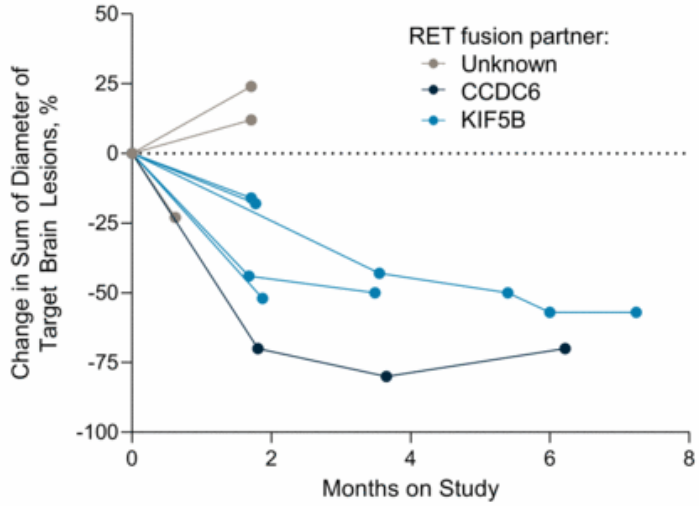
BLU-667 is Active Regardless of CNS Involvement



CNS, central nervous system
Patients enrolled by 14 Nov 18, data cut-off 28 Apr 19.

BLU-667 is Active Against Intracranial Metastases

Shrinkage of Brain Metastases[a]



- 7 of 9 (78%) patients had shrinkage of measurable brain metastases
- No patients at 400 mg QD starting dose had progression due to new CNS involvement

[a]Data shown for 9 patients with brain lesion(s) identified as RECIST 1.1 target lesions at baseline. Data cut-off date: 28 Apr 2019.

Brain metastases

49yo male

Diagnosis : Lung adenocarcinoma
Molecular profile : fusion RET-KIF5B, intermediate tumor mutation burden

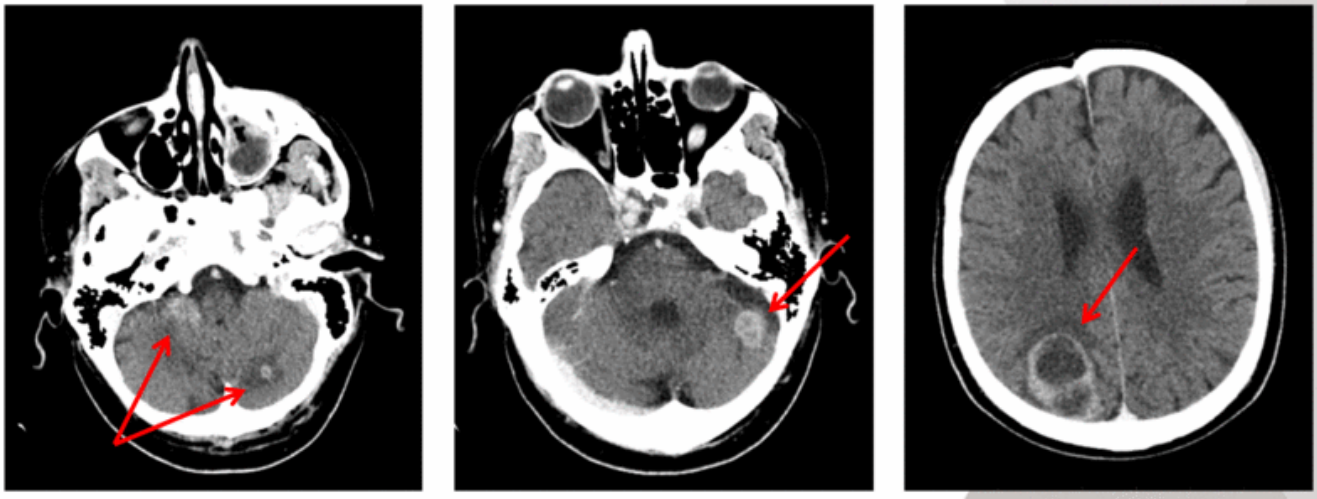
Previous treatments :

- **October 2016 :** adenocarcinoma cT3N3M0 : **concurrent chemoradiotherapy**
- **May 2017 :** brain metastasis : **Pemetrexed** (PR)
- **October 2017 :** brain progression = **SABR** (cerebellum) + **cyberknife**
- **March 2018 :** thoracic and brain progression (irradiated and non-irradiated brain metastasis)
  PACLITAXEL-BEVACIZUMAB
- **July 2018 :** cerebral progression (no local treatment feasible) **PEMBROLIZUMAB**
- **October 2018:** progression disease (lung/brain) **DOCETAXEL**
- **December 2018 :** brain/lung progression

Brain metastases

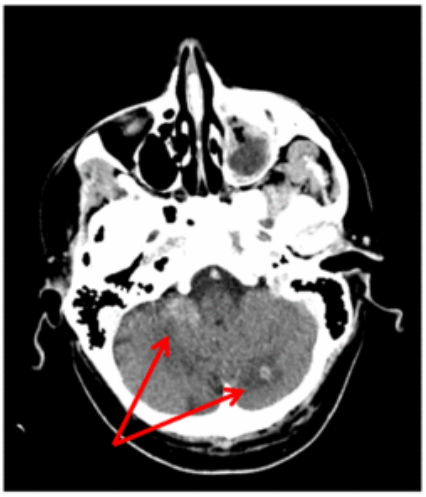
Baseline December 26, 2018

Phase I trial: BLU-667 400mg QD
- C1D1 January 11, 2019
- Then 300 mg QD (asymptomatic Gr3 CPK)

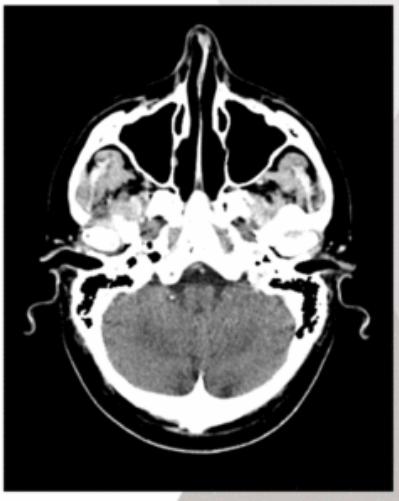


Radiological assessment

Baseline: December 26, 2018

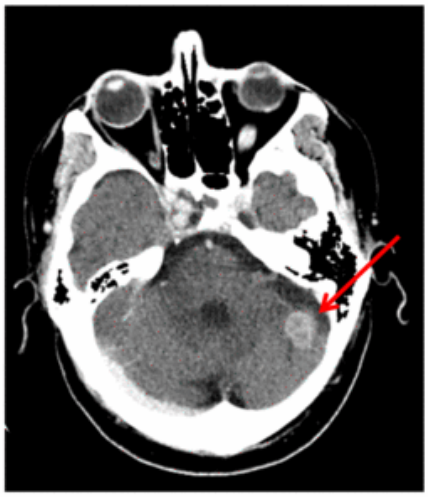


March 5, 2019

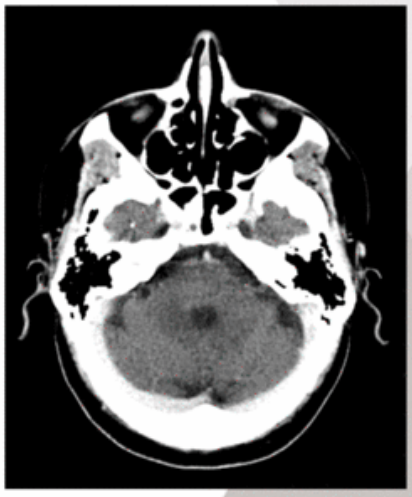


Radiological assessment

Baseline: December 26, 2018

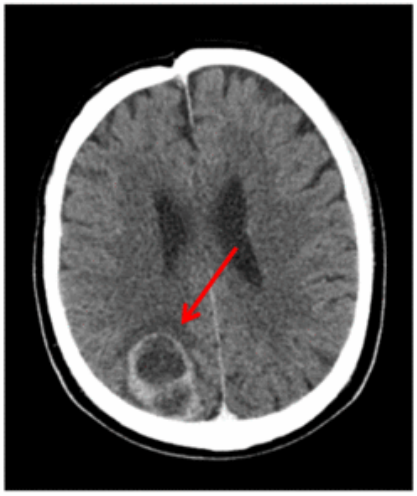


March 5, 2019

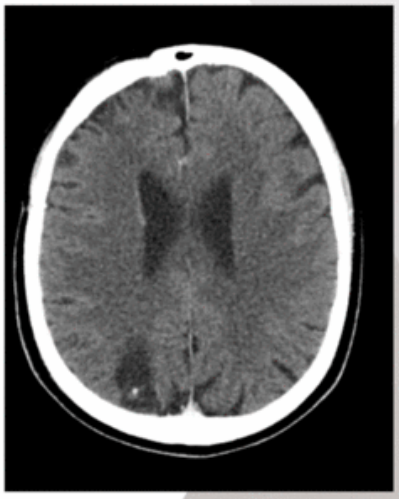


Radiological assessment

Baseline: December 26, 2018



March 5, 2019



BLU-667 is Well Tolerated by Patients with RET Fusion+ Advanced NSCLC

	RET Fusion+ Advanced NSCLC 400 mg QD Starting Dose (N=120)			
	Treatment-Emergent (≥15% overall)		Treatment-Related	
Adverse Events	All	Grade ≥3	All	Grade ≥3
Constipation	30%	2%	17%	2%
Neutropenia[a]	26%	13%	26%	13%
AST increased	24%	5%	20%	2%
Fatigue	21%	3%	13%	3%
Hypertension	20%	13%	13%	10%
Anemia	18%	7%	11%	4%
Diarrhea	18%	2%	9%	-
Pyrexia	18%	-	2%	-
ALT increased	17%	3%	13%	2%
Cough	17%	-	3%	-
Dry mouth	17%	-	12%	-

Additional grade ≥3 treatment related AEs (≥2%): increased CPK (3%), leukopenia[b] (3%).

Among 120 pts with advanced NSCLC receiving BLU-667 starting dose of 400 mg QD:

- Treatment-related toxicity is generally low-grade and reversible
- 7% discontinued BLU-667 due to treatment-related toxicity*
  - Pneumonitis, respiratory distress/ hypoxemia, mucositis/colitis, myelosuppression, gait disturbance, anemia

** Across the entire study (n=276), rate of discontinuation due to treatment-related toxicity is 4%.*

[a]Combined term including decreased neutrophils and neutropenia. [b]Combined term including leukopenia and white blood cell count decreased. AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase. Data cut-off date: 28 Apr 2019.

2nd line TKI

58yo female

Diagnosis : Lung adenocarcinoma
Molecular profile : fusion RET-KIF5B, intermediate TMB

Previous treatments :

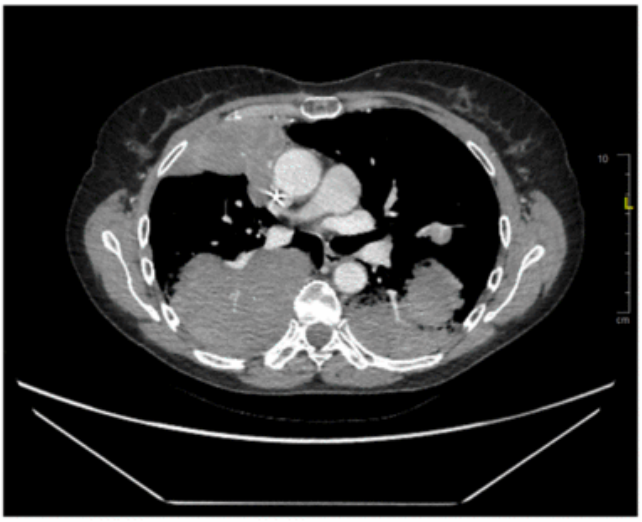
- December 2013 right upper lobectomy pT3 N0 R1
- Adjuvant chemotherapy with **Vinorelbine and cisplatin**
- Adjuvant mediastinal radiotherapy
- Pulmonary relapse in May 2016
- **NIVOLUMAB** from Jun. 2016 to Mar. 2017 : progressive disease (low pace)
- **NIVOLUMAB + a SRC inhibitor** from April to September 2017
- **Specific RET TKI** from April 19th to May 15th 2018 : response but definitive stop for toxicity

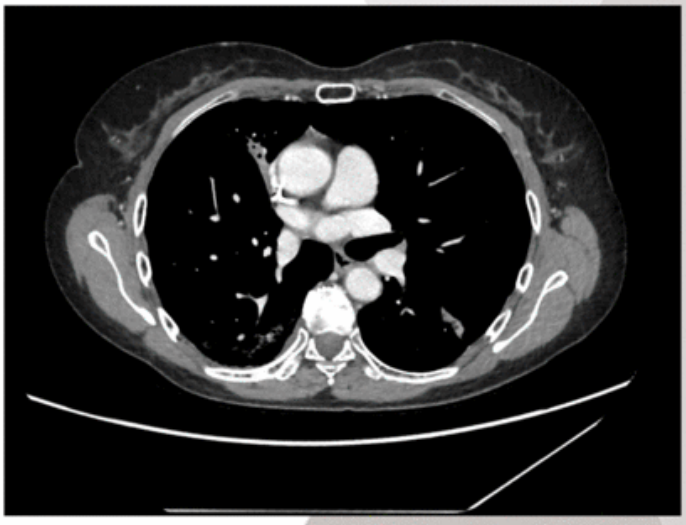
Radiological Assessment

Baseline : Jan. 14, 2019

PR -47%

May 20, 2019





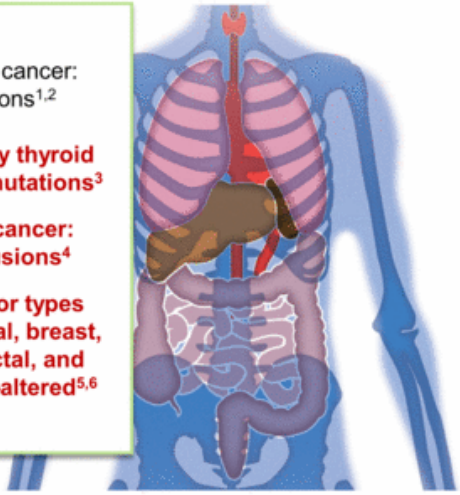
RET Alterations: Diverse Oncogenic Drivers Lacking Targeted Therapeutic Approach

Non-small cell lung cancer:
~1-2% RET fusions[1,2]

Advanced medullary thyroid cancer: >90% RET mutations[3]

Papillary thyroid cancer: ~10-20% RET fusions[4]

Multiple other tumor types including esophageal, breast, melanoma, colorectal, and leukemia: <1% RET-altered[5,6]



Patients with RET-mutant MTC and other RET-altered cancers may benefit from highly targeted therapy

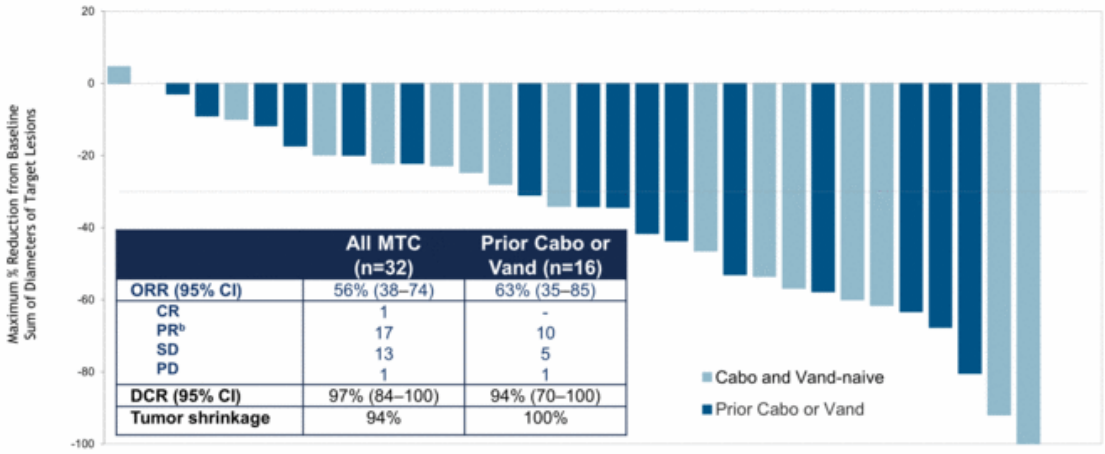
- Multikinase inhibitors are approved for MTC, but have important limitations:[7]
  - Modest efficacy (28-45% ORR)
  - Off-target toxicity often requiring dose modification or discontinuation
  - Emergence of resistance

No selective RET inhibitors are approved

1. Lipson, et al. Nat Med 2012; 2. Takeuchi, et al. Nat Med 2012; 3. Romei, et al. Oncotarget 2018; 4. Santoro, et al. J Clin Invest 1992; 5. Kato, et al. Clin Cancer Res 2017.
6. Ballerini, et al. Leukemia 2012; 7. Drilon, et al. Nature Reviews Clinical Oncology, 2017.

Results: Advanced RET-Mutated MTC Antitumor Activity – Tumor Response

RET-mutated MTC (400 mg QD starting dose)[a]

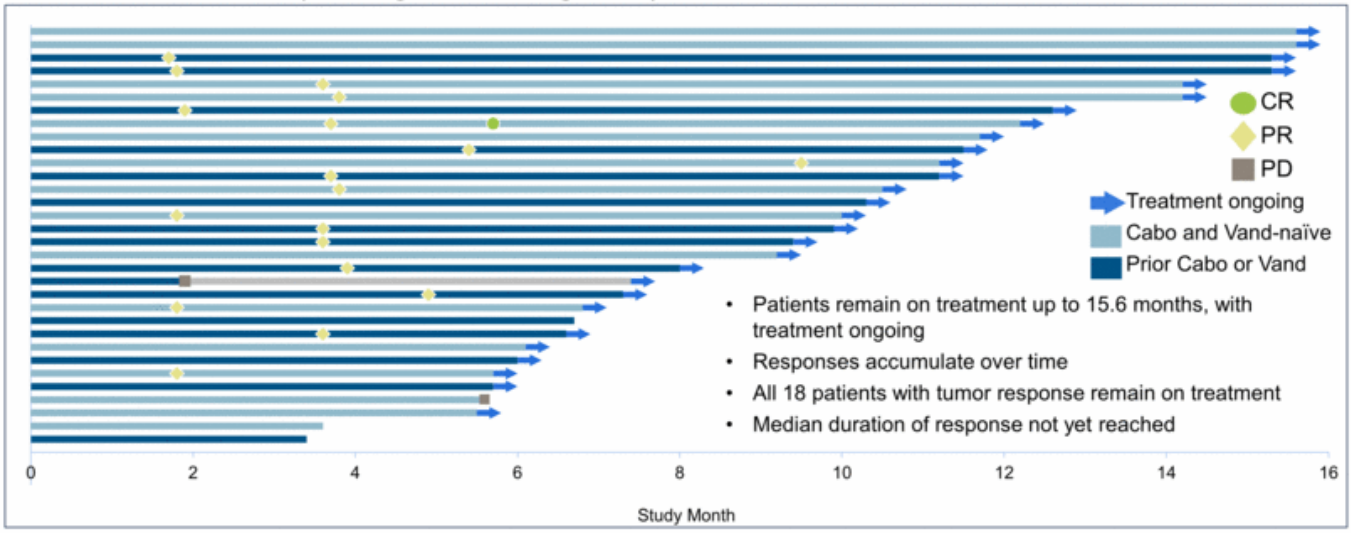


	All MTC (n=32)	Prior Cabo or Vand (n=16)
ORR (95% CI)	56% (38–74)	63% (35–85)
CR	1	-
PR[b]	17	10
SD	13	5
PD	1	1
DCR (95% CI)	97% (84–100)	94% (70–100)
Tumor shrinkage	94%	100%

[a]Data for response-evaluable patients enrolled by November 14, 2018 with follow-up through a data cut-off date of April 28, 2019. Response-evaluable population includes patients with measurable disease and ≥1 evaluable post-treatment disease assessment. [b] Two responses are pending confirmation.

Results: Advanced RET-Mutated MTC
Antitumor Activity – Treatment and Response Duration

RET-mutated MTC (400 mg QD starting dose)[a]



[a]Data for response-evaluable patients enrolled by November 14, 2018 with follow-up through a data cut-off date of April 28, 2019. Response-evaluable population includes patients with measurable disease and ≥1 evaluable post-treatment disease assessment.

Results: Advanced RET-Mutated MTC

Tolerability

Among 64 pts with RET-mutated MTC receiving BLU-667 starting dose of 400 mg QD:

- Treatment-related toxicity is generally low-grade and reversible
- No patients discontinued BLU-667 due to treatment-related toxicity (4% across the entire study)

	RET-mutated MTC (400 mg QD Starting Dose; N=64)			
	Treatment-Emergent [≥15% overall; n (%)]		Treatment-Related n (%)	
Adverse Event Term	All	Grade ≥3	All	Grade ≥3
Hypertension	26 (41)	15 (23)	19 (30)	10 (16)
Constipation	21 (33)	1 (2)	12 (19)	1 (2)
Neutropenia[a]	17 (27)	7 (11)	15 (23)	7 (11)
Anemia	14 (22)	3 (5)	6 (9)	1 (2)
Aspartate aminotransferase increased	14 (22)	-	9 (14)	-
Leukopenia[b]	14 (22)	1 (2)	11 (17)	-
Alanine transaminase increased	13 (20)	-	8 (13)	-
Diarrhea	13 (20)	3 (5)	6 (9)	1 (2)
Headache	12 (19)	-	5 (8)	-
Blood creatinine increased	11 (17)	-	7 (11)	-
Fatigue	11 (17)	-	6 (9)	-
Hypocalcemia	11 (17)	4 (6)	4 (6)	1 (2)

Additional grade ≥3 treatment related AEs (≥2%): blood creatine phosphokinase increased (5%).
[a]Combined term including decreased neutrophil count. [b]Combined term including decreased white blood cell count.

BLU-667 has Activity in Other RET Fusion+ Malignancies

- PR in 2/2 patients with metastatic pancreatic cancer
  - 67 yo male, CCDC6-RET fusion, continues with confirmed PR (53% shrinkage) at ~6 months
  - 31 yo male, TRIM33-RET and JMJD1C-RET fusions, continues treatment after PR(41% shrinkage) at first response assessment
- PR in a patient with intrahepatic bile duct carcinoma
  - 51 yo female, NCOA4-RET fusion, continues with confirmed PR (67% shrinkage) at ~15 months
- ORR 83% (5/6)* in RET-fusion papillary thyroid cancer
- Safety profile similar to what was seen in RET fusion+ NSCLC

* Confirmation of response is pending for two patients. Data cut-off date: 28 Apr 2019.

Conclusions

- BLU-667 demonstrates broad and durable anti-tumor activity in advanced RET-altered cancers
  - Highly active regardless of RET alteration, tumor type, treatment history or CNS involvement
  - RET fusion+ NSCLC
    - 60% ORR in NSCLC patients previously treated with platinum-based chemotherapy
    - 71% response rate in (5/7) NSCLC patients naïve to prior systemic therapy
    - Strong activity against intracranial metastases
  - RET mutation+ MTC and other RET-altered cancers
    - 63% ORR in MTC patients previously treated with an multikinase inhibitor
    - Responses observed in papillary thyroid cancer, pancreatic cancer and intrahepatic bile duct carcinoma
  - Well tolerated at 400 mg QD with most AEs grade 1 or 2
- FDA breakthrough therapy designations granted for RET fusion+ NSCLC and RET mutation+ MTC
- Data support broad registration-directed development program across patient populations, including expansion of the ARROW trial in treatment-naïve NSCLC patients

Acknowledgments

- Participating patients and families
- BLU-667-1101 Investigators and research coordinators
  - The University of Texas MD Anderson Cancer Center, Houston, TX, United States
  - Oregon Health & Science University, Portland, OR, United States
  - Massachusetts General Hospital Cancer Center, Boston, MA, United States
  - University of Pennsylvania, Philadelphia, PA, United States
  - University of California Irvine Medical Center, Irvine, CA, United States
  - University of Miami, Miami, FL, United States
  - Georgetown University Medical Center, Washington, District of Columbia, United States
  - University of Washington, Seattle, WA, United States
  - University of Michigan, Ann Arbor, MI, United States
  - Cornell University, New York, NY, United States
  - University of Colorado, Aurora, CO, United States
  - Washington University School of Medicine, St. Louis, MO, United States
  - Mayo Clinic, Rochester, MN, United States
  - Mayo Clinic, Jacksonville, FL, United States
  - Mayo Clinic, Phoenix, AZ, United States
  - Texas Oncology, Dallas, TX, United States
  - Thoraxklinik Heidelberg, Heidelberg, Germany
  - Universitatsklinikum Essen, Essen, Germany
  - Pius-Hospital Oldenberg, Oldenberg, Germany
  - Vall d'Hebron University Hospital, Barcelona, Spain
  - Hospital Universitario 12 de Octubre, Madrid, Spain
  - Hospital Universitario Ramon y Cajal, Madrid, Spain
  - Hospital Clinic Barcelona, Barcelona, Spain
  - Hospital Duran I Reynals, Barcelona, Spain
  - Centre Leon Berard, Lyon, France
  - Gustave Roussy, Villejuif, France
  - Institut Claudius Regaud, Toulouse, France
  - CHU de Rennes, Rennes, France
  - CHRU de Lille, Lille, France
  - Institut Bergonie, Bordeaux, France
  - University College of London NHS Foundation Trust, London, UK
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  - The Christie NHS Foundation Trust, Manchester, UK
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  - Grande Ospedale Metropolitano Niguarda, Milan, Italy
  - University Medical Center Gronigen, Gronigen, Netherlands
  - National Cancer Centre Singapore, Singapore, Singapore
  - Seoul National University Hospital, Seoul, Republic of Korea
  - Asan Medical Center, Seoul, Republic of Korea
  - Severance Hospital, Seoul, Republic of Korea
  - National Taiwan University Hospital, Taipei, Taiwan
- Colleagues at Blueprint Medicines Corporation

BLU-667 program strategy

Andy Boral, M.D., Ph.D.
Chief Medical Officer, Blueprint Medicines

A powerful scientific platform with a focused research strategy

Difficult-to-drug

Kinase targets that are difficult to drug with existing technologies

Treatment-resistant

Kinase targets characterized by alterations promoting resistance to existing therapies

Novel biology

New kinase targets identified via computational and cell biology

BLU-667 highlights our ability to rapidly design innovative precision therapies

BLU-667 is a highly selective and potent RET inhibitor

BLU-667 selectively inhibits RET versus other kinases

Biochemical potency for RET versus other kinases (IC_{50}, fold difference)

Anti-targets	VEGFR-2	JAK1	JAK2	TRKC
BLU-667	88x	20x	158x	59x

- BLU-667 is ≥100x more selective for RET than 96% of kinases tested

BLU-667 potently inhibits common RET fusions and mutations

Biochemical potency against common RET alterations (IC_{50}, nM)

RET alteration	WT RET	CCDC6-RET	M918T	RET V804L	RET V804M
BLU-667	0.4 nM	0.4 nM	0.4 nM	0.3 nM	0.4 nM

- Potent in vivo activity against RET-KIF5B and RET-CCDC6, including in intracranial models

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Subbiah, et al. Cancer Discovery, 2018.

BLU-667 has differentiated preclinical activity

Selectivity for VEGFR-2

Cellular activity against p-VEGFR-2 (IC_{50}, nM)

Anti-target	p-VEGFR-2
BLU-667	65 nM
Loxo-292	54 nM

Inhibition of gatekeeper mutations predicted to drive resistance

Cellular anti-proliferative activity against KIF5B-RET the most common RET fusion in NSCLC [IC50, nM (fold difference)]

RET fusion	KIF5B-RET	KIF5B-RET V804L	KIF5B-RET V804M	KIF5B-RET V804E
BLU-667	10.1 nM (1x)	8.1 nM (0.8x)	14.1 nM (1.4x)	8.1 nM (0.8x)
Loxo-292	10.5 nM (1x)	28.4 nM (2.7x)	78.8 nM (7.5x)	126 nM (12x)

Blueprint Medicines internal data on file.

Emerging BLU-667 clinical profile reflects original purpose-built design

- High response rates and durable anti-tumor activity in NSCLC and MTC patients regardless of RET genotype
- Clinical responses in 2 of 4 patients previously treated with Loxo-292
- Strong activity against brain metastases in patients with NSCLC
- Preliminary evidence of clinically active and tolerable combination with osimertinib in patients with EGFR-mutant NSCLC
- Clinical responses in multiple patients with other RET-altered cancers
- Well-tolerated with low discontinuation rates in advanced cancer populations

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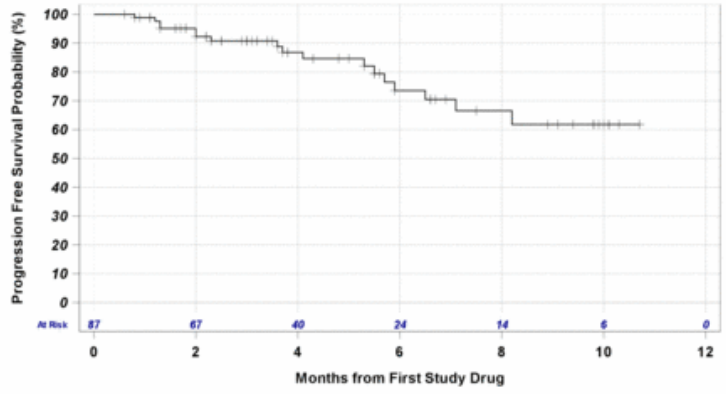
Data presented at ASCO 2019 Annual Meeting. Data cut-off: April 28, 2019. Data for BLU-667 in combination with osimertinib presented at September 2018 International Association for the Study of Lung Cancer 19th World Conference on Lung Cancer and published online in *Cancer Discovery*.

Preliminary PFS for BLU-667 in previously treated NSCLC supports advancing development into first-line setting

ARROW trial – BLU-667

RET fusion+ NSCLC previously treated with platinum-based chemo[1]

Median PFS not reached



Alectinib – ALK+ NSCLC	Median PFS
Previously treated with crizotinib[2]	8.9 months
Previously untreated[3]	25.7 months

Osimertinib – EGFR+ NSCLC	Median PFS
Previously treated with systemic therapy[4]	10.1 months
Previously untreated[4]	18.9 months

[1] BLU-667 PFS analysis. Data cut-off: April 28, 2019. [2] Ou, et al. ASCO presentation, 2015. [3] Alectinib prescribing information. [4] Osimertinib prescribing information. PFS, progression free survival.

Responses in 2 of 4 patients previously treated with Loxo-292

Patient 1

- RET-mutant MTC
- Initiated BLU-667 at 200 mg QD
- Confirmed PR with treatment ongoing >1 year

Patient 2

- RET-mutant MTC
- Initiated BLU-667 at 400 mg QD
- SD with radiographic tumor reduction
- Treatment ongoing >4 months

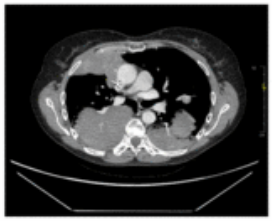
Patient 3

- RET-fusion NSCLC
- Initiated BLU-667 at 400 mg QD
- Discontinued BLU-667 due to progression

Patient 4

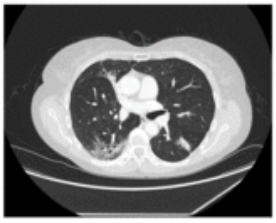
- RET-fusion NSCLC
- Initiated BLU-667 at 400 mg QD
- Confirmed PR with treatment ongoing >17 weeks

Baseline



January 2019

PR: -47%



May 2019

Courtesy Professor Besse, Gustave Roussy Cancer Center

Data cut-off: May 24, 2019

Key BLU-667 program next steps

Status	Planned next steps
1. Previously treated NSCLC and MTC • 60%+ ORRs; mDORs not reached • Well tolerated to date • FDA breakthrough therapy designations	• Submit NDA for previously treated NSCLC in Q1 2020 • Submit NDA for previously treated MTC in 1H 2020
2. First-line NSCLC • 71% ORR in treatment-naïve NSCLC • Preliminary FDA feedback	• Amend ARROW trial to expand enrollment of treatment-naïve patients and support potential expedited development • Initiate confirmatory Phase 3 trial in 1L NSCLC in 2H 2019
3. Other RET-altered cancers • Clinical responses in multiple other RET-altered cancers	• Continue to enroll basket cohorts to support development in a broad tumor-agnostic population • Initiate Phase 2 trial in resistant EGFR-mutant NSCLC in combination with osimertinib in 2H 2019

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Data presented at ASCO 2019 Annual Meeting. Data cut-off date: April 28, 2019.

Questions and Answers

Updated avapritinib data in patients with advanced systemic mastocytosis

- 24th EHA Congress
- Amsterdam, The Netherlands
- Saturday, June 15
- Oral abstract: S830

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Thank you