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): **October 6, 2018**

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. ☐

Item 7.01 Regulation FD Disclosure.

On October 6, 2018, Blueprint Medicines Corporation issued a press release announcing the presentation of updated data for RET-altered medullary thyroid cancer ("MTC") patients and papillary thyroid cancer patients from its ongoing Phase 1 ARROW clinical trial evaluating BLU-667 for the treatment of RET-altered non-small cell lung cancer, MTC and other advanced solid tumors. The data were presented on Saturday, October 6, 2018 in an oral presentation at the 88th Annual Meeting of the American Thyroid Association (the "ATA Annual Meeting") in Washington, D.C. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K, and a copy of the presentation at the ATA Annual Meeting is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.1 and 99.2, 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	Press release issued by Blueprint Medicines Corporation on October 6, 2018
99.2	Presentation by Blueprint Medicines Corporation on October 6, 2018

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: October 9, 2018

By: /s/ Tracey L. McCain
Tracey L. McCain
Chief Legal Officer

Blueprint Medicines Announces Updated Data from Phase 1 ARROW Clinical Trial Showing Broad, Durable Activity of BLU-667 in Advanced RET-Altered Medullary and Papillary Thyroid Cancers

90 percent of evaluable MTC and PTC patients had tumor reductions
62 percent response rate in MTC patients treated with 300 to 400 mg once daily for at least 24 weeks
Patients with longest treatment durations remain on therapy for more than 15 months

CAMBRIDGE, Mass., October 6, 2018 – Blueprint Medicines Corporation (NASDAQ: BPMC), a leader in discovering and developing targeted kinase medicines for patients with genomically defined diseases, today announced the presentation of updated data from the ongoing Phase 1 ARROW clinical trial of BLU-667, an investigational precision therapy targeting RET alterations, including resistance mutations. The new results showed that BLU-667 was highly active and well-tolerated in patients with advanced RET-altered medullary thyroid cancer (MTC) and papillary thyroid cancer (PTC), with increased activity observed with higher dose levels and longer treatment durations.

The reported data showed 90 percent of evaluable patients with MTC and PTC had radiographic tumor reductions, regardless of RET alteration type or prior multi-kinase inhibitor (MKI) therapy. In addition, the response rate was 62 percent in patients with MTC treated once daily (QD) with BLU-667 at doses of 300 to 400 mg for at least 24 weeks. In the MTC and PTC populations, all responders across dose levels and all patients treated at 400 mg QD remain on study. Safety results were consistent with prior data, and the majority of adverse events (AEs) were Grade 1. These results were as of a data cutoff date of September 14, 2018 and were reported today in an oral presentation at The 88th Annual Meeting of the American Thyroid Association (ATA).

“Existing treatment of medullary and papillary thyroid cancer with multi-kinase inhibitors is limited by frequent dose modifications or interruptions due to off-target toxicities, reducing the opportunity for a meaningful or sustained response,” said Andy Boral, M.D., Ph.D., Chief Medical Officer of Blueprint Medicines. “These new data showed selectively targeting RET alterations with BLU-667 was well-tolerated and enabled durable responses. Importantly, response rates were high for patients with prolonged time on therapy at higher dose levels, demonstrating that potent and sustained target inhibition leads to improved patient outcomes. We believe these results begin to reveal the potential of BLU-667 to transform the care of patients with RET-altered thyroid cancer, and we look forward to seeing the data continue to mature as additional patients are treated at the recommended phase 2 dose for longer durations.”

Based on the encouraging data reported to date, Blueprint Medicines has expanded enrollment targets for the ARROW trial to further evaluate the safety and efficacy of BLU-667 in a broader patient population and, ultimately, to support potential registration.

Data Highlights from the Ongoing Phase 1 ARROW Clinical Trial

The data presented included all patients enrolled in the Phase 1 ARROW clinical trial as of May 9, 2018 and included follow-up on these patients through the data cutoff date of September 14, 2018. Of the 69 patients who had been treated with BLU-667 in the dose escalation and expansion portions of the trial, 42 had RET-altered thyroid cancer, including 37 with MTC and five with PTC. In the dose escalation

portion, patients were treated at dose levels ranging from 30 mg to 600 mg QD or up to 300 mg twice daily. In the expansion portion, patients were treated at the recommended phase 2 dose of 400 mg QD.

Clinical Activity Data

As of the data cutoff date, 35 patients with MTC and four patients with PTC were evaluable for response assessment by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Overall, 90 percent of MTC and PTC patients with measurable target lesions had radiographic tumor reductions.

In patients with MTC, response assessments showed increased clinical activity with higher dose levels and longer treatment durations. Across all evaluable MTC patients, the overall response rate (ORR) was 49 percent, including one patient with a confirmed complete response (CR) and 16 patients with a partial response (PR; two pending confirmation). In patients with MTC treated with 300 to 400 mg QD for at least 24 weeks, the response rate was 62 percent, including one patient with a confirmed CR and seven patients with a confirmed PR.

In patients with PTC, two of four evaluable patients had a confirmed PR, and all evaluable patients with PTC had radiographic tumor shrinkage.

The data also showed encouraging evidence of durable activity. All patients with MTC and PTC who responded to BLU-667 remain on treatment as of the data cutoff date. In addition, all patients treated at 400 mg QD are continuing on therapy. Patients with the longest treatment durations remain on therapy for more than 15 months.

Anti-tumor activity was observed regardless of prior MKI therapy or RET alteration. Similar response rates were observed in MTC patients who were MKI-experienced (47 percent; 8/17 patients) and MKI-naïve (50 percent; 9/18 patients). In addition, clinical responses were observed in patients with common activating mutations in MTC (e.g., M918T) and fusion partners in PTC (e.g., NCO4A and CCDC6). A clinical response was also observed in the one evaluable MTC patient with a germline V804M gatekeeper mutation.

Safety Data

The reported data showed that across 69 patients, BLU-667 was well-tolerated as of the data cutoff date. Most AEs were Grade 1, and only two patients discontinued therapy due to a treatment-related AE (Grade 3 increased alanine aminotransferase in a patient with liver metastases and Grade 2 pneumonitis). Treatment-emergent AEs (regardless of relationship to BLU-667) reported by investigators (≥15 percent) most commonly were constipation (35 percent), increased aspartate aminotransferase (33 percent), anemia (30 percent), hypertension (30 percent), decreased white blood cell count (29 percent), diarrhea (28 percent), neutropenia (28 percent), increased alanine aminotransferase (25 percent), increased blood creatinine (23 percent), fatigue (19 percent) and headache (17 percent). Grade 3 or higher treatment-related AEs occurring in two or more patients included anemia, hypertension, decreased white blood cell count, diarrhea and neutropenia.

About the Phase 1 ARROW Clinical Trial of BLU-667

ARROW is a Phase 1 clinical trial designed to evaluate the safety, tolerability and efficacy of BLU-667 in multiple ascending doses in adults with RET-altered non-small cell lung cancer (NSCLC), MTC and other

advanced solid tumors. The trial consists of two parts: a dose escalation portion and an expansion portion. Enrollment in the dose escalation portion is complete, and the expansion portion has been initiated and is actively enrolling patients in six defined cohorts at the recommended phase 2 dose of 400 mg QD: (1) RET-altered NSCLC patients previously treated with an MKI, (2) RET-altered NSCLC patients who have not previously received any MKI treatment, (3) MTC patients previously treated with an MKI, (4) MTC patients who have not previously received any MKI treatment, (5) patients with other RET-altered solid tumors and (6) RET-altered solid tumor patients with prior selective RET tyrosine kinase inhibitor. Trial objectives include assessing response, pharmacokinetics, pharmacodynamics and safety. The trial is designed to enroll approximately 190 patients across all six expansion cohorts, at multiple sites in the United States, European Union and Asia.

Patients and physicians interested in the ARROW clinical trial can contact the Blueprint Medicines study director at arrow@blueprintmedicines.com or 1-617-714-6707. Additional details are available at www.arrowtrial.com or www.clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT03037385).

About RET-Altered Solid Tumors

RET activating fusions and mutations are a key disease driver in many cancer types, including NSCLC and MTC. RET fusions are implicated in approximately 1 to 2 percent of patients with NSCLC and approximately 10 percent of patients with PTC, while RET mutations are implicated in approximately 60 percent of patients with MTC. In addition, oncogenic RET alterations are observed at low frequencies in colorectal, breast, pancreatic and other cancers, and RET fusions have been observed in patients with treatment-resistant, EGFR-mutant NSCLC.

Currently, there are no approved therapies that selectively target RET-driven cancers, though there are several approved MKIs with RET activity being evaluated in clinical trials. Thus far, clinical activity attributable to RET inhibition has been uncertain for these inhibitors, likely due to insufficient inhibition of RET and off-target toxicities. There is a need for precision therapies that provide durable clinical benefit by selectively targeting RET alterations and resistance mutations.

About BLU-667

BLU-667 is an investigational, once-daily oral precision therapy specifically designed for highly potent and selective targeting of oncogenic RET fusions, mutations and resistance mutations. In preclinical studies, BLU-667 consistently demonstrated sub-nanomolar potency against the most common RET fusions, activating mutations and resistance mutations. In addition, BLU-667 demonstrated markedly improved selectivity for RET compared to approved MKIs, including more than 80-fold improved potency for RET versus VEGFR2. By suppressing primary and secondary mutants, BLU-667 has the potential to overcome and prevent the emergence of clinical resistance. This approach is expected to enable durable clinical responses across the range of RET alterations, with a favorable safety profile.

BLU-667 was discovered by Blueprint Medicine’s research team based on its proprietary compound library. The company is developing BLU-667 for the treatment of people with RET-altered NSCLC, MTC and other solid tumors. Blueprint Medicines has an exclusive collaboration and license agreement with CStone Pharmaceuticals for the development and commercialization of BLU-667 and certain other drug candidates in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains development and commercial rights for BLU-667 in the rest of the world.

About Blueprint Medicines

Blueprint Medicines is developing a new generation of targeted and potent kinase medicines to improve the lives of patients with genomically defined diseases. Its approach is rooted in a deep understanding of the genetic blueprint of cancer and other disease driven by the abnormal activation of kinases. Blueprint Medicines is advancing multiple programs in clinical development for subsets of patients with gastrointestinal stromal tumors, hepatocellular carcinoma, systemic mastocytosis, non-small cell lung cancer, medullary thyroid cancer and other advanced solid tumors, as well as multiple programs in research and preclinical development. For more information, please visit www.blueprintmedicines.com.

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 plans and timelines for the clinical development of BLU-667; expectations regarding the potential benefits of BLU-667 in treating patients with RET-altered thyroid cancers, including patients with RET-altered MTC or PTC; expectations regarding the potential to treat patients at the recommended phase 2 dose for longer durations and Blueprint Medicines' strategy, business plans and focus. 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. 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 delay of any current or planned clinical trials or the development of Blueprint Medicines' drug candidates, including avapritinib, BLU-554, BLU-667 and BLU-782; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates; 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, including companion diagnostic tests for BLU-554 for FGFR4-driven hepatocellular carcinoma, avapritinib for PDGFRα D842V-driven gastrointestinal stromal tumors and advanced systemic mastocytosis and BLU-667 for RET-driven non-small cell lung cancer; the success of Blueprint Medicines' 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 in the section entitled "Risk Factors" in Blueprint Medicines' Quarterly Report on Form 10-Q for the quarter ended June 30, 2018, as filed with the Securities and Exchange Commission (SEC) on August 1, 2018, 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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ARROW BLU-667

Clinical activity of BLU-667, a highly selective RET inhibitor, in advanced *RET*-altered thyroid cancers: updated results from the phase 1 ARROW study

Mimi I. Hu, Matthew Taylor, Lori Wirth, Viola Zhu, Robert Doebele, Dae Ho Lee, Ignacio Matos, Christina Baik, Marcia Brose, Giuseppe Curigliano, Gilberto de Lima Lopes, Dong-Wan Kim, Daniel Tan, Chia-Chi Lin, Michael Palmer, Meera Tugnait, Hui Zhang, Brenton Mar, Corinne Clifford, Beni Wolf, Elena Garralda, Sai-Hong Ignatius Ou, Vivek Subbiah, Justin Gainor

88th Annual Meeting of the American Thyroid Association
Washington, DC • October 6, 2018

blueprint MEDICINES

NCT03037385

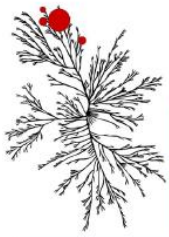
Disclosures

I have the following financial relationships to disclose:

- **Research support:** Sanofi-Genzyme
- **Consultant:** Blueprint Medicines Corporation
- **Advisory board:** Loxo Oncology

BLU-667 is an investigational agent discovered and currently in development by Blueprint Medicines Corporation (Blueprint Medicines)

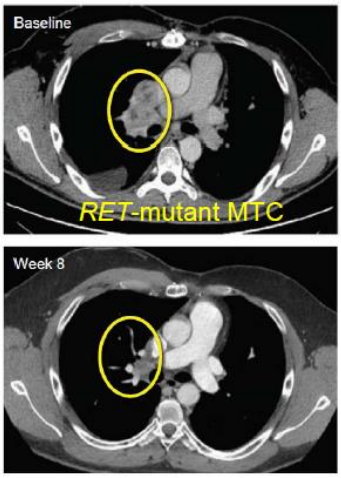
BLU-667 is designed to treat *RET*-altered cancers



BLU-667 potently inhibits RET alterations and resistance mutants while sparing VEGFR2

	Biochemical IC50 (nM)			
	RET M918T Most common in MTC	RET V804M Gatekeeper resistance in MTC	CCDC6-RET Occurs in PTC	VEGFR2
BLU-667	0.4	0.4	0.4	35
Cabozantinib	8	45	34	2
Vandetinib	7	3597	20	4
Sorafenib	23	32	ND	21
Lenvatinib	3	360	4	0.7

PHASE 1, PART 1:
PROOF OF CONCEPT



VEGFR, vascular endothelial growth factor receptor; IC50, half maximal inhibitory concentration; MTC, medullary thyroid cancer; CCDC6, coiled-coil domain containing 6; PTC, papillary thyroid cancer; ND, not determined. Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com) (CSTI). The foregoing website is maintained by CSTI, and the authors and Blueprint Medicines are not responsible for its content

Hu et al. International Thyroid Oncology Group (ITOG) 2018
Subbiah et al. American Association for Cancer Research (AACR) 2018 (clinical trials plenary presentation)
Subbiah et al. Precision Targeted Therapy with BLU-667 for *RET*-Driven Cancers. Cancer Discovery, July 2018

ARROW trial: first-in-human study with BLU-667

PART 1: Dose escalation – *complete*

Objective: *Determine MTD/RP2D* ✓

Proof of concept ✓

BOIN design
Advanced MTC, NSCLC*, or other solid tumor*

MTD/RP2D 400 mg PO daily

*All NSCLC and other solid tumors were RET-altered in cohorts higher than 30 mg QD

Part 1: *62 patients treated*
53 treated at 30 – 600 mg QD
9 treated at 200 – 300 mg divided BID dosing

PART 2: Dose expansion – ongoing

Objective: *Determine Overall Response Rate*

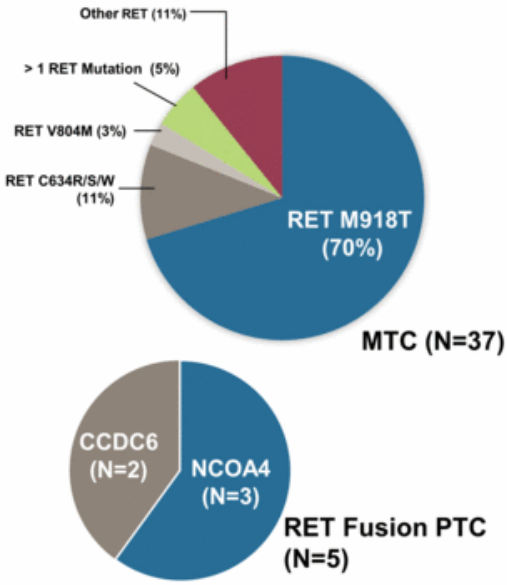
- ***RET*-altered NSCLC with prior MKI**
- ***RET*-altered NSCLC with no prior MKI**
- **MTC with prior MKI**
- **MTC with no prior MKI**
- **Other *RET*-altered solid tumors (including PTC)**
- ***RET*-altered solid tumors with prior selective RET TKI**

MTD, maximum tolerated dose; RP2D, recommended Part 2 dose; BOIN, Bayesian optimal interval; MTC, medullary thyroid cancer; NSCLC, non–small cell lung cancer; QD, once daily; BID, twice daily; PO, orally; ORR, overall response rate; MKI, multikinase inhibitor; PTC, papillary thyroid cancer; TKI, tyrosine kinase inhibitor. NCT03037385

Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018

Patient demographics and baseline characteristics

Parameter	Total (N=69)
Age (years), median (range)	57 (19-85)
Sex, male, n (%)	42 (61)
ECOG, PS, n (%) 0	26 (38)
1-2	43 (62)
Metastatic disease, n (%)	65 (94)
Prior systemic therapy, n (%)	51 (74)
Multikinase inhibitor	21 (30)
Number of prior regimen, median (range)	1 (0-8)
Tumor type, n (%)	
Medullary thyroid cancer	**37 (54)**
RET fusion papillary thyroid cancer	**5 (7)**
RET fusion non–small cell lung cancer	23 (33)
RET fusion intrahepatic bile duct carcinoma	1 (1)
RET mutation retroperitoneal paraganglioma	1 (1)
Non-RET altered solid tumors	2 (3)

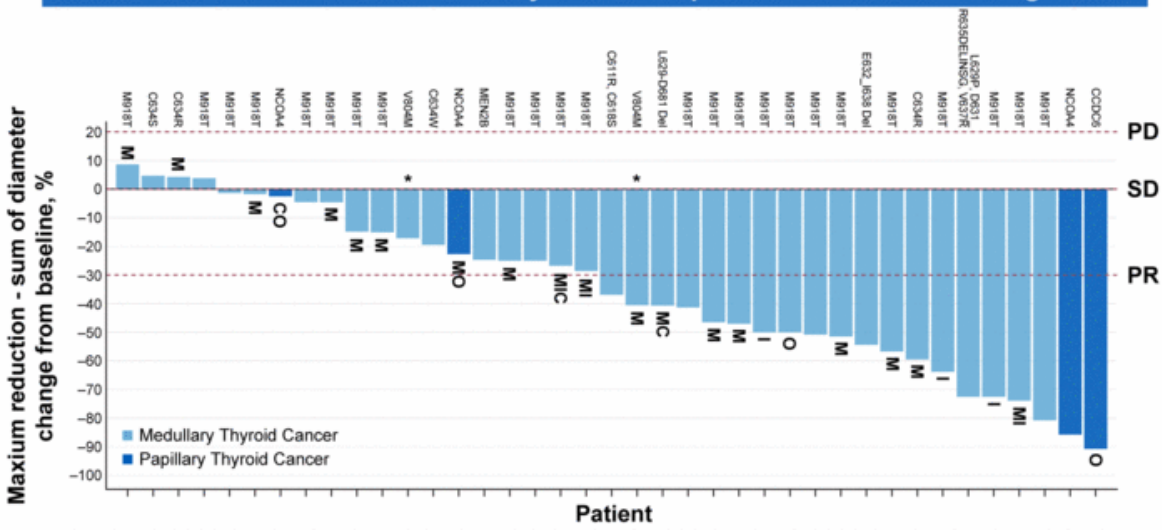


ECOG, Eastern Cooperative Oncology Group; PS, performance status; MKI, multikinase inhibitor; MTC, medullary thyroid cancer; PTC, papillary thyroid cancer; NSCLC, non–small cell lung cancer; CCDC6, coiled-coil domain containing 6; NCOA4, nuclear receptor coactivator 4.

Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018

BLU-667 has profound activity in *RET*-altered thyroid cancer

90% of evaluable *RET*-altered thyroid cancer patients had tumor shrinkage

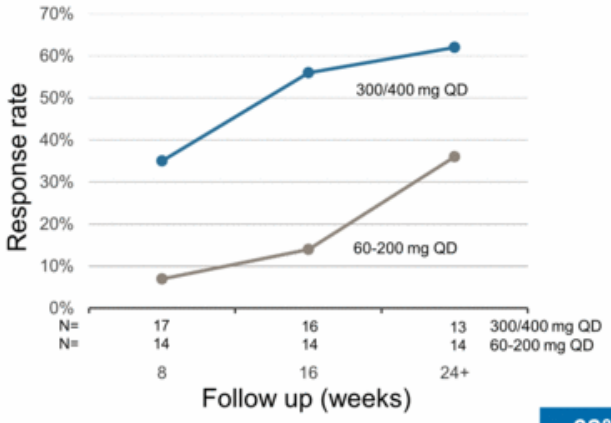


Responses seen regardless of RET alteration, including RET V804M,* or prior treatment

NCO4A, nuclear receptor coactivator 4; CCDC6, coiled-coil domain containing 6; M, prior MKI therapy; C, prior chemotherapy; O, other therapy; I, prior immunotherapy; PD, progressive disease; SD, stable disease; PR, partial response.

Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018

Response rate in MTC patients increases with dose and duration of therapy



MTC Response Evaluable# Patients

Best response n, (%)	Total All doses All cycles (N=35)	300/400 mg QD		
		At 8 weeks (N=17)	At 16 weeks (N=16)	At 24+ weeks (N=13)
ORR	**17 (49)**	6 (35)	9 (56)	**8 (62)**
CR	1 (3)	1 (6)	1 (6)	1 (8)
PR	16 (46)	5 (29)	8 (50)	7 (54)
SD	18 (51)	10 (59)	7 (44)	5 (39)
PD	0 (0)	0 (0)	0 (0)	0 (0)
Pending confirmation:	2 PR	1 CR, 5 PR	3 PR	

62% Response Rate at 24+ weeks in MTC at 300/400 mg QD

#Evaluable patients at a specific week considers only post baseline assessments up to at that week of therapy (based on cycle start), or those that discontinued therapy or progressed prior to that.

MTC, medullary thyroid cancer; QD, once daily; ORR, overall response rate; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; RECIST, Response Evaluation Criteria in Solid Tumors. Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018.

High ORR in MTC patients treated with BLU-667 regardless of prior MKI Treatment

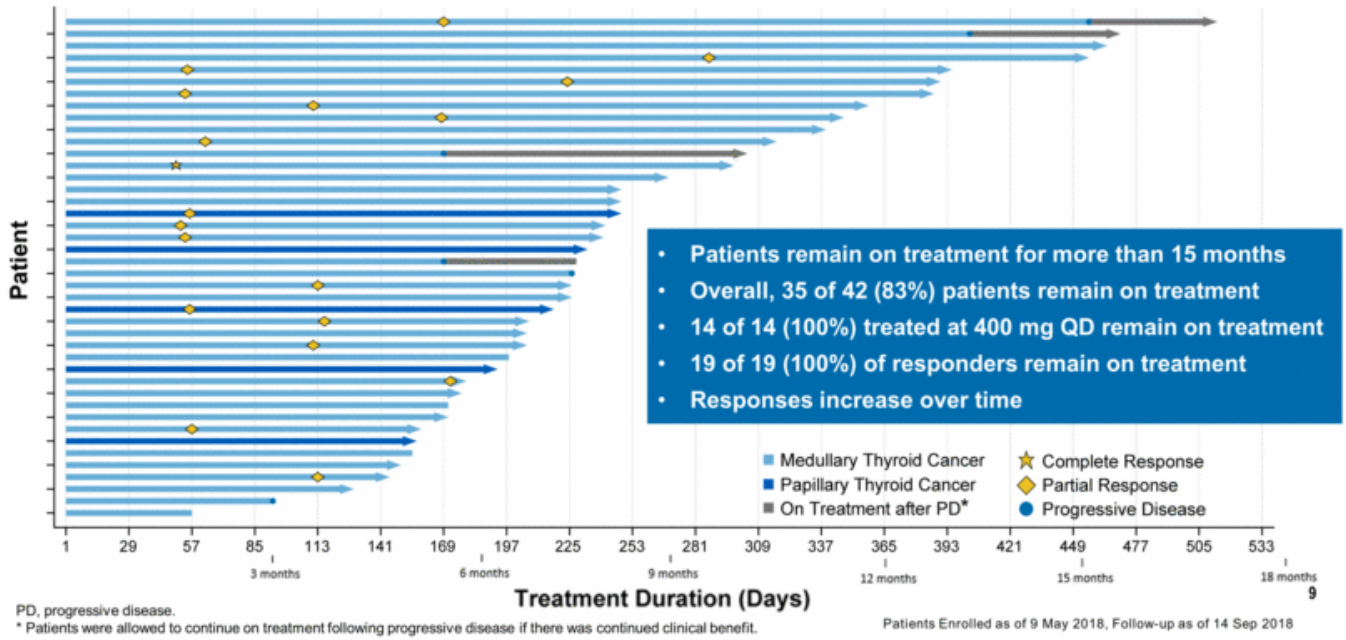
MTC Response Evaluable# Patients

Best Response	Total (n=35) n (%)	No prior MKI (n=18) n (%)	Prior MKI (n=17) n (%)
ORR (CR+PR)	**17 (49)**	**9 (50)**	**8 (47)**
CR	1 (3)	1 (6)	-
PR*	16 (46)	8 (44)	8 (47)
SD	18 (51)	9 (50)	9 (53)

MKI, multikinase inhibitor; ORR, overall response rate; CR, complete response; PR, partial response; SD, stable disease; RECIST, Response Evaluation Criteria in Solid Tumors.
*2 PRs pending confirmation
#Evaluable patients at all cycles include all dosed patients with RECIST target lesions with 1 or more post-baseline assessments or progressed or ended therapy for any reason.

Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018

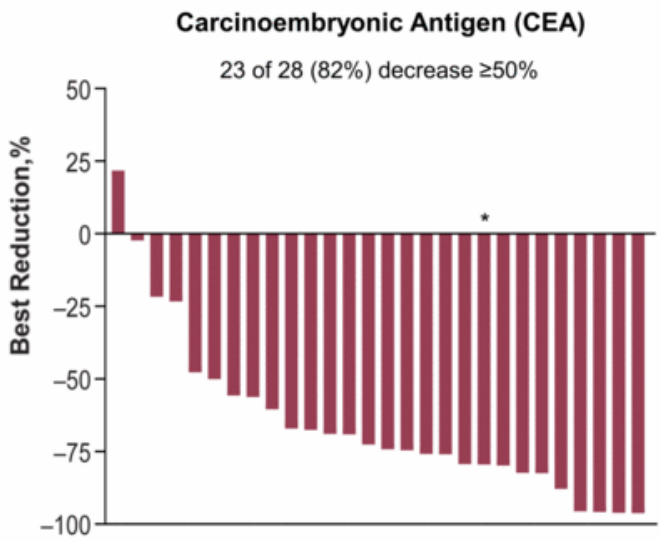
BLU-667 shows durable responses in thyroid cancer patients

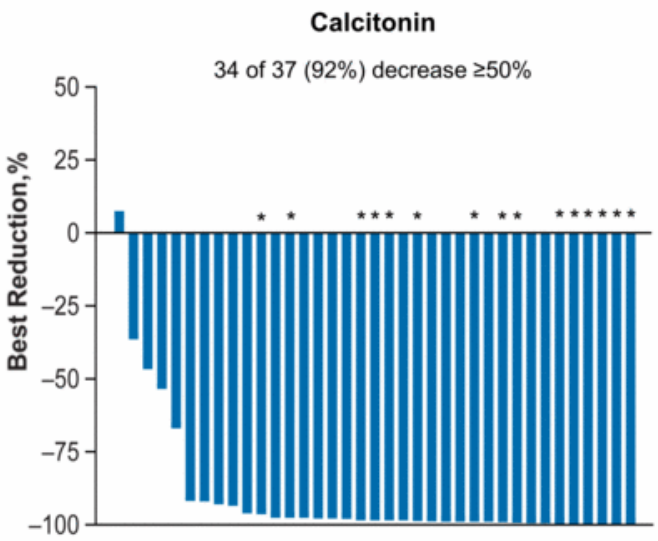


PD, progressive disease.
* Patients were allowed to continue on treatment following progressive disease if there was continued clinical benefit.

Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018

Significant declines in MTC tumor markers

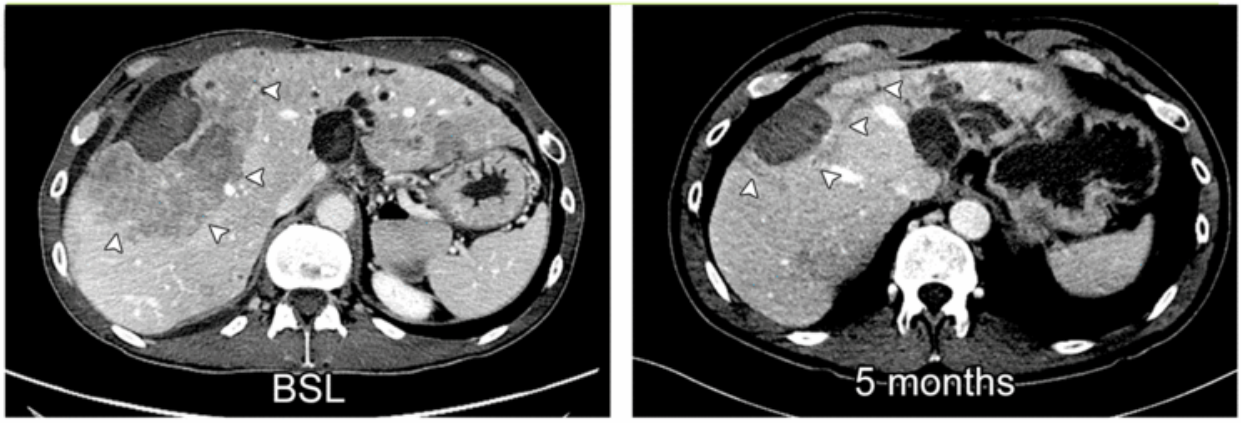




MTC, medullary thyroid cancer; CEA, carcinoembryonic antigen.
*Tumor marker normalized.

Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018

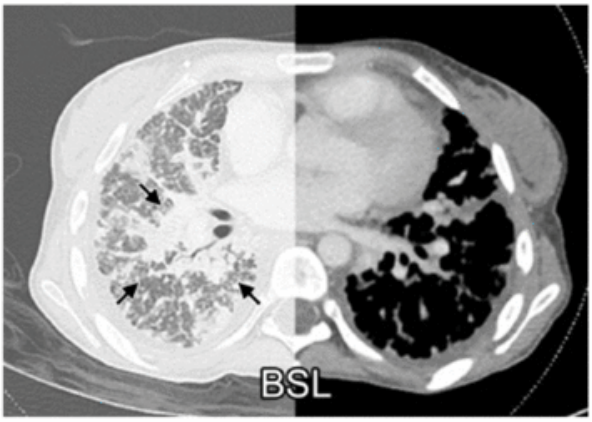
BLU-667 demonstrates potent activity in germline *RET* V804M mutant MTC

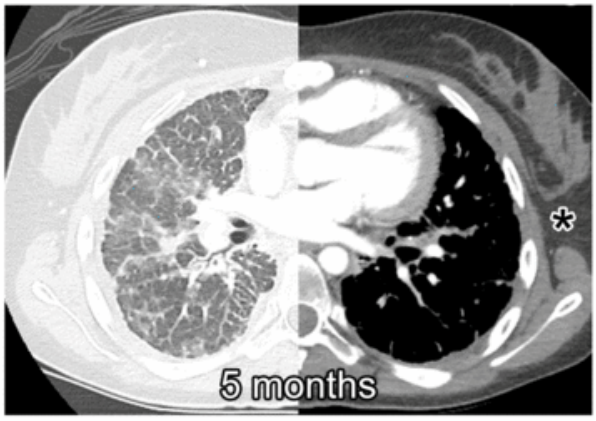


- 52-year-old male gastroenterologist with MTC (germline *RET* V804M gatekeeper mutation) with metastases to neck and mediastinal lymph nodes, lungs, liver and bone
- Progressive disease in liver on sunitinib (AE's: anorexia, weight loss, diarrhea, hand/foot syndrome, fatigue)
- Initiated BLU-667 at 100 mg BID and escalated to 400 mg QD at C3D1
- By C5D1, showed -41% (PR) reduction in liver metastases; gaining weight (BMI increased from 18.9 to 23.5), no diarrhea
- Remains on treatment in Cycle 7 with continued PR

MTC, medullary thyroid cancer; BSL, baseline; PD, progressive disease; AE, adverse event; BID, twice daily; QD, once daily; PR, partial response; BMI, body mass index. Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018

BLU-667 induced dramatic improvement in young PTC patient





- 23-year-old woman with PTC, sclerosing variant (*CCDC6-RET* fusion) who presented 6 years ago with symptomatic diffuse lung metastases requiring supplemental oxygen (O_2) since diagnosis; treated with I-131 (total activity 351 mCi) with subsequent fibrosis
- Progressed on sorafenib and early this year on lenvatinib (increasing O_2 needs, pleural effusions and intubated 3 times over 6 wks)
- Initiated BLU-667 at 400 mg once daily → RECIST SD (no target lesion/non-target lymphangitic lung metastases)
- Symptomatic response: O_2 weaned monthly to room air within 5 months, baseline BMI 14.8 steadily increased to 22.3 after 6 mos
- Remains on treatment at Cycle 8 and plans to start college and get her driver's license this Fall

PTC, papillary thyroid cancer; BSL, baseline; CCDC6, coiled-coil domain containing 6; O2, oxygen; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; BMI, body mass index. Patient had non-measurable disease at baseline and is not represented on current waterfall plot. Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018

Safety - BLU-667 is well tolerated

All doses and patients, N=69							
	Treatment-emergent AEs (≥15% overall)					Treatment-related AEs	
Adverse Event	Any event n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 3	Grade 4
Constipation	24 (35)	22 (32)	2 (3)	-	-	-	-
Aspartate aminotransferase increased	23 (33)	20 (29)	3 (4)	-	-	-	-
Anemia	21 (30)	8 (12)	7 (10)	6 (9)	-	4 (6)	-
Hypertension	21 (30)	5 (7)	5 (7)	11 (16)	-	6 (9)	-
White blood cell count decreased	20 (29)	7 (10)	10 (15)	3 (4)	-	3 (4)	-
Diarrhea	19 (28)	11 (16)	3 (4)	5 (7)	-	4 (6)	-
Neutropenia	19 (28)	5 (7)	5 (7)	6 (9)	3 (4)	5 (7)	2 (3)
Alanine aminotransferase increased	17 (25)	16 (23)	-	1 (1)	-	1 (1)	-
Blood creatinine increased	16 (23)	15 (28)	1 (1)	0	-	0	-
Fatigue	13 (19)	9 (13)	3 (4)	1 (1)	-	1 (1)	-
Headache	12 (17)	9 (13)	2 (3)	1 (1)	-	1 (1)	-

Most AEs were Grade 1

Only 2 discontinuations for related AEs*

AE, adverse event; ALT, alanine aminotransferase.
*Discontinuations for related AEs: ↑ALT (gr3) and pneumonitis (gr2)

Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018

Conclusions

- **BLU-667** has demonstrated:
  - Responses across *RET* genotypes, which increase with dose and time on treatment
    - **Durable and high ORR of 62%** at 300/400 mg QD in patients with MTC at 24+ weeks
    - **100%** of MTC patients treated at 400 mg daily remain on treatment
    - **ORR of ~50%** in MTC patient regardless of prior MKI treatment
    - Patients remain on treatment for more than 15 months
    - **100%** of responders remain on treatment
- BLU-667 is well tolerated at efficacious doses in MTC and PTC patients
- Results warrant further clinical development in MTC and PTC
- **ARROW** trial Part 2 dose expansion is open and enrolling globally in the United States, Europe, and Asia

ORR, overall response rate; QD, once daily; MTC, medullary thyroid cancer; MKI, multikinase inhibitor; PTC, papillary thyroid cancer. Patients Enrolled as of 9 May 2018, Follow-up as of 14 Sep 2018

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