The 2020 Blueprint

JUNE 5, 2019

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, BLU-667, BLU-554 and BLU-782 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; expectations regarding the Company’s existing cash, cash equivalents and investments and the future financial performance of the Company; 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. (collectively, “Roche”) and its collaboration with CStone Pharmaceuticals (“CStone”).

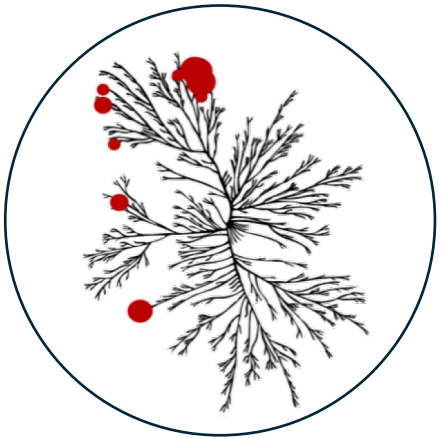
These and other risks and uncertainties are described in greater detail under “Risk Factors” in the Company’s Quarterly Report on Form 10-Q for the period ended March 31, 2019, as filed with the Securities and Exchange Commission (“SEC”) on May 9, 2019, and any other filings the Company has made or may 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 June 5, 2019, 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.

Precision therapies for people with cancer and rare diseases

A NEW WAY OF LOOKING AT KINASE MEDICINES

SELECTIVE



avapritinib

NON-SELECTIVE

Rydapt® (midostaurin)

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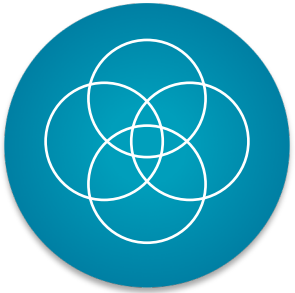
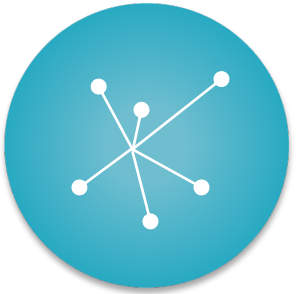
Our vision for building the leading precision therapy company

Rapid, reproducible product development

Robust scientific platform to design selective kinase medicines



Disciplined portfolio management focused on therapeutic area leadership

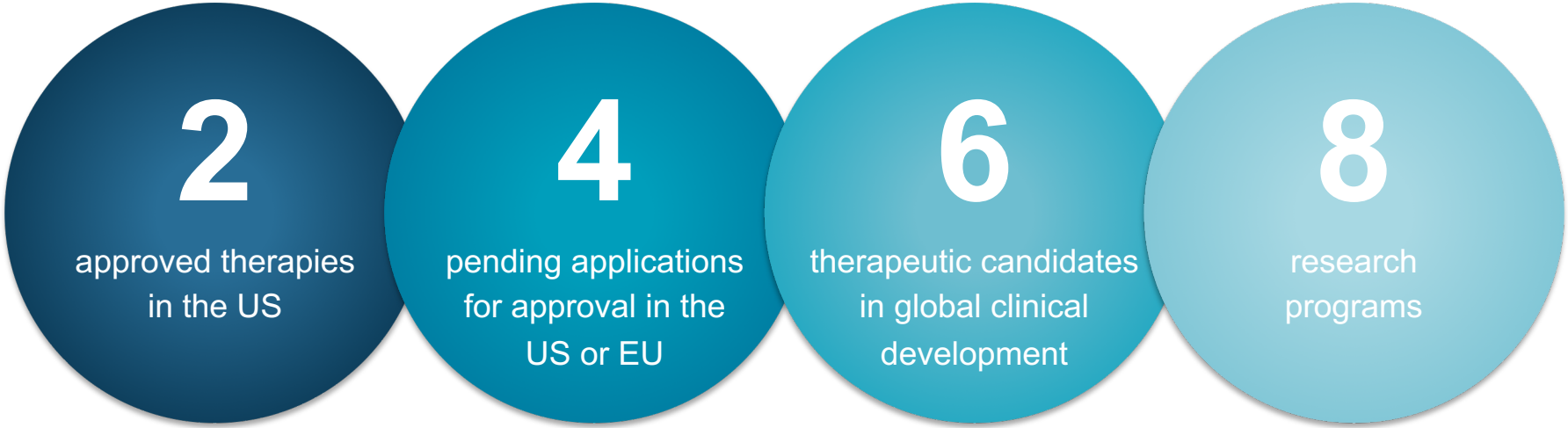


Effective and nimble commercial organization with global reach

Reinvestment of revenue to sustain constant innovation cycle

The 2020 Blueprint

ANTICIPATED ACHIEVEMENTS BY YEAR-END 2020

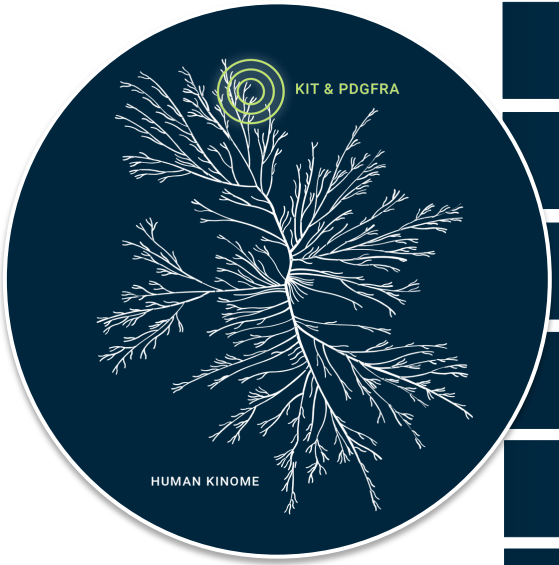


Rapidly advancing pipeline of investigational precision therapies

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					Roche **

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. 1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line.

Avapritinib: an investigational precision therapy with broad potential



LATE CLINICAL DEVELOPMENT	U.S. REGULATORY SUBMISSION PLANS
PDGFRA Exon 18 mutant GIST	June 2019
4L GIST	June 2019
3L GIST	2020
2L GIST*	
Advanced SM	Q1 2020
Indolent and smoldering SM	

* Trial planned to initiate 2H 2019.
Target GIST populations have unresectable or metastatic disease. Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com) (CSTI). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.

Beyond imatinib, there are no highly effective therapies for advanced GIST

ALL GIST

1L Gleevec®	2L Sutent®	3L Stivarga®	4L No Approved Therapy
ORR ~51%	ORR ~7%	ORR ~5%	ORR ~0%
PFS ~19 months	PFS ~6 months	PFS ~4.8 months	PFS 1.8 months*

PDGFRα D842V GIST

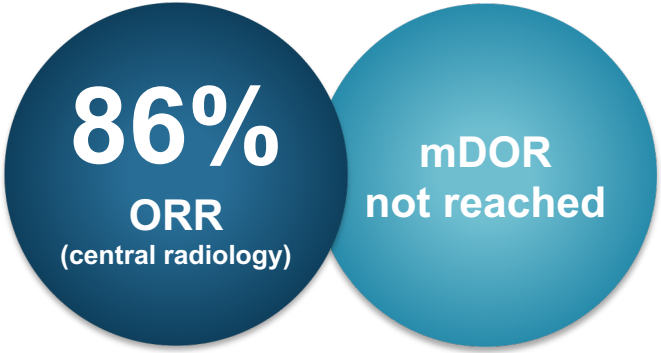
ORR ~0%

PFS ~3 months

* Re-challenged with Gleevec.

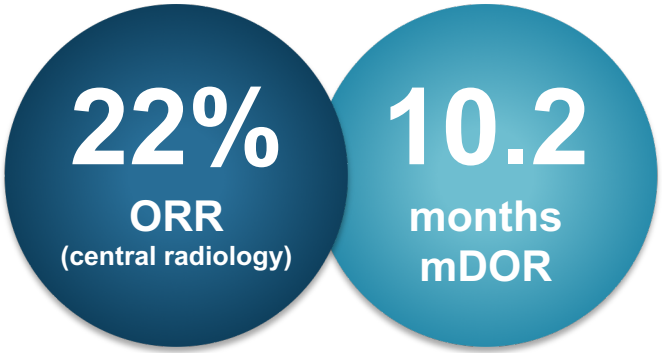
Data forming the basis of planned avapritinib new drug application

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



Breakthrough Therapy Designation[2]

4L GIST (n=111)[1]



Safety Results (N=204):

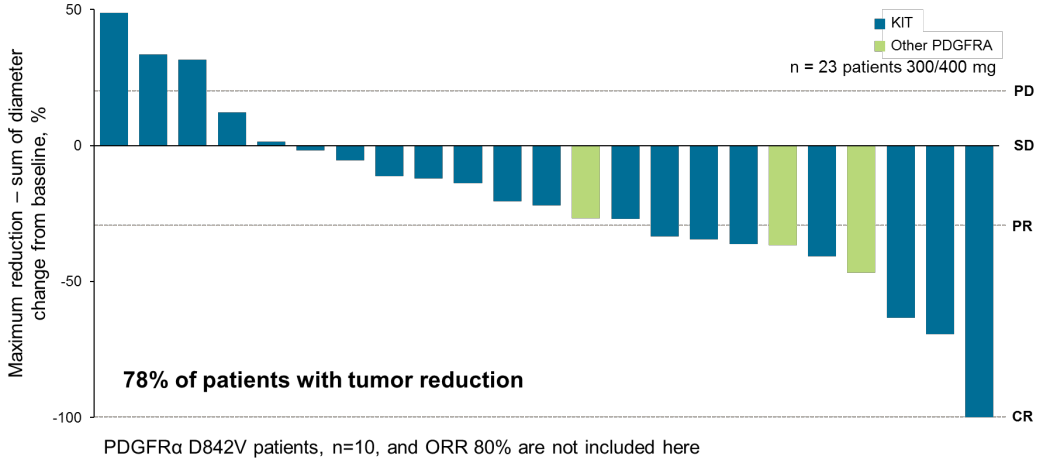
- Avapritinib was generally well-tolerated and most AEs reported by investigators were Grade 1 or 2
- Grade ≥3 treatment-related AEs included anemia, fatigue, blood bilirubin increased, cognitive effects and diarrhea
- Relative dose intensity was 86% at 300 mg QD, the recommended dose for planned marketing 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.

Preliminary Phase 1 NAVIGATOR trial data in 3L/4L Stivarga®-naïve GIST support ongoing confirmatory Phase 3 VOYAGER trial

Preliminary 26% ORR for avapritinib[1]



PDGFRα D842V patients, n=10, and ORR 80% are not included here

VOYAGER

3L/4L GIST R, 1:1

- avapritinib
- Stivarga®

Primary endpoint: PFS

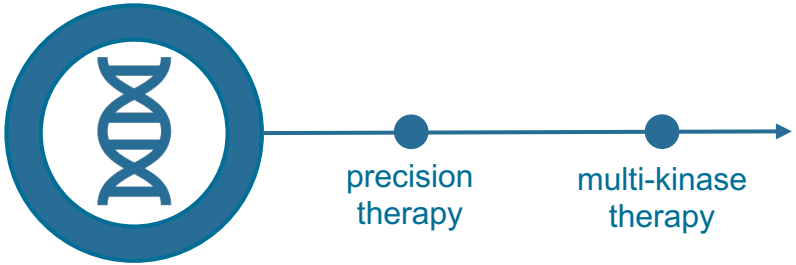
Expect to complete VOYAGER trial enrollment in 2H 2019

[1] Data presented at the CTOS Annual Meeting in November 2018. Data cutoff date: October 15, 2018.
R, randomized.

Plan to initiate COMPASS-2L precision medicine trial in 2L GIST in 2H 2019

Treatment in standard sequence

Initial treatment and sequence tailored to each patient's molecular profile



Goal: maximize opportunity for durable response / disease control

TODAY Increased understanding of GIST molecular profile & mutational sensitivity of current / emerging treatments **TOMORROW**

blueprint™ MEDICINES

Avapritinib selectively targets the genomic driver of systemic mastocytosis

~95% of patients have KIT D816V mutation[1]

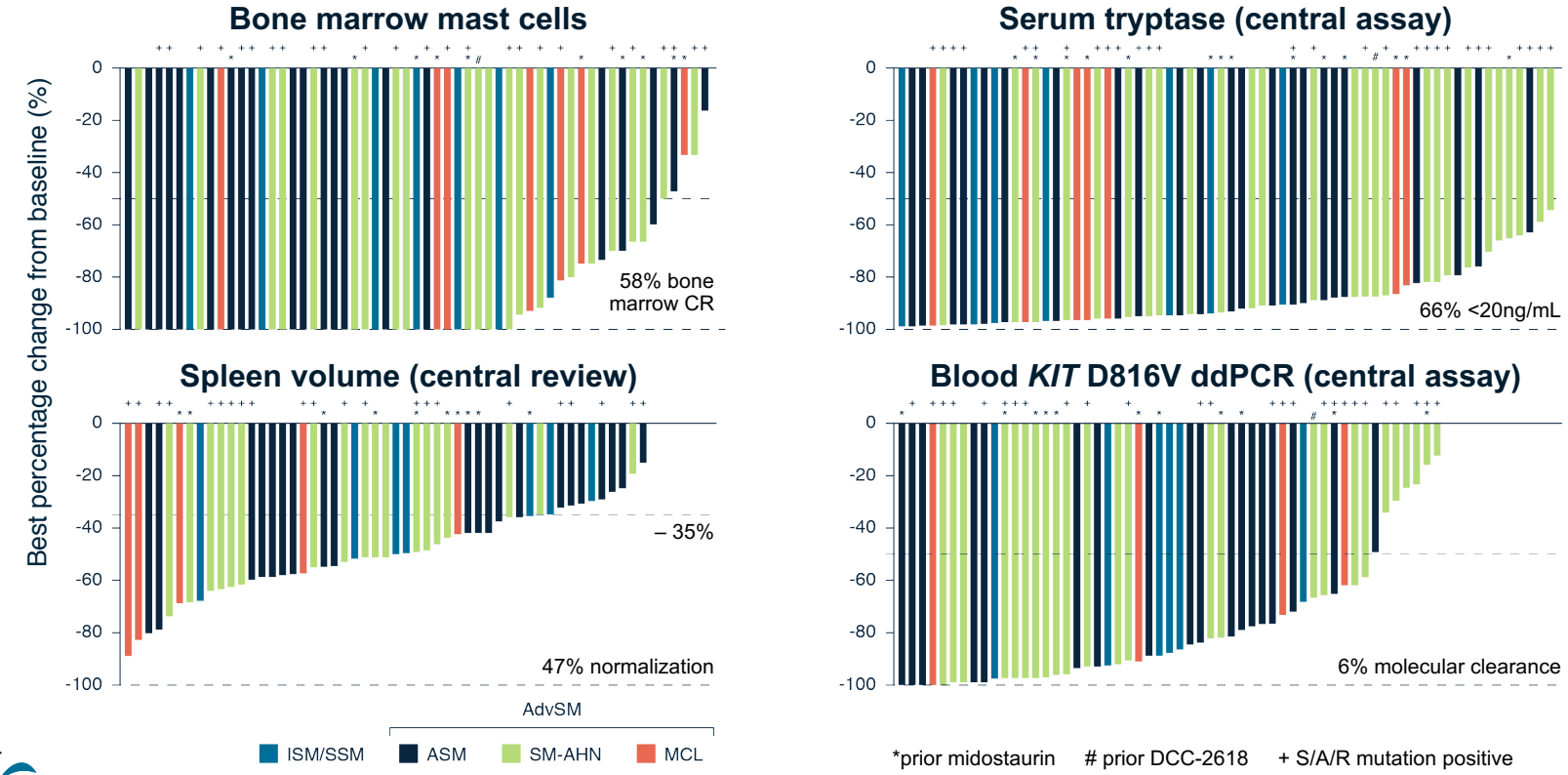
Spectrum

Patient impact

- Debilitating symptoms
- Increasing organ dysfunction and damage
- Decreased overall survival[2]

[1] Garcia-Montero AC et al, 2006.
[2] Based on published natural history data.

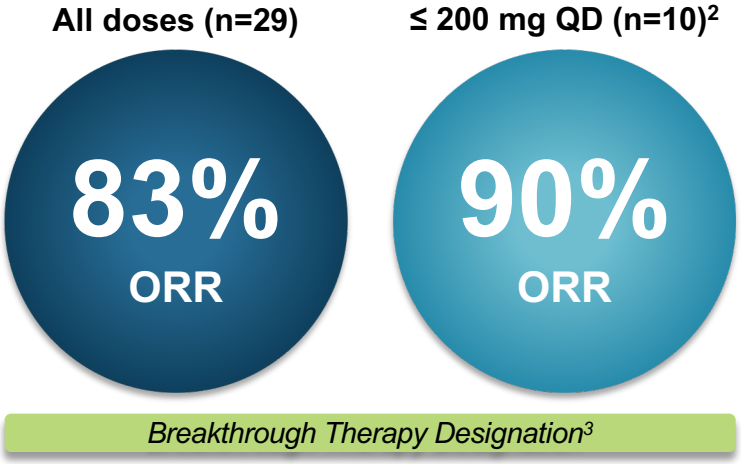
Decline in mast cell burden in evaluable patients across all patient subtypes



Data previously presented at ASH Annual Meeting in December 2018. Data cutoff date: September 30, 2018.

Results show deep and durable clinical responses in advanced SM

Best response per IWG-MRT-ECNM criteria[1]



Prolonged duration of response

- Ongoing treatment durations up to 31 months
- Median duration of response was not reached

Responses deepened over time

- Median time to initial response was 2 months
- Median time to CR/CRh was 9 months

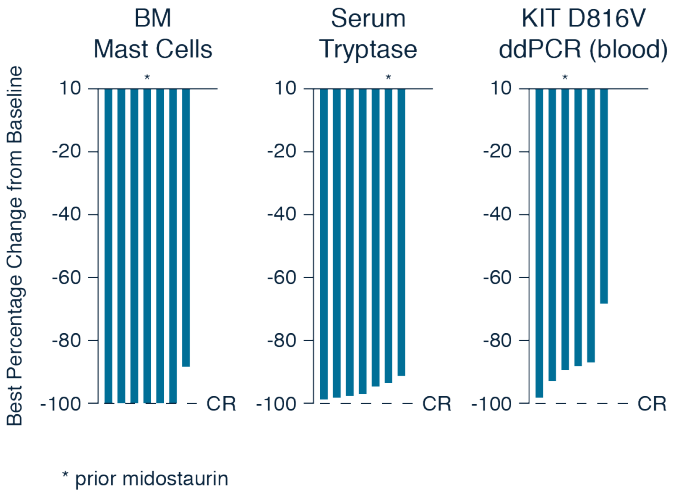
Safety (n=67)

- Avapritinib was generally well-tolerated and most adverse events reported by investigators were Grade 1 or 2
- 66% had Grade 3 and 4 treatment-related AEs; most commonly hematologic AEs in patients with prior cytopenias
- Across all doses, 4% of patients discontinued treatment due to treatment-related AEs

[1] Data presented at ASH Annual Meeting in December 2018. Data cutoff date: September 30, 2018. Pending confirmation: 3 transitioning from confirmed response to a deeper response, 3 transitioning from SD to first response. [2] Started at ≤200mg QD. 90% have not dose escalated above 200mg **as of the data cutoff date.** [3] Avapritinib granted Breakthrough Therapy Designation for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia.
CR/CRh, complete response with a full or partial recovery of peripheral blood counts.

Preliminary Phase 1 data show the potential of avapritinib to impact ISM

Evaluable indolent and smoldering SM patients in Phase 1 EXPLORER trial



* prior midostaurin

PIONEER

Part 1: Dose-finding

Part 2: Efficacy

Part 3: Extension

25 mg QD

50 mg QD

100 mg QD

RP2D R, 1:1

avapritinib

placebo

Open-label extension

Plan to present initial PIONEER trial data from Part 1 in 2H 2019

Data presented at ASH Annual Meeting in December 2018. Data cutoff date: September 30, 2018.
BM, bone marrow; R, randomized; RP2D, recommended Phase 2 dose.

Avapritinib is a differentiated precision therapy for advanced GIST and SM

Selective and potent inhibitor of genomic drivers in GIST and SM

- ✓ **Robust clinical activity with prolonged duration of response** in PDGFRA Exon 18 GIST and 4L GIST, populations with no approved therapies
  - Plan to submit NDA in June 2019 and MAA in Q3 2019
- ✓ **Deep and durable responses** in advanced SM, with remarkable consistency across disease subtypes
  - Plan to submit NDA in Q1 2020
- ✓ **Breakthrough therapy designations** for PDGFRα D842V GIST and advanced SM
- Ongoing or planned clinical trials in 3L and 2L GIST and indolent SM present **significant expansion opportunities**

Opportunity to address multiple patient populations

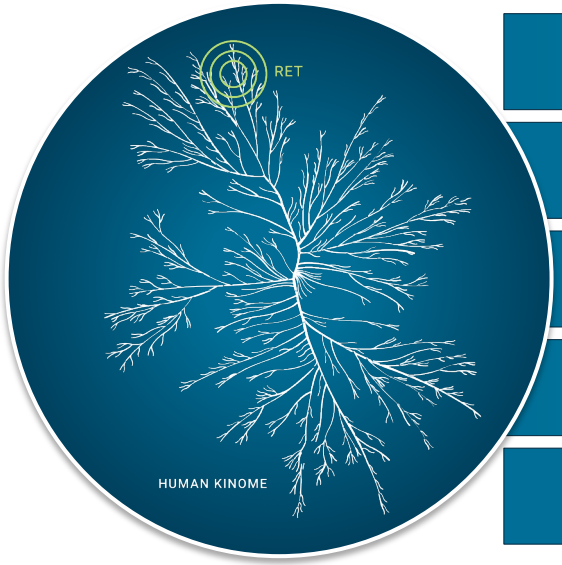
Advanced GIST

Systemic mastocytosis

~30,000 patients across GIST and SM populations in major countries*

*Represents estimated number of patients with PDGFRA-driven GIST; 2L, 3L, 4L KIT-driven GIST; and advanced, smoldering and indolent SM in major countries (US, France, Germany, Italy, Spain, the United Kingdom and Japan). NDA, new drug application (U.S.); MAA, marketing authorization application (Europe).

BLU-667: an investigational precision therapy for RET-altered cancers



	LATE CLINICAL DEVELOPMENT	U.S. REGULATORY SUBMISSION PLANS
2L RET-fusion NSCLC		Q1 2020
1L RET-fusion NSCLC*		
EGFR-mutant NSCLC (+osimertinib)*		
2L RET-mutant MTC		1H 2020
Other RET-altered solid tumors		

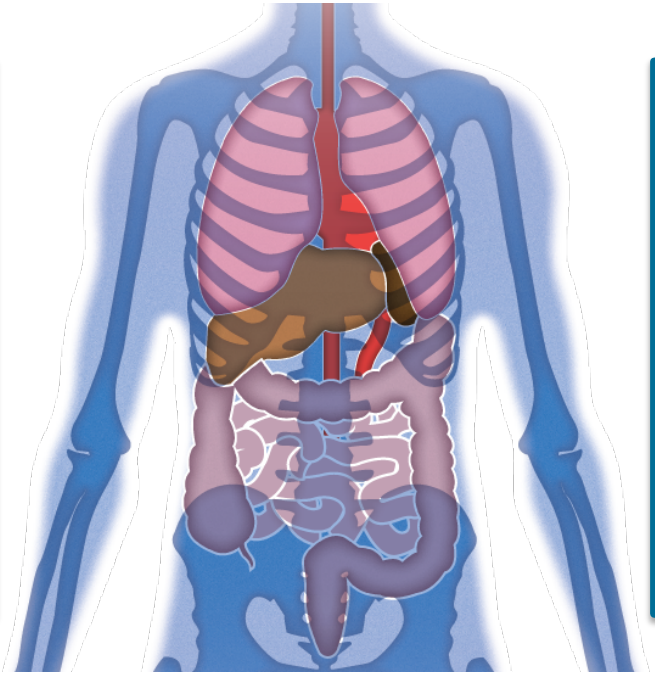
* Trial planned to initiate 2H 2019.
Target NSCLC and MTC populations have unresectable or metastatic disease. Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com) (CSTI). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.

RET alterations: oncogenic drivers lacking a 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]

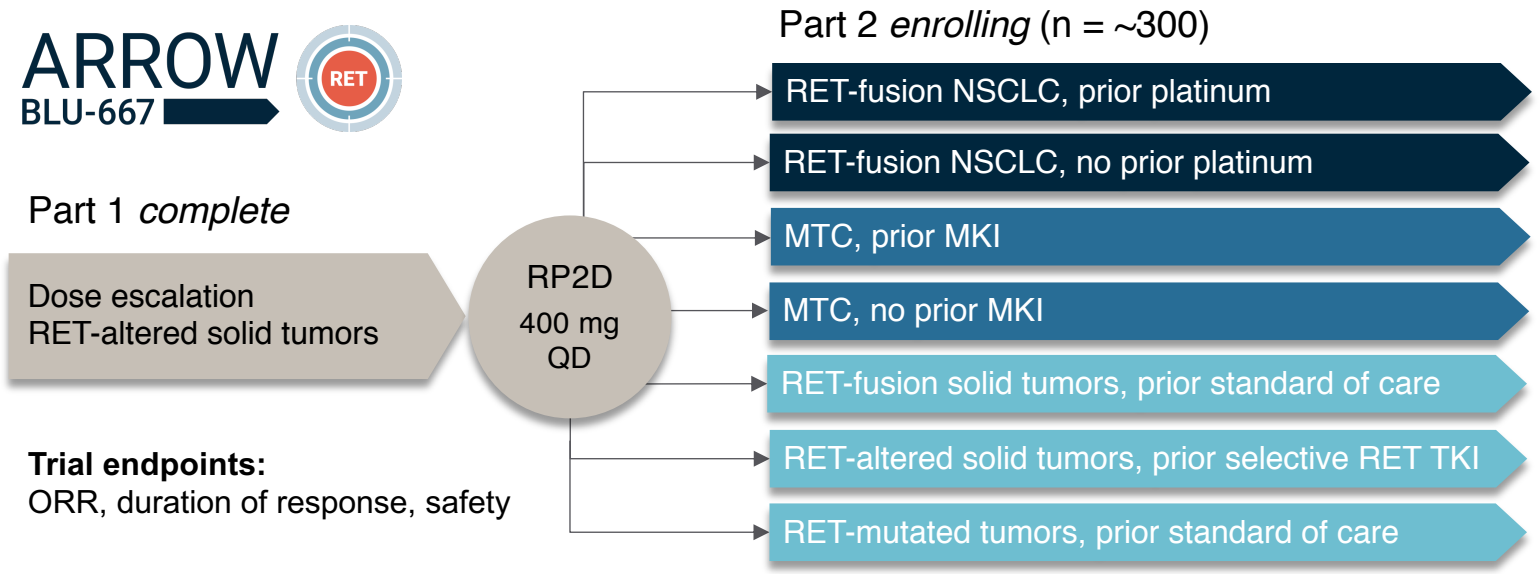


Multiple other tumor types <1% RET-altered, including:[5,6]

esophageal
pancreatic
breast
melanoma
colorectal
leukemia

[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.

Updated ARROW trial data presented at ASCO 2019



Safety[1] (n=226)

- BLU-667 was well-tolerated and most AEs were Grade 1 or 2 and reversible
- Across all patients, 4% discontinued due to treatment-related AEs

[1] Data presented at ASCO Annual Meeting in June 2019. Includes NSCLC and MTC patients treated at the recommended Phase 2 dose of 400 mg QD and enrolled as of November 14, 2018 with follow-up through a data cutoff date of April 28, 2019. MKI, multi-kinase inhibitor; TKI, tyrosine kinase inhibitor

NSCLC patients with RET fusions have no highly effective treatment options

- **Chemotherapy:** nonspecific, low response rates, significant toxicity
- **Checkpoint inhibition:** Preliminary evidence for lack of benefit in RET-altered NSCLC[1]
- **Multi-kinase inhibitors:** ↓ activity, ↑ off-target toxicity[2,3]
- Growing understanding of RET-driven resistance
- No selective RET inhibitors are approved

[1] Mazieres, et al. JCO 2018. [2] Drilon, et al. Lancet 2017. [3] Yoh, et al. Lancet Respir Med 2017.

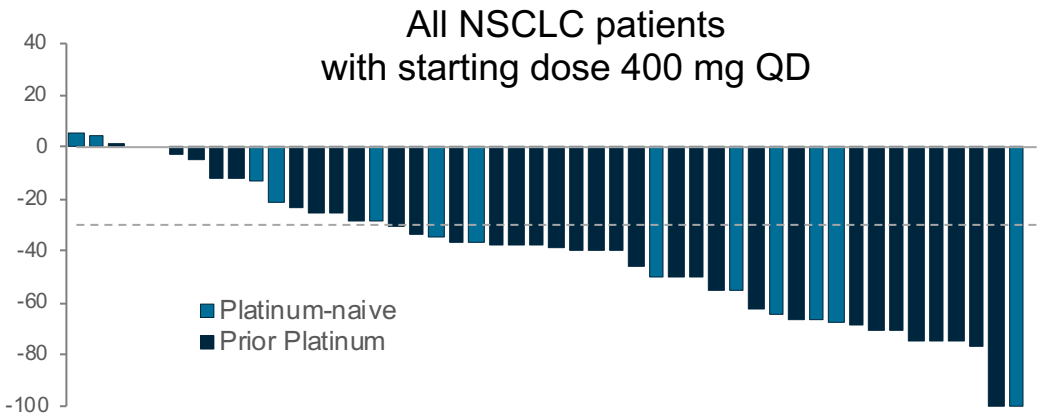
BLU-667 showed robust and durable clinical activity in RET fusion NSCLC

60%
Confirmed ORR

RET-fusion NSCLC with prior platinum chemotherapy

400 mg QD, n=35

Breakthrough Therapy Designation[1]

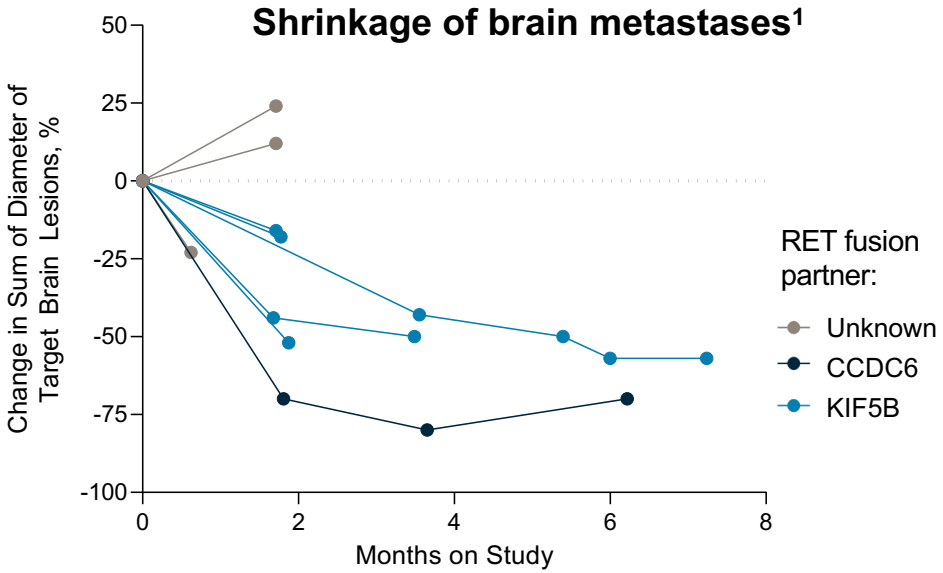


ADDITIONAL RESULTS

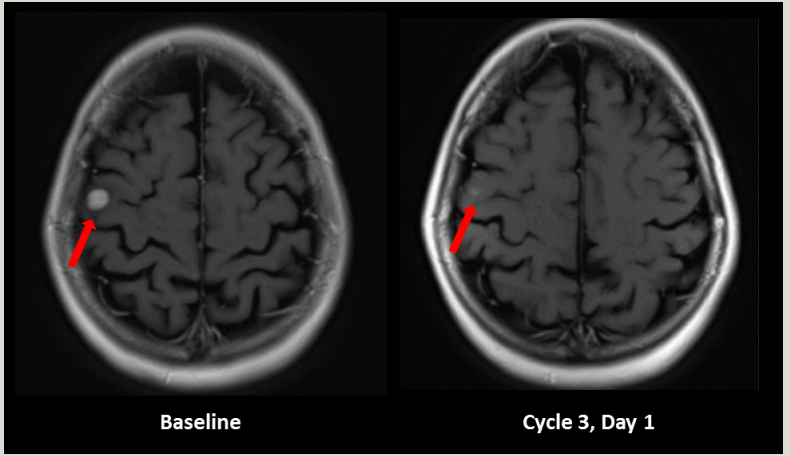
- Across all NSCLC patients, 96% disease control rate
- 71% ORR in patients naïve to prior systemic therapy
- Median duration of response not reached; 82% of responders remain on treatment with durations up to 15.6 months

Data presented at ASCO Annual Meeting in June 2019. Includes NSCLC patients treated at the recommended Phase 2 dose of 400 mg QD and enrolled as of November 14, 2018 with follow-up through a data cutoff date of April 28, 2019. [1] BLU-667 granted Breakthrough Therapy Designations for RET fusion-positive NSCLC that has progressed following platinum-based chemotherapy.

BLU-667 showed strong activity against NSCLC brain metastases



- 78% had shrinkage of measurable brain metastases
- No patients had progression due to new CNS involvement



- 52-year-old woman, RET fusion+ NSCLC, prior platinum and checkpoint inhibitor
- Near-complete resolution of previously untreated target brain metastasis after two months of BLU-667 400 mg QD
- Continues to receive treatment with ongoing confirmed PR (70% shrinkage) at ~6 months

[1] Data presented at ASCO Annual Meeting in June 2019 for 9 patients with brain lesion(s) identified as RECIST 1.1 target lesions at baseline. All patients treated at 400 mg QD. Data cut-off: April 28, 2019. Case courtesy of Dr. Stephen Liu, Georgetown University, Washington, D.C.

RET-altered thyroid cancer patients may benefit from highly targeted therapy

- **Multi-kinase inhibitors** are approved for MTC, but have important limitations:[1]
  - 25-44% ORR
  - Off-target toxicity often requiring dose modification or discontinuation
  - Emergence of resistance
- No selective RET inhibitors are approved

[1] Drillon, et al. Nature Reviews Clinical Oncology, 2017.

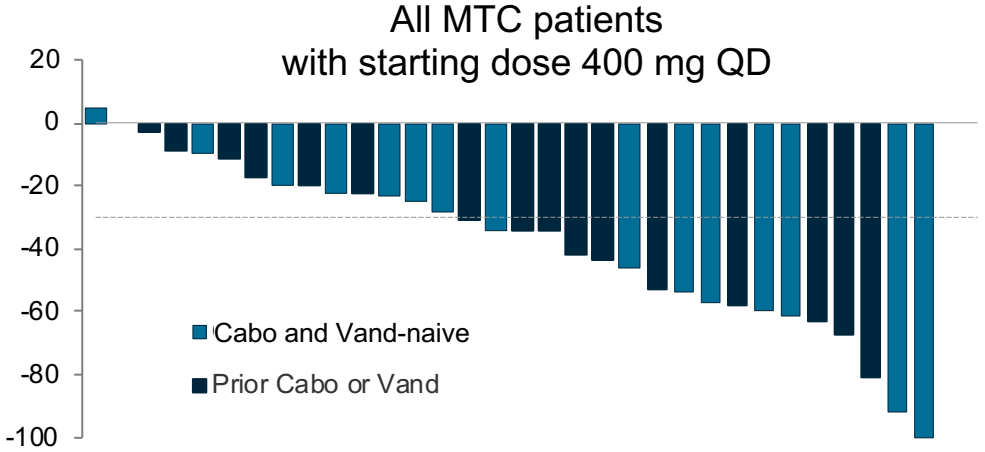
BLU-667 shows robust and durable clinical activity in patients with MTC and other RET-altered cancers

63%
ORR[1]

RET-mutant MTC previously treated with an MKI

400 mg QD, n=16

Breakthrough Therapy Designation[2]



ADDITIONAL RESULTS

- Across all MTC patients, 97% disease control rate
- Median duration of response not reached; all responders remain on treatment with durations up to 15.6 months
- 83% ORR in papillary thyroid cancer[3]
- Additional clinical responses observed in pancreatic cancer and intrahepatic bile duct carcinoma

Data presented at ASCO Annual Meeting in June 2019. Includes MTC patients treated at the recommended Phase 2 dose of 400 mg QD and enrolled as of November 14, 2018 with follow-up through a data cutoff date of April 28, 2019. [1] Two responses pending confirmation. [2] BLU-667 granted Breakthrough Therapy Designations for RET-mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments. [3] Six patients were evaluable for response assessment (3 confirmed PRs, 2 PRs pending confirmation). Cabo, cabozantinib; Vand, vandetininb.

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 alteration, 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

Resistant EGFR mutation+ NSCLC

Growing understanding of RET-driven resistance

RET mutation+ MTC

~90% of advanced MTC

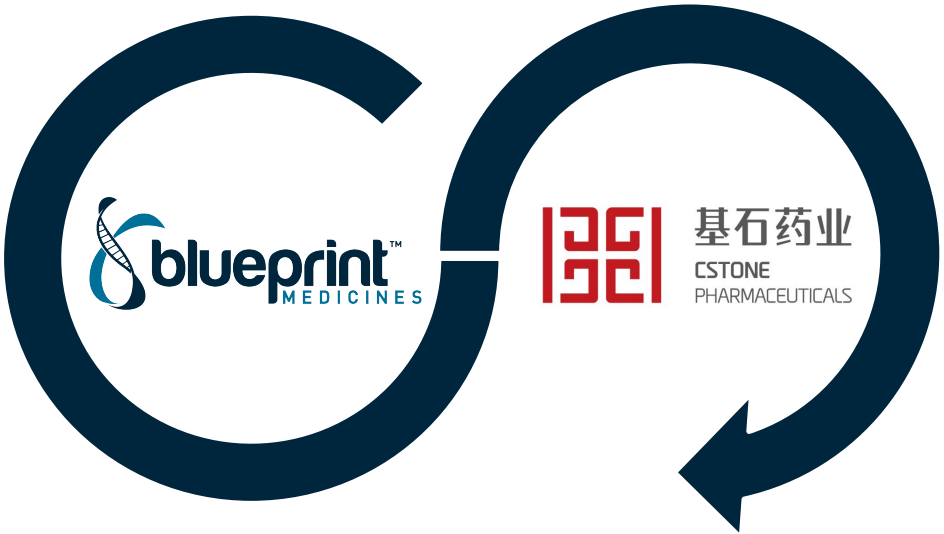
Tumor agnostic RET+ cancers

Low variable RET frequency across tumor types

Data reported at ASCO 2019 Annual Meeting in June 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.

Strategic collaboration accelerates BLU-554 clinical development program

- Leader in targeted kinase medicines
- Three clinical programs with demonstrated proof-of-concept
- Retain all rights in the rest of the world



- Deep development experience and network in China
- Growing oncology portfolio including immunotherapies
- Exclusive rights in Greater China[1]

First patient dosed in China in ongoing Phase 1 trial of BLU-554 in TKI-naïve HCC

Chinese health authorities have cleared IND for BLU-554 and anti-PD-L1 combination trial in HCC

[1] Greater China consists of Mainland China, Hong Kong, Macau and Taiwan.

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

Platform enables additional pipeline programs, including BLU-782 for fibrodysplasia ossificans progressiva

Based on current operating plans, expect existing cash balance will fund operations into the middle of 2021*

Program	Anticipated milestones for 2019-2020	Anticipated Timing
Avapritinib – GIST	Submit NDA for PDGFRA Exon 18 mutant GIST and 4L GIST	June 2019
	Submit MAA for PDGFRα D842V mutant GIST and 4L GIST	Q3 2019
	Complete enrollment of Phase 3 VOYAGER trial in 3L GIST	2H 2019
	Initiate Phase 3 COMPASS-2L precision medicine trial in 2L GIST	2H 2019
	Submit NDA for 3L GIST	2020
Avapritinib – SM	Present updated data from Phase 1 EXPLORER trial in advanced SM	June 2019
	Present initial data from Phase 2 PIONEER trial in indolent and smoldering SM	2H 2019
	Complete enrollment of Phase 2 PATHFINDER trial in advanced SM	2H 2019
	Submit NDA for advanced SM	Q1 2020
BLU-667 – RET	Initiate Phase 3 trial in 1L RET-fusion NSCLC	2H 2019
	Initiate Phase 2 trial of BLU-667 and osimertinib in EGFR-mutant NSCLC harboring an acquired RET alteration	2H 2019
	Submit NDA for previously 2L RET-fusion NSCLC and 2L RET-mutant MTC	Q1 and 1H 2020, respectively
BLU-554 – HCC	Initiate Phase 1 combination trial of BLU-554 and CS-1001, CStone Pharmaceuticals' anti-PD-L1 inhibitor, in China	2H 2019
BLU-782 – FOP	Initiate Phase 2 trial in patients with FOP	Q4 2019
Research portfolio	Provide a research portfolio update, including disclosure of up to 2 new targets, at an R&D day	2019
	Nominate at least one new wholly-owned discovery program	2019

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* Includes estimated net proceeds of $327.2M from April 2019 follow-on public offering and excludes any potential option fees and milestone payments under the Roche and CStone collaborations

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