A blueprint for a healthier tomorrow

July 15, 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, BLU-554, BLU-667 and BLU-782 and the ability of Blueprint Medicines Corporation (the “Company”) to implement those clinical development plans; the potential benefits of the Company’s current and future drug candidates in treating patients; plans and timelines for regulatory submissions, filings or discussions, including a first New Drug Application for avapritinib for the treatment of PDGFRα D842V-driven gastrointestinal stromal tumors (“GIST”); plans and timelines for the development and commercialization of companion diagnostics for the Company’s current or future drug candidates; plans and timelines for current or future discovery programs; plans and timelines for any current or future collaborations with strategic partners; expectations regarding the Company’s existing cash, cash equivalents and investments or the future financial performance of the Company; expectations regarding potential milestones; and the Company’s strategy, 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-554, BLU-667 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; 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, including companion diagnostic tests for BLU-554 for FGFR4-driven hepatocellular carcinoma, avapritinib for PDGFRα D842V-driven GIST and BLU-667 for RET-driven non-small cell lung cancer; 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.

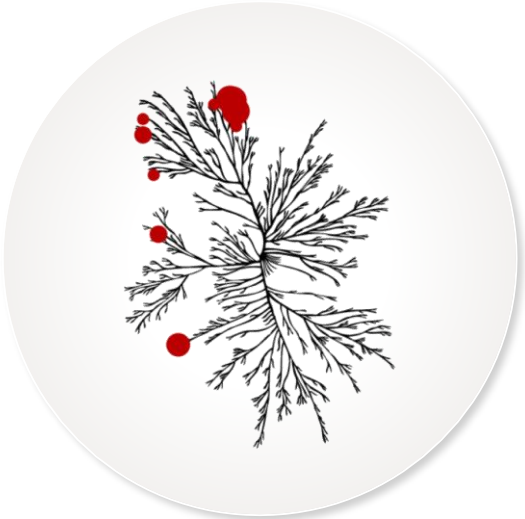
These and other risks and uncertainties are described in greater detail under “Risk Factors” in the Company’s Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, as filed with the Securities and Exchange Commission (“SEC”) on May 2, 2018, and any other filings the Company has made or 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.

A new way of looking at kinase medicines

Highly selective kinase medicines offer potential for
improved potency, less off-target activity and increased probability of clinical success

SELECTIVE



AVAPRITINIB

NON-SELECTIVE

SUNITINIB

MIDOSTAURIN

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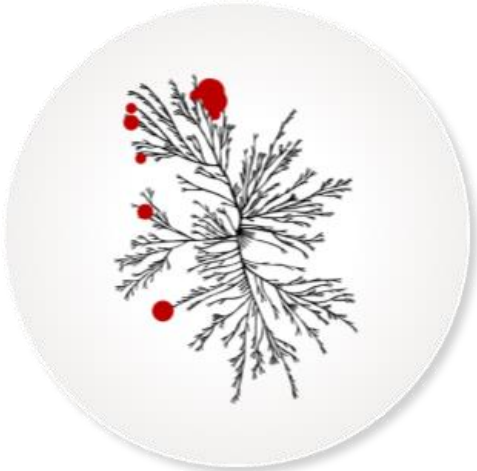
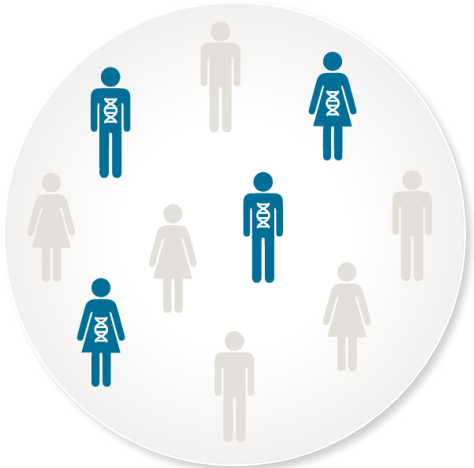
Clinical strategy to rapidly bring transformative medicines to patients

GENOMIC DRIVER OF DISEASE ❯ **HIGHLY SELECTIVE KINASE MEDICINE** ❯ **SELECTED PATIENT POPULATION** ❯



Proprietary compound library



TARGET OUTCOMES

- Achieve rapid clinical proof-of-concept
- Early go/no-go decisions
- Expedited development & regulatory approval
- Clear commercial value proposition

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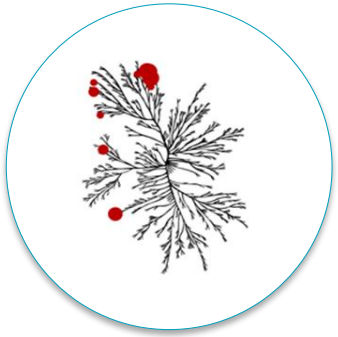
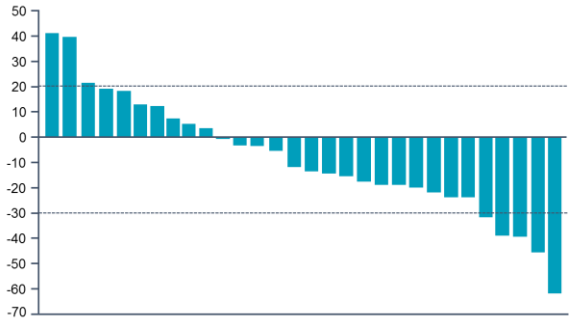
Five compelling proof-of-concept datasets over 18 months

avapritinib

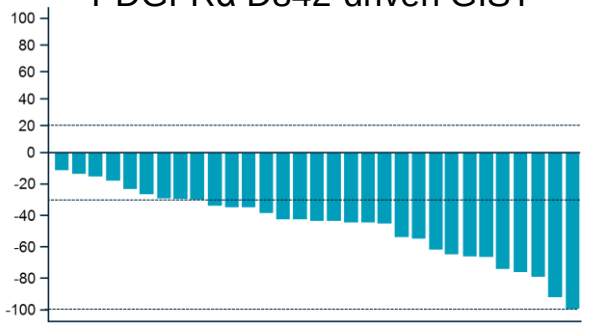


3L+ KIT-driven GIST



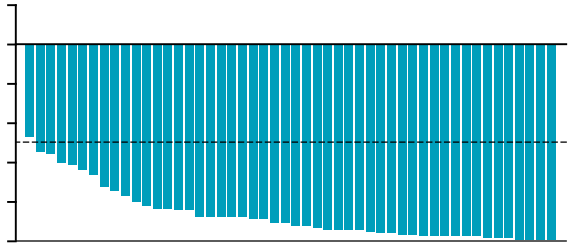
Maximum reduction in target tumors

PDGFRα D842-driven GIST



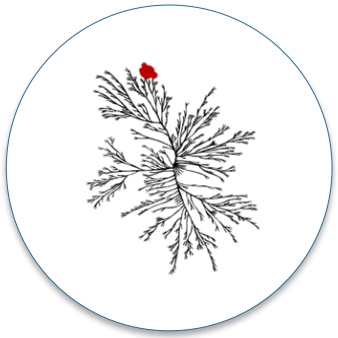
Maximum reduction in target tumors

Advanced Systemic Mastocytosis

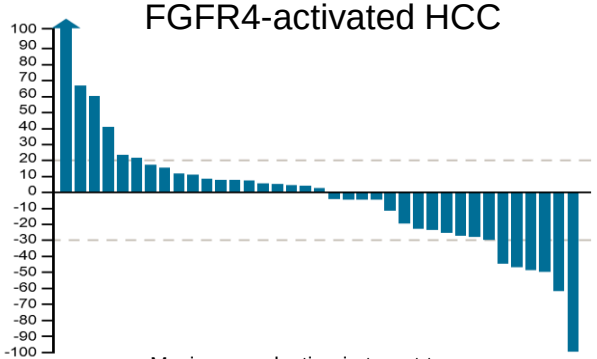


Maximum reduction in serum tryptase

BLU-554

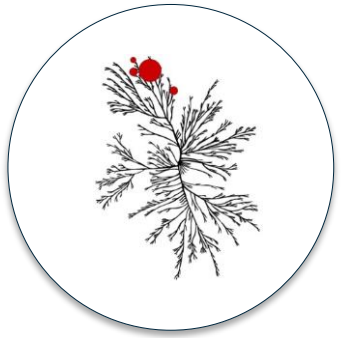


FGFR4-activated HCC

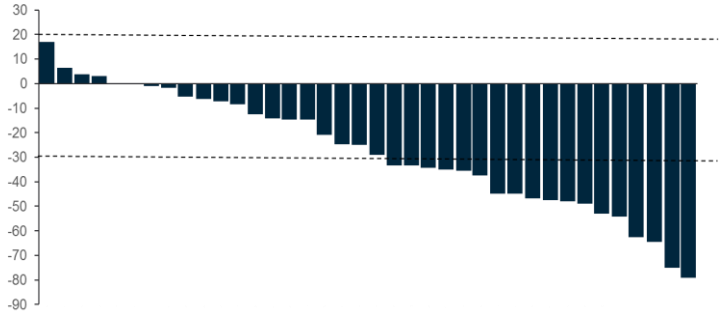


Maximum reduction in target tumors

BLU-667



RET-altered Solid Tumors



Maximum reduction in target tumors

Avapritinib GIST data presented at November 2017 CTOS Annual Meeting. Data cutoff: October 11, 2017; Avapritinib systemic mastocytosis data presented at June 2018 Congress of the European Hematology Association. Data cutoff: April 30, 2018; BLU-554 data presented at September 2017 ESMO Congress. Data cutoff: August 18, 2017; BLU-667 data presented at April 2018 AACR Annual Meeting. Data cutoff: April 6, 2018. 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; GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; 3L+, third-line or later treatment.

Realizing our vision for Blueprint Medicines

DRUG CANDIDATE (TARGET)	DISCOVERY	PRECLINICAL	PHASE 1-2	PIVOTAL	COMMERCIAL RIGHTS
avapritinib (KIT & PDGFRα)	Phase 1 NAVIGATOR – Advanced PDGFRα-driven GIST Phase 1 NAVIGATOR – Advanced 3L+ (KIT-driven) GIST Phase 1 NAVIGATOR – 2L (KIT-driven) GIST Phase 3 VOYAGER – Advanced 3L GIST Phase 1 EXPLORER – Advanced systemic mastocytosis (SM) Phase 2 PATHFINDER – Advanced systemic mastocytosis (planned mid 2018) Phase 2 PIONEER – Indolent and smoldering systemic mastocytosis (planned by end of 2018)				*
BLU-554 (FGFR4)	Phase 1 – Advanced hepatocellular carcinoma				
BLU-667 (RET)	Phase 1 ARROW – Advanced NSCLC, thyroid and other cancers[1]				
BLU-782 (ALK2)	Fibrodysplasia ossificans progressiva				
3 undisclosed kinase targets					
Immunokinase targets	Up to 5 cancer immunotherapy programs; development stage undisclosed				Roche **

2L, second-line; 3L, third-line; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis

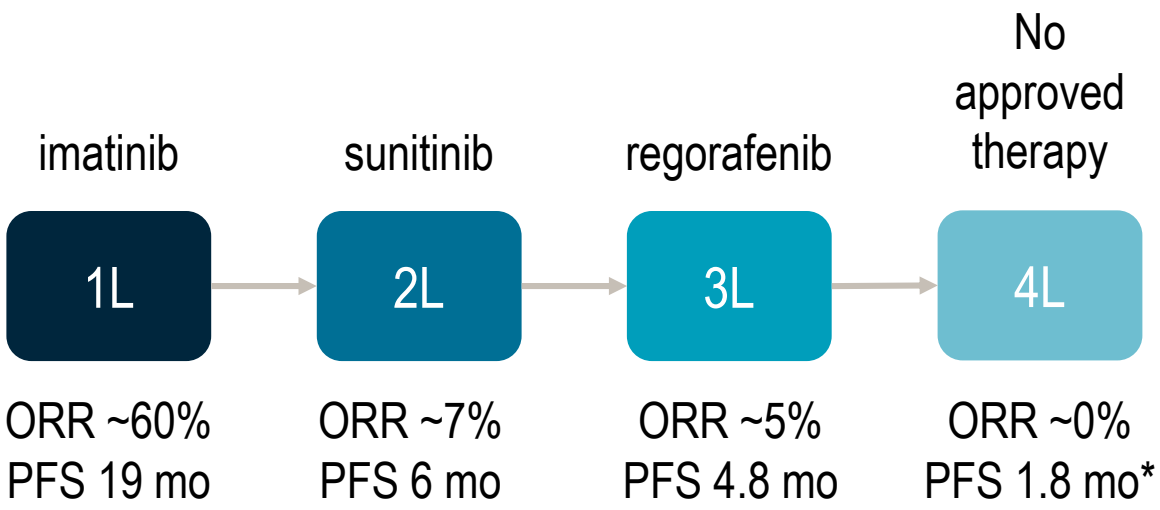
[1] ARROW trial includes a basket cohort that consists of other advanced solid tumors with RET alterations.

* 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.

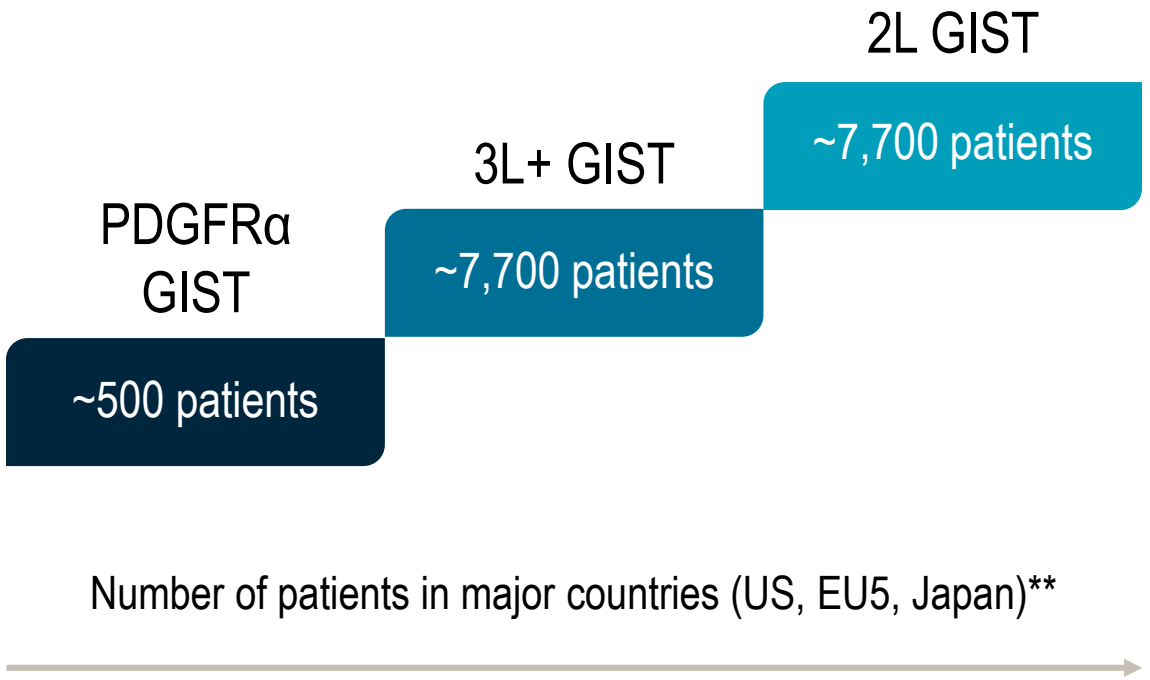
Potent and selective KIT and PDGFRα inhibition with avapritinib has the potential to address important medical needs in GIST

No highly effective therapies beyond imatinib



- Approved agents are ineffective against PDGFRα D842V GIST

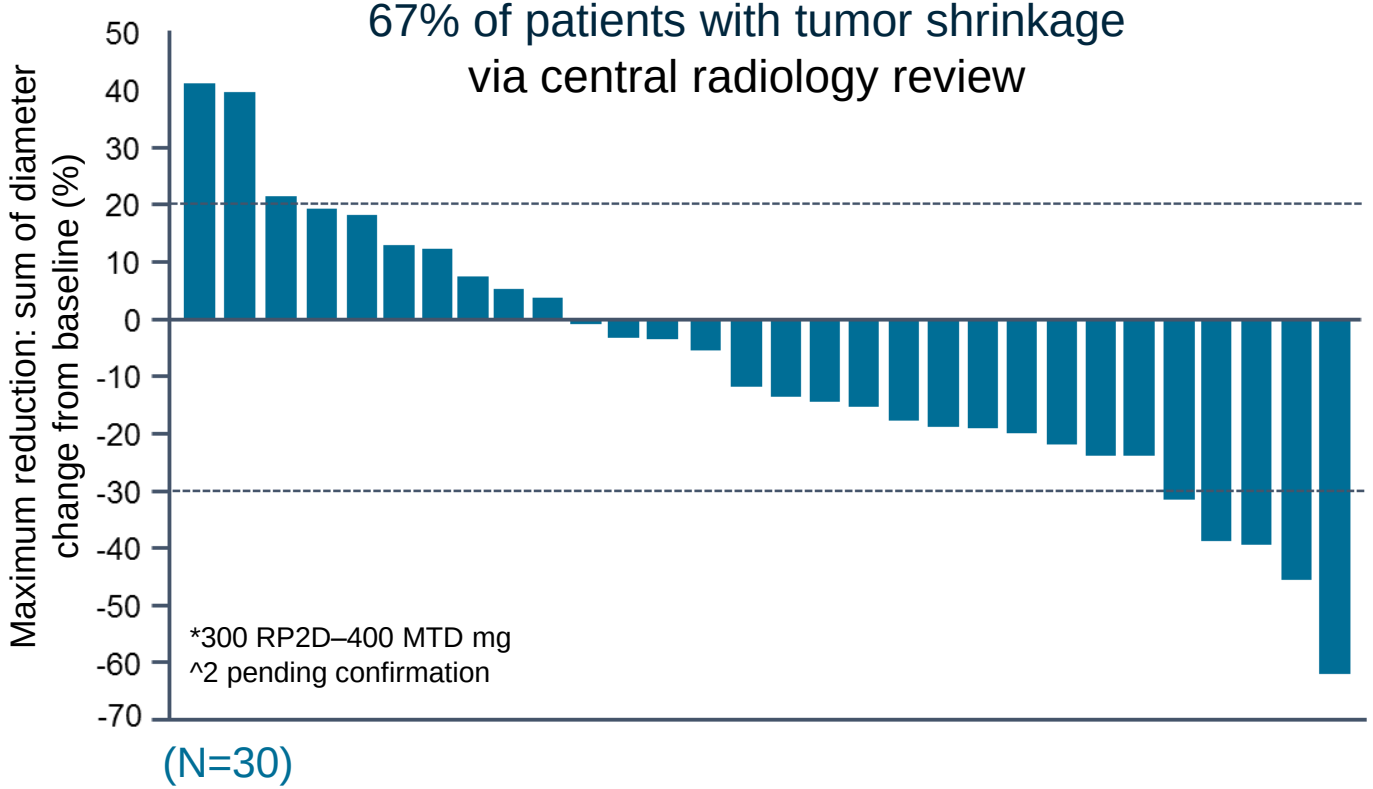
Significant global opportunity



ORR, overall response rate; PFS, progression free survival.
* Imatinib re-challenged. ** Represents estimated incidence of GIST patients (regardless of alteration) and PDGFRα D842V-driven GIST patients in major countries (US, EU5 and Japan). 3L+ GIST includes estimated incidence for 3L and 4L GIST.

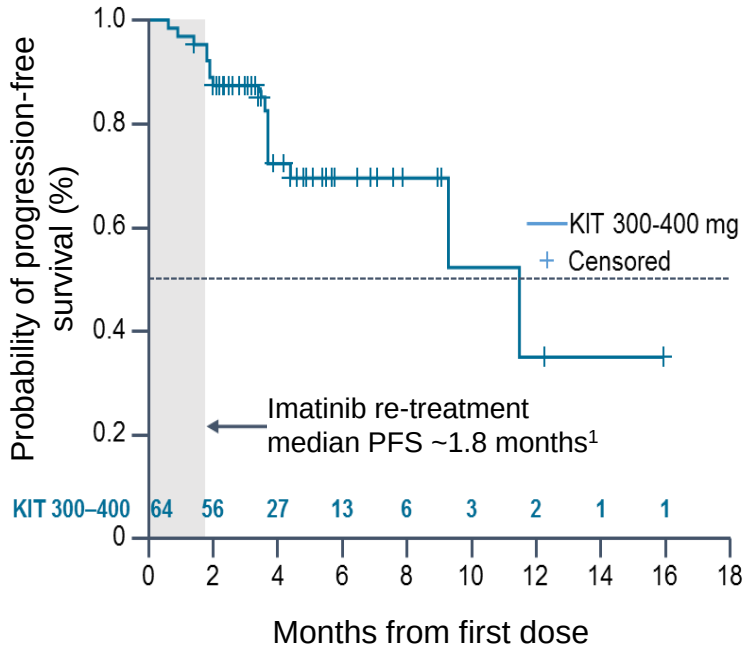
Tumor reduction and prolonged PFS observed in 3L+ KIT- driven GIST patients

67% of patients with tumor shrinkage via central radiology review



(N=30)

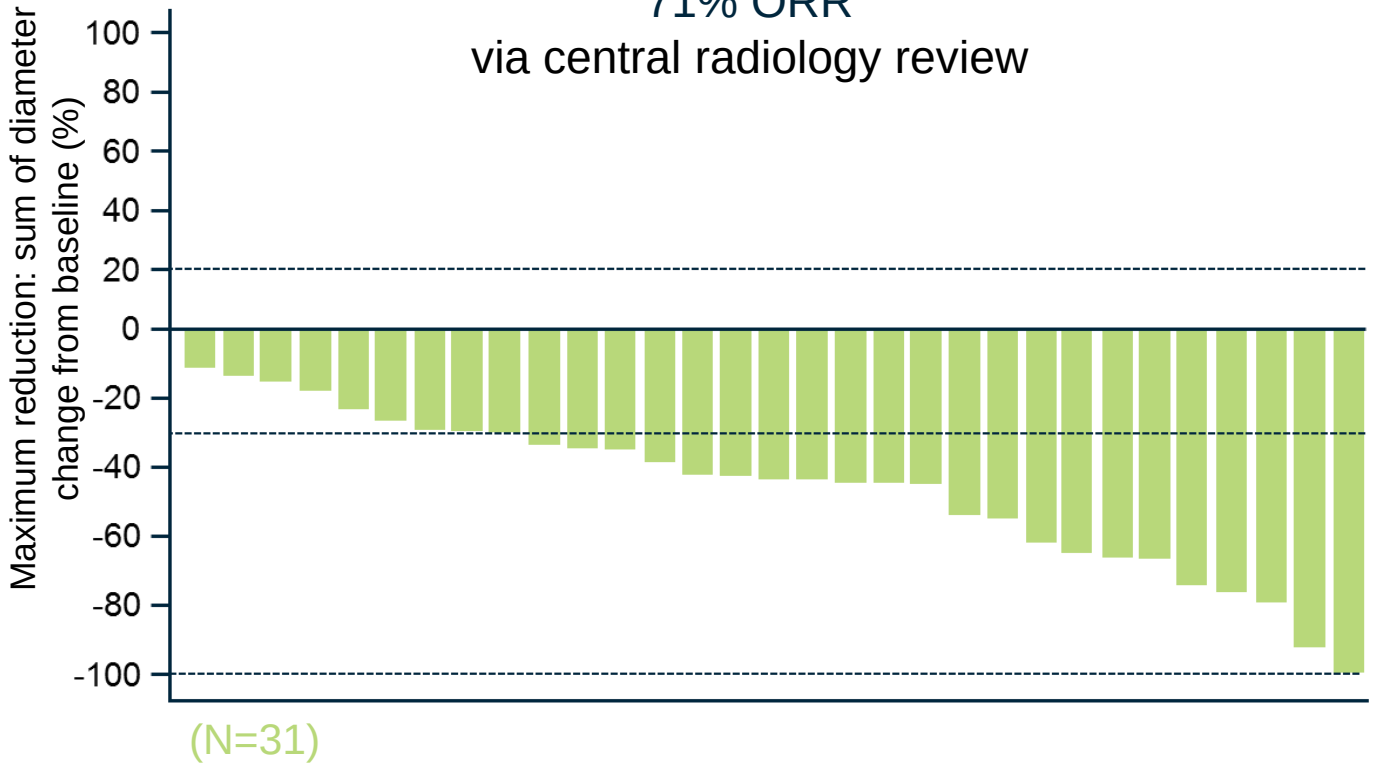
Median PFS 11.5 months; PFS at 6 months 69%



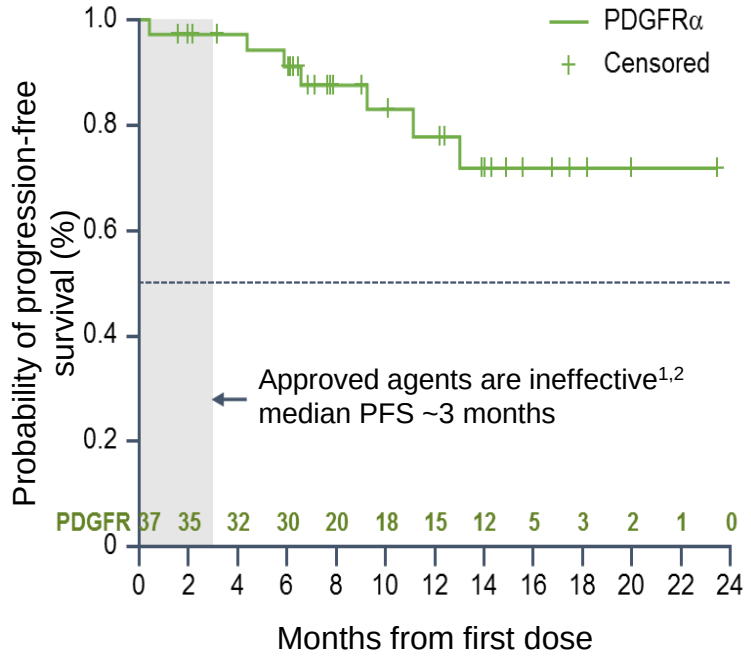
[1] Kang et al. Lancet Oncol. 2013;14(12):1175–82.
DCR, disease control rate; MTD, maximum tolerated dose; PD, progressive disease; PR, partial response; SD, stable disease.
Data previously presented in November 2017 at the CTOS Annual Meeting. Data cutoff: October 11, 2017.

Tumor reduction and prolonged PFS observed in PDGFRα D842-mutant GIST

71% ORR
via central radiology review



Median PFS not reached;
PFS at 12 months 78%



[1] Cassier et al. Clin Cancer Res. 2012;18(16):4458–64. [2] Yoo et al. Cancer Res Treat. 2016;48(2):546–52
CR, complete response.
Data previously presented in November 2017 at the CTOS Annual Meeting. Data cutoff: October 11, 2017.

Safety results showed avapritinib was generally well-tolerated in patients with GIST

- Most AEs were Grade 1 or 2
- Across all grades, the most common AEs included nausea (56%), fatigue (53%), periorbital edema (43%), vomiting (41%), peripheral edema (34%), anemia (31%), diarrhea (31%), increased lacrimation (30%), cognitive effects (30%), decreased appetite (28%), dizziness (23%), constipation (22%), and hair color changes (22%)
- Investigators reported treatment-related Grade ≥3 AEs in 39 patients (34%), including anemia (9%), fatigue (7%), hypophosphatemia (4%), nausea (4%) and cognitive effects (3%)
- Six patients (5%) discontinued treatment with avapritinib due to AEs

AE, adverse event. Data previously presented in November 2017 at the CTOS Annual Meeting. Data cutoff: October 11, 2017.
Cognitive effects are an aggregated category of individual cognitive events, each of which was observed in fewer than 20% of patients.

Highly selective inhibition of D816V mutant KIT with avapritinib has broad potential applications across all subtypes of SM

~90-95% of patients have KIT D816V mutation[1]

Spectrum

- Indolent SM (ISM)
- Smoldering SM (SSM)
- Aggressive SM (ASM)
- SM with Associated Hematologic Neoplasm (SM-AHN)
- Mast Cell Leukemia (MCL)

Advanced SM

Cases[2]

~16,300 patients | ~1,800 patients | ~2,600 patients

Patient impact

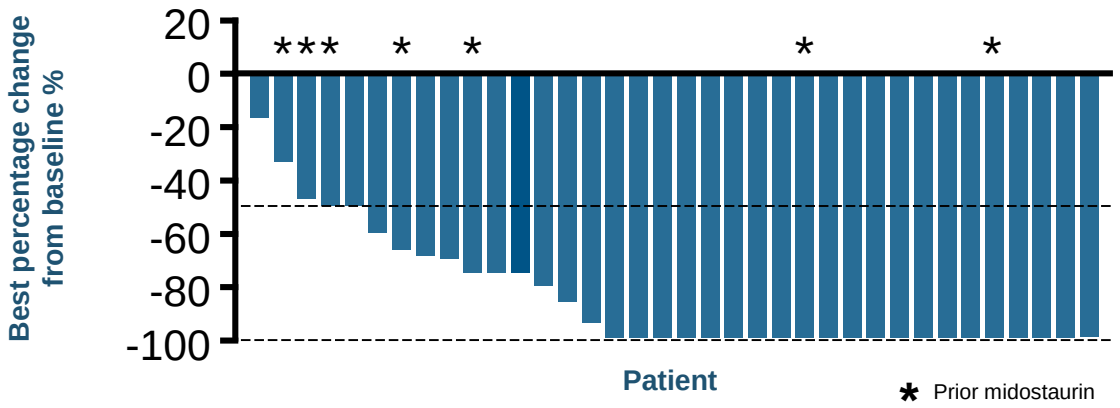
- Debilitating symptoms
- Increasing organ dysfunction and damage
- Decreased overall survival[3]

1 Garcia-Montero AC et al, 2006.
2 Represents estimated prevalence regardless of alteration in major countries (US, EU5 and Japan).
3 Based on published natural history data.

Strong clinical activity in systemic mastocytosis across outcome measures regardless of dose or disease subtype

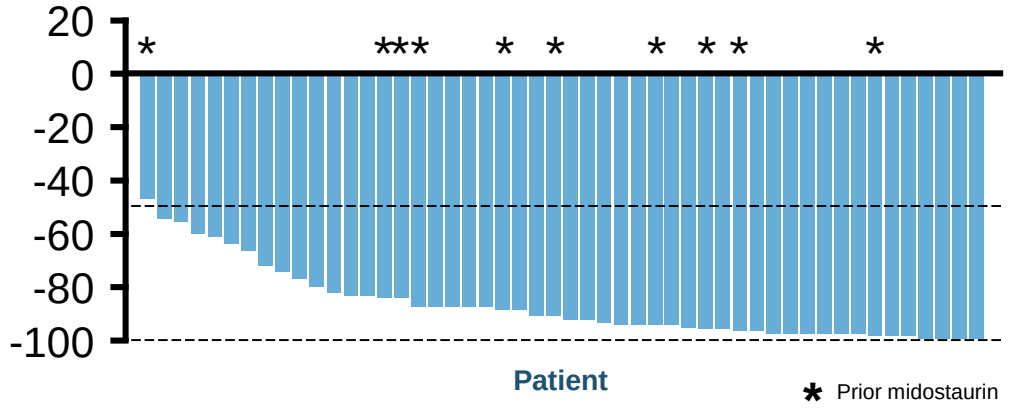
58% had bone marrow complete response (CR)

Bone marrow mast cells (n=36)



98% had >50% reduction in serum tryptase

Serum tryptase (n=50)



- **83% objective response rate per IWG criteria[1]**
- **Clinical activity observed at all dose levels tested, with duration of response up to 22 months**
- Most AEs reported by investigators were Grade 1 or 2; grade ≥3 treatment-related AEs reported in 28 patients (54%)
- Three discontinuations due to treatment-related AEs

[1]ORR defined as CR/CRh + PR + clinical improvement; responses pending confirmation: ASM, 1 PR; SM-AHN, 2 PR; MCL, 2 CR
CRh, complete response with partial recovery of peripheral blood counts; IWG criteria, International Working Group-Myeloproliferative Neoplasms Research and Treatment and European Competence Network on Mastocytosis criteria.
Data previously presented in June 2018 at the Congress of the European Hematology Association. Data cutoff: April 30, 2018.

Plan to submit first New Drug Application for avapritinib for the treatment of PDGFRα D842V-driven GIST in 1H 2019

	Advanced GIST		Systemic Mastocytosis (SM)		
Trial	NAVIGATOR	VOYAGER	EXPLORER	PATHFINDER	PIONEER
Phase	• Phase 1	• Phase 3	• Phase 1	• Phase 2	• Phase 2
Populations	• PDGFRα D842V* • 3L+ (KIT-driven) • 2L	• 3L* • 4L*	• Advanced SM	• Advanced SM*	• Indolent SM* • Smoldering SM*
Status	• Enrollment of PDGFRα and 3L+ cohorts complete • 2L expansion cohort enrolling	• Global, randomized trial enrolling	• Expansion cohorts enrolling	• Planned initiation by middle of 2018	• Planned initiation by year end 2018

* Potential for registration-enabling trial (base-case)

Growing portfolio of highly selective investigational kinase medicines

BLU-667

- Non-small cell lung cancer
- Medullary thyroid cancer
- Other RET-altered solid tumors

BLU-554

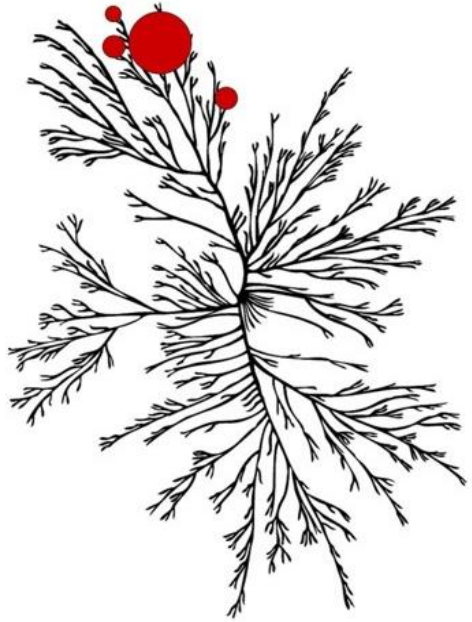
- Hepatocellular carcinoma

BLU-782

- Fibrodysplasia ossificans progressiva

BLU-667 was designed to treat RET-altered cancers

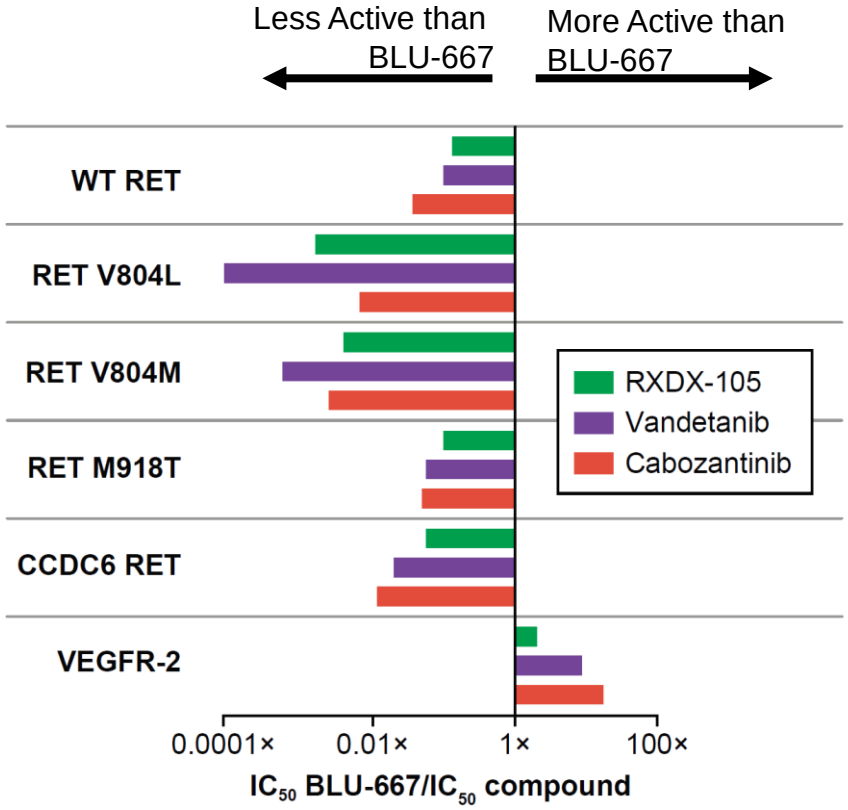
Highly selective for RET versus other kinases



Sub-nanomolar potency across RET alterations

Variant	Biochemical IC_{50} (nM)
RET wildtype	0.4
RET V804L	0.3
RET V804M	0.4
RET M918T	0.4
CCDC6-RET	0.4

More potent than multi-kinase inhibitors



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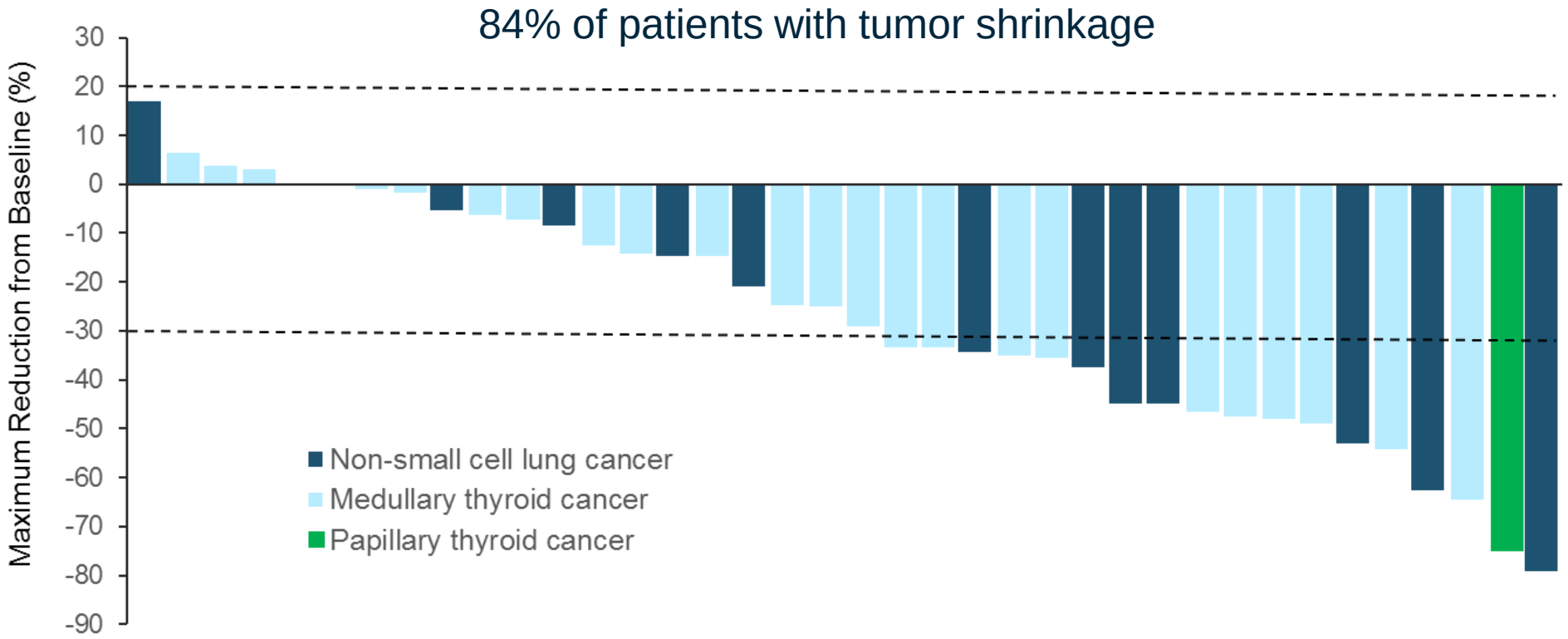
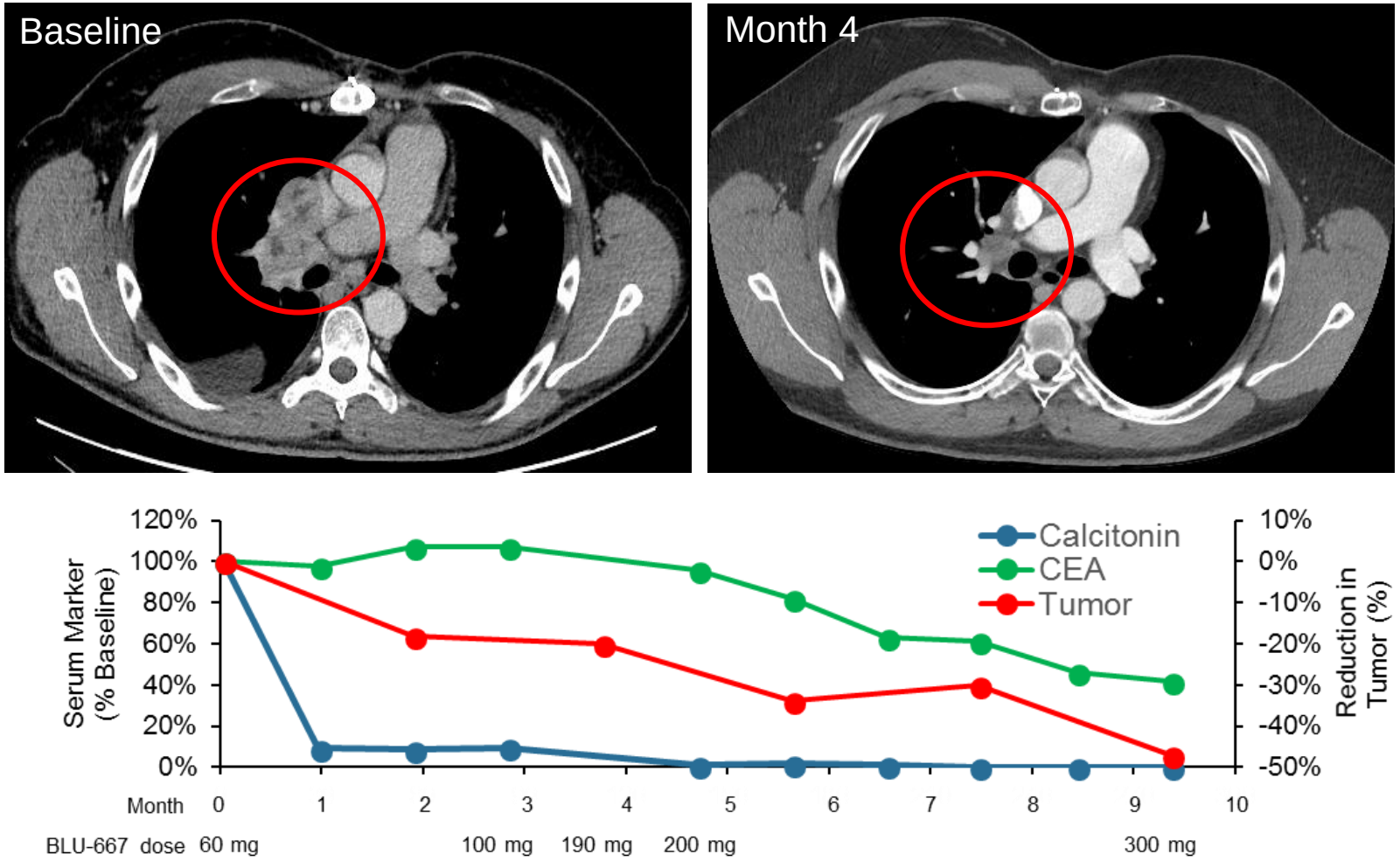
BLU-667 demonstrates broad anti-tumor activity regardless of RET genotype, tumor type or prior therapy



- Most AEs reported by investigators were Grade 1
- Grade 3 treatment-related AEs reported in 8 patients (16%); no Grade 4/5 treatment-related AEs
- Only 1 discontinuation due to a treatment-related AE
- 41 of 53 patients (77%) remained on treatment as of the data cut-off

Data previously presented at AACR Annual Meeting in April 2018. Data cut-off: April 6, 2018.

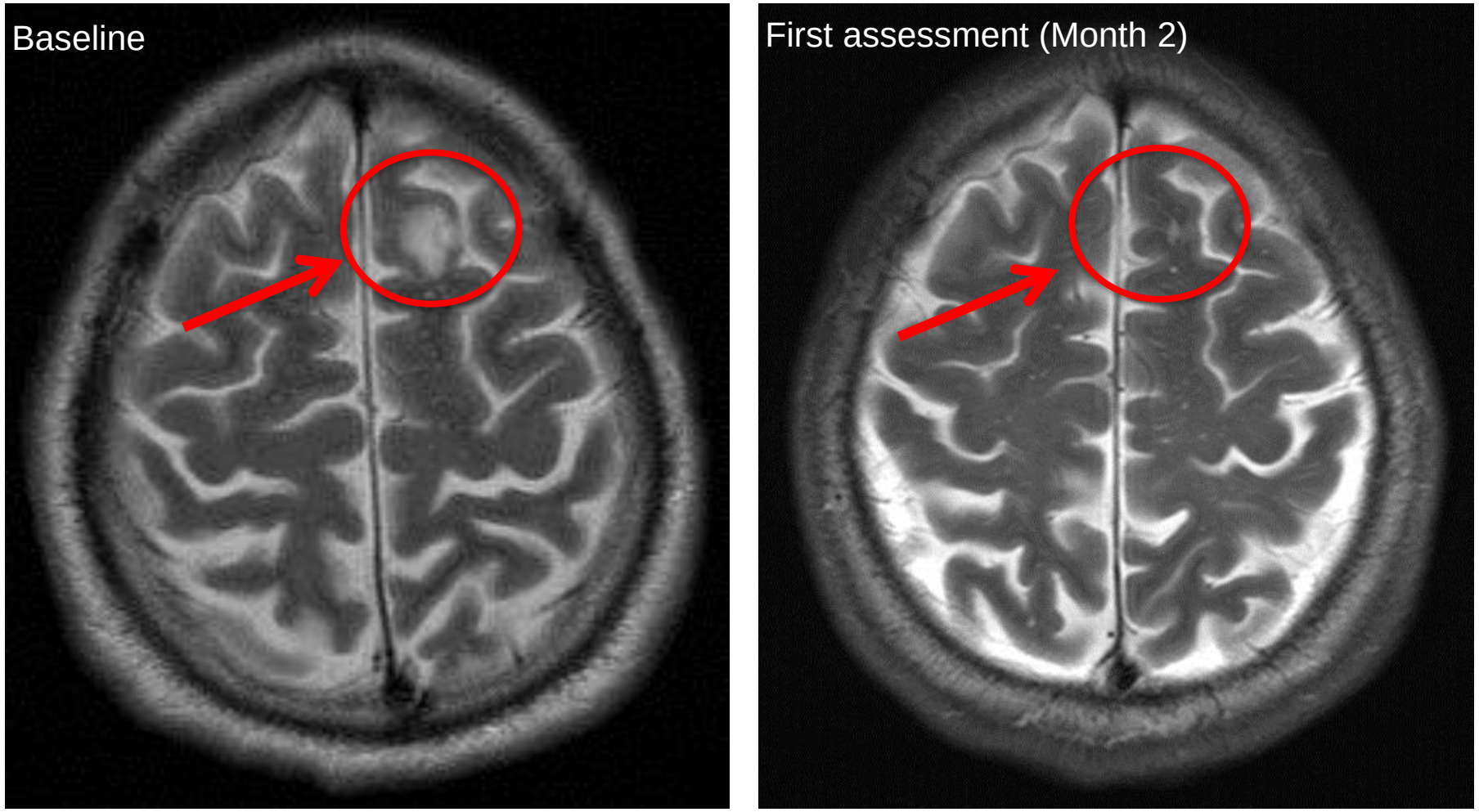
Potent activity against highly invasive RET-mutant MTC



27-year-old male; RET L629-D361 Del; initiated at 60 mg; ongoing at 400 mg with confirmed PR

Data previously presented at AACR Annual Meeting in April 2018. Data cut-off: April 6, 2018.

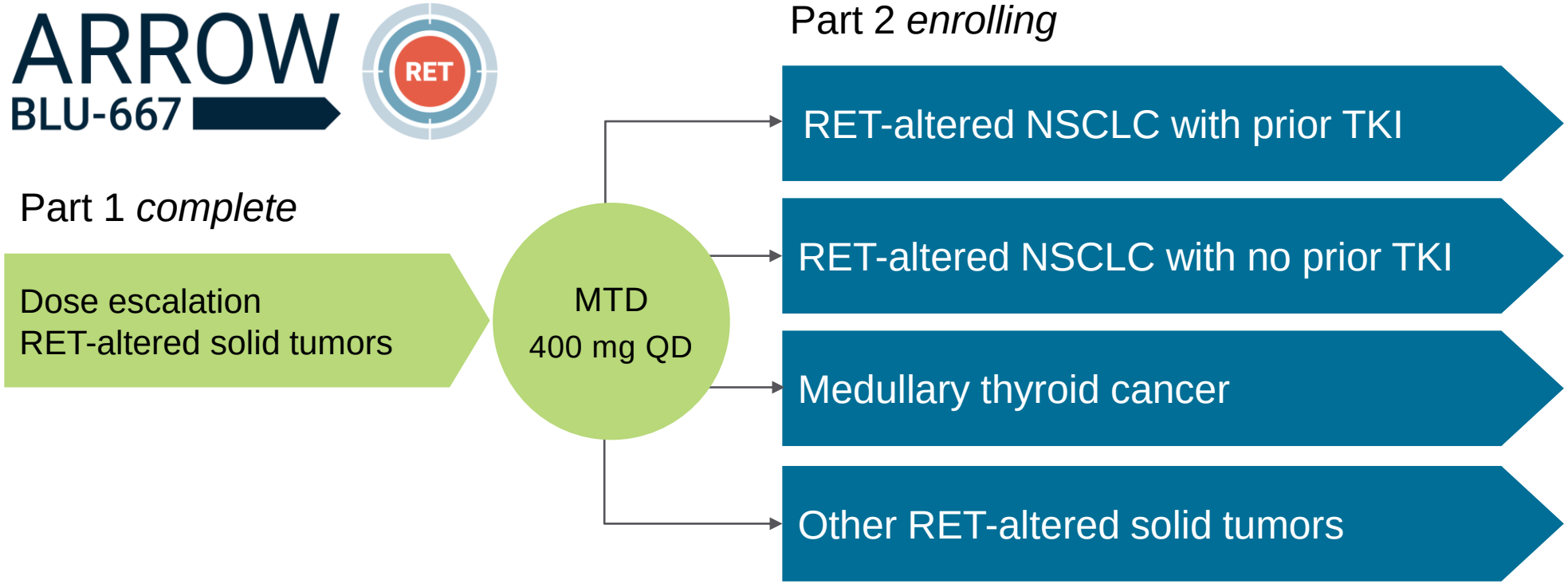
Activity against KIF5B-RET NSCLC brain metastases



69-year-old male; initiated at 400 mg; ongoing at month 4

Data previously presented at AACR Annual Meeting in April 2018. Data cut-off: April 6, 2018; Images courtesy of Drs Gainor, J and Lin, J of MGH.

Expansion portion of ARROW trial initiated and enrolling globally

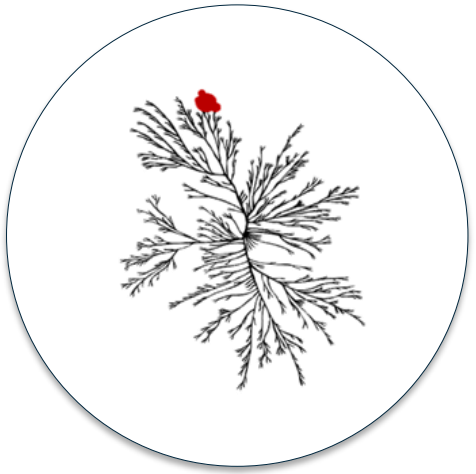


Key Part 2 objectives: evaluate efficacy (ORR and DOR) and safety at the MTD

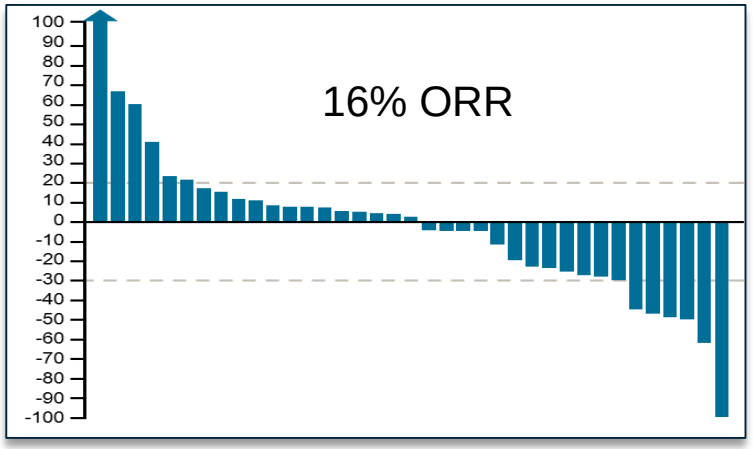
DOR, duration of response; ORR, overall response rate; QD, once daily; TKI, tyrosine kinase inhibitor

Strategic collaboration with CStone Pharmaceuticals accelerates and expands BLU-554 clinical development program

Highly selective FGFR4 inhibitor



Clinical proof-of-concept in patients with FGFR4-activated HCC



- Most AEs were Grade 1 or 2
- Grade ≥3 AEs in ≥5 patients included anemia, diarrhea and AST/ALT elevation

Expansion of BLU-554 clinical program in China

Monotherapy

Ongoing global Phase 1 expansion in TKI-naïve patients

Combination therapy

Planned proof-of-concept trial with PD-L1 inhibitor (CS1001) in patients in China

ALT, analine aminotransferase; AST, aspartate aminotransferase
Data previously presented at September 2017 ESMO Congress. Data cutoff: August 18, 2017.
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Realizing our vision for Blueprint Medicines

Deliver transformational genomically targeted medicines to patients

2014 – 2015

- STRATEGY
- LIBRARY
- TEAM

2016 – 2017

3 CLINICAL CANDIDATES WITH PROOF-OF-CONCEPT

2018 – 2019

4	CLINICAL CANDIDATES
6+	TUMOR TYPES & RARE DISEASES
2	TUMOR AGNOSTIC CLINICAL TRIALS
~9	RESEARCH PROGRAMS*

* Includes up to 5 programs under the cancer immunotherapy collaboration with Roche.

Cash to fund operating expenses and capital expenditures into 2H 2020*

SHARES OUTSTANDING *as of 3/31/18*	OUTSTANDING DEBT *as of 3/31/18*	CASH, CASH EQUIVALENTS AND INVESTMENTS *as of 3/31/18*
43.8 million (basic) 47.9 million (fully diluted)	***$1.1 million***	***$621.1 million***

$40M upfront payment from CStone Pharmaceuticals

$10M milestone payment from Roche for achieving research milestone

* Cash guidance includes $40M upfront payment under collaboration with CStone Pharmaceuticals and $10M milestone payment under collaboration with Roche but excludes any potential additional option fees, milestone payments or other payments under these collaborations.

2018 key priorities and anticipated milestones

Avapritinib	✓ Completed enrollment of registration-enabling Phase 1 NAVIGATOR trial in PDGFRα-driven GIST by mid-2018 ✓ Engaged global regulatory authorities on path to registration in SM in 1H 2018 • Engage global regulatory authorities on path to registration in GIST in 1H 2018 ✓ Initiate registration-enabling Phase 3 VOYAGER trial in 3L GIST in Q2 2018 • Initiate registration-enabling Phase 2 PATHFINDER trial in advanced SM by mid-2018 • Initiate registration-enabling Phase 2 PIONEER trial in indolent SM and smoldering SM by end of 2018 • Present updated Phase 1 data across multiple GIST and SM patient populations in 2018
Portfolio	✓ Presented data from Phase 1 trial of BLU-667 in RET-altered cancers and initiated expansion in 1H 2018 ✓ Initiated TKI-naïve cohort in Phase 1 trial of BLU-554 in advanced HCC in Q1 2018
Research	✓ Initiated IND-enabling studies for BLU-782 in fibrodysplasia ossificans progressiva in Q1 2018 ✓ Nominated additional wholly-owned discovery program in Q2 2018 • Plan to nominate at least one additional discovery program in 2018

Thank you