2020 Blueprint
global business strategy

Jeff Albers, Chief Executive Officer

Cowen 39th Annual Health Care Conference

MARCH 12, 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; Blueprint Medicines’ “2020 Blueprint” strategy, key goals and anticipated milestones; 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, 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; 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 avapritinib for PDGFRα D842V-driven gastrointestinal stromal tumors (“GIST”), BLU-667 for RET-driven non-small cell lung cancer (“NSCLC”) and BLU-554 for FGFR4-driven hepatocellular carcinoma (“HCC”); 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”).

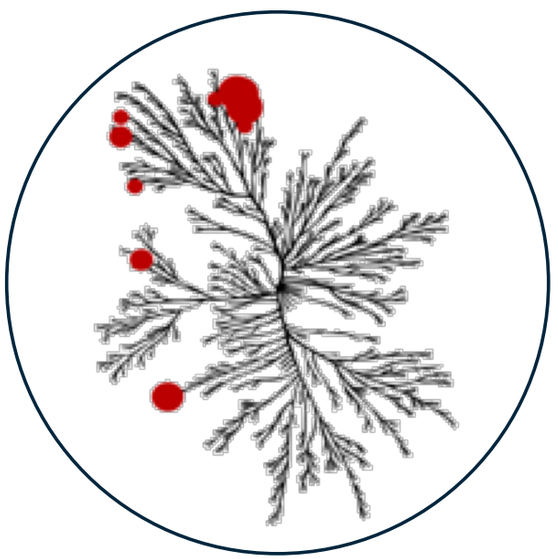
These and other risks and uncertainties are described in greater detail under “Risk Factors” in the Company’s Annual Report on Form 10-K for the year ended December 31, 2018, as filed with the Securities and Exchange Commission (“SEC”) on February 26, 2019, and any other filings the Company has made 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.

Precision therapies for people with cancer and rare diseases

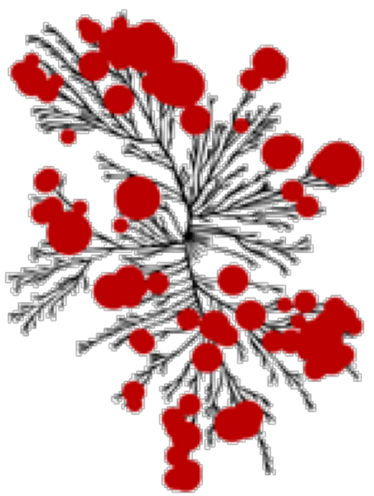
A NEW WAY OF LOOKING AT KINASE MEDICINES

SELECTIVE



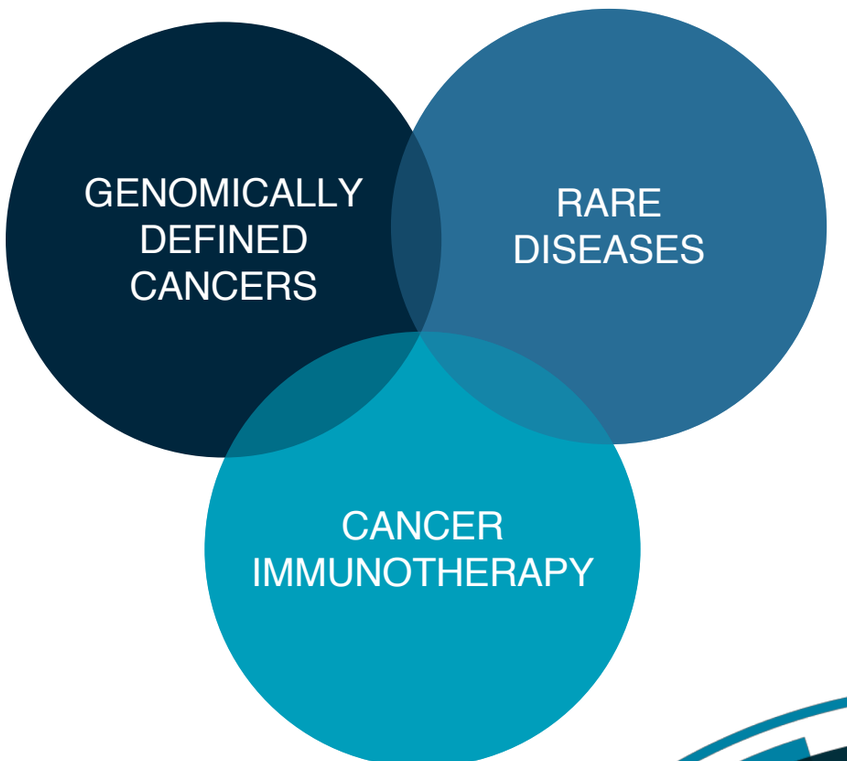
avapritinib

NON-SELECTIVE



Rydapt® (midostaurin)

WITH A FOCUS ON CORE AREAS OF EXPERTISE

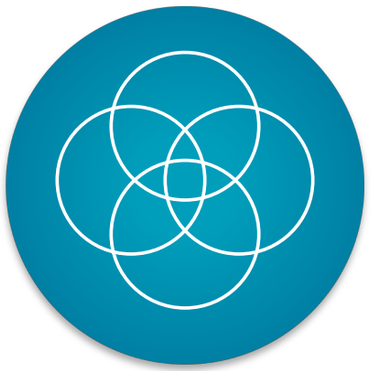


Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com) (CSTI).
The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.

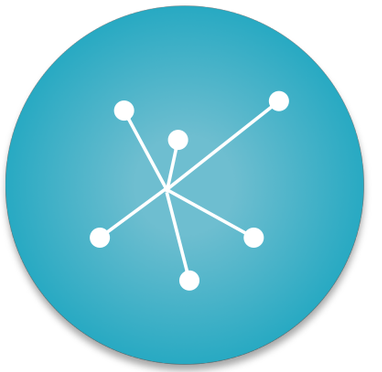
Our vision for building the leading precision therapy company

Rapid, reproducible product development

Robust scientific platform to design selective kinase medicines



Disciplined portfolio management focused on therapeutic area leadership

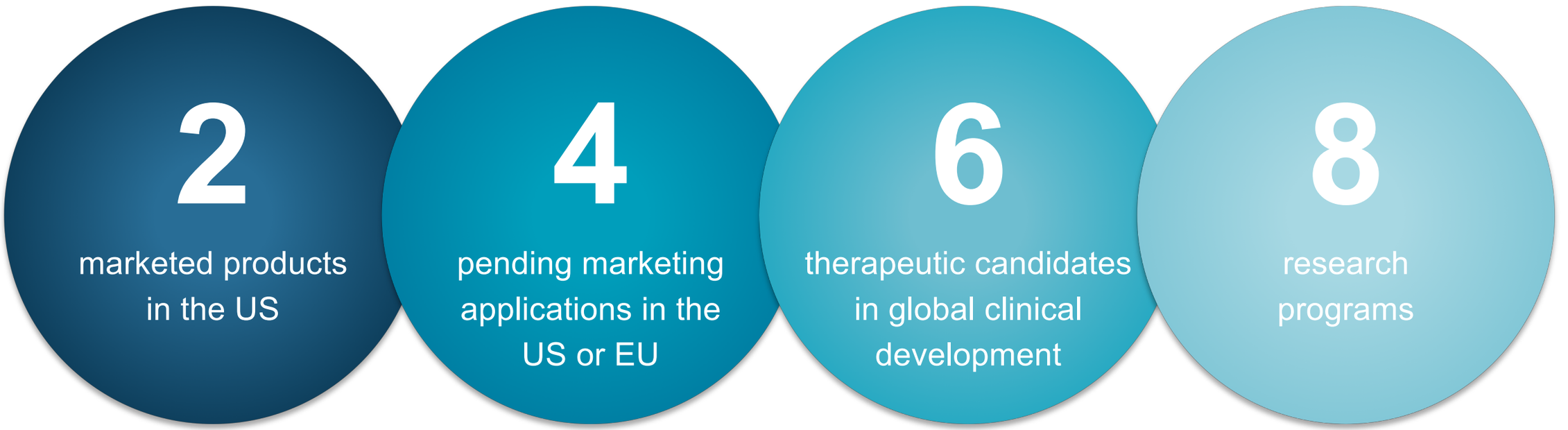


Effective and nimble commercial organization with global reach

Reinvestment of revenue to sustain constant innovation cycle

Our “2020 Blueprint” strategy to make this vision a reality

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 Q2 2019		 *
	4L GIST [1]			NDA planned Q2 2019		
	3L GIST [1]			NDA planned 2020		
	2L GIST [1]		trial planned 2H 2019			
	Advanced SM			NDA planned 2020		
	Indolent and smoldering SM					
BLU-667 (RET)	2L RET-fusion NSCLC [1]			NDA planned 1H 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 progressiva. [1] Unresectable or metastatic disease. [2] Phase 1 trial in healthy volunteers.

* 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.

Avapritinib: an investigational precision therapy with broad commercial potential

Avapritinib

KIT and PDGFRA inhibitor

DEVELOPMENT STATUS

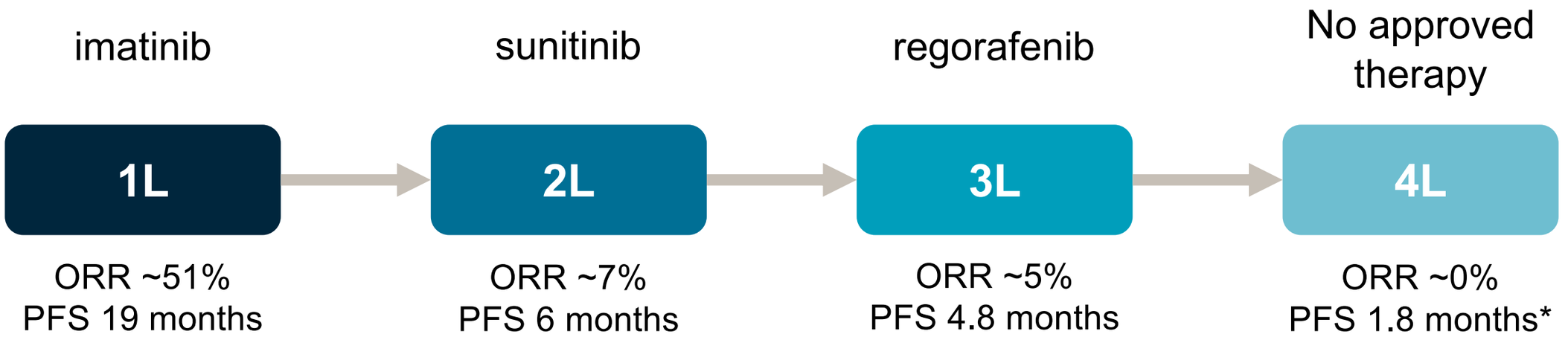
- Plan to submit NDA for PDGFRA Exon 18 mutant GIST and 4L GIST in Q2 2019
  - ORR and DOR per central radiology are primary endpoints for registration
- 5 ongoing or planned registration-enabling studies for avapritinib in multiple GIST and SM populations

POTENTIAL OPPORTUNITY

- Blueprint Medicines retains global commercial rights, excluding Greater China*
- ~30,000 patients across GIST and SM populations in major markets**
- Scalable commercial footprint initially focused on driving patient identification and treatment through engagement with recognized centers of excellence

*CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib in Mainland China, Hong Kong, Macau and Taiwan.
**Represents estimated number of patients with PDGFRA-driven GIST; 2L, 3L, 4L KIT-driven GIST; and advanced, smoldering and indolent SM in major markets (US, France, Germany, Italy, Spain, the United Kingdom and Japan).
DOR, duration of response; NDA, new drug application; ORR, overall response rate.
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



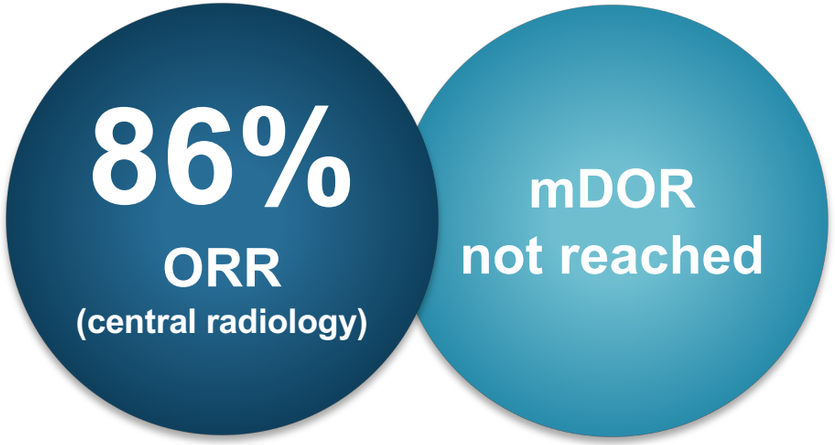
- All approved agents are ineffective against PDGFRα D842V GIST -

Genetic drivers	PDGFRA D842V ~5-6%	KIT ~80%

PFS, progression free survival.
* Imatinib re-challenged.

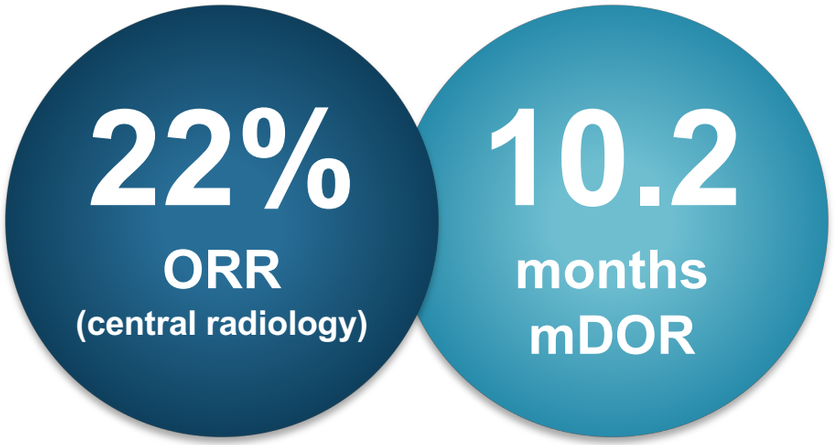
Top-line NAVIGATOR trial data support planned NDA submission in Q2 2019

PDGFRA Exon 18 mutant GIST (n=43)*



*Breakthrough Therapy Designation***

4L GIST (n=111)*



Top-line safety results (N=237):

- Data consistent with those previously reported at the CTOS 2018 Annual Meeting
- Avapritinib was well-tolerated and most adverse events reported by investigators were Grade 1 or 2
- Across all doses, only 9.7% of patients discontinued treatment due to treatment-related adverse events

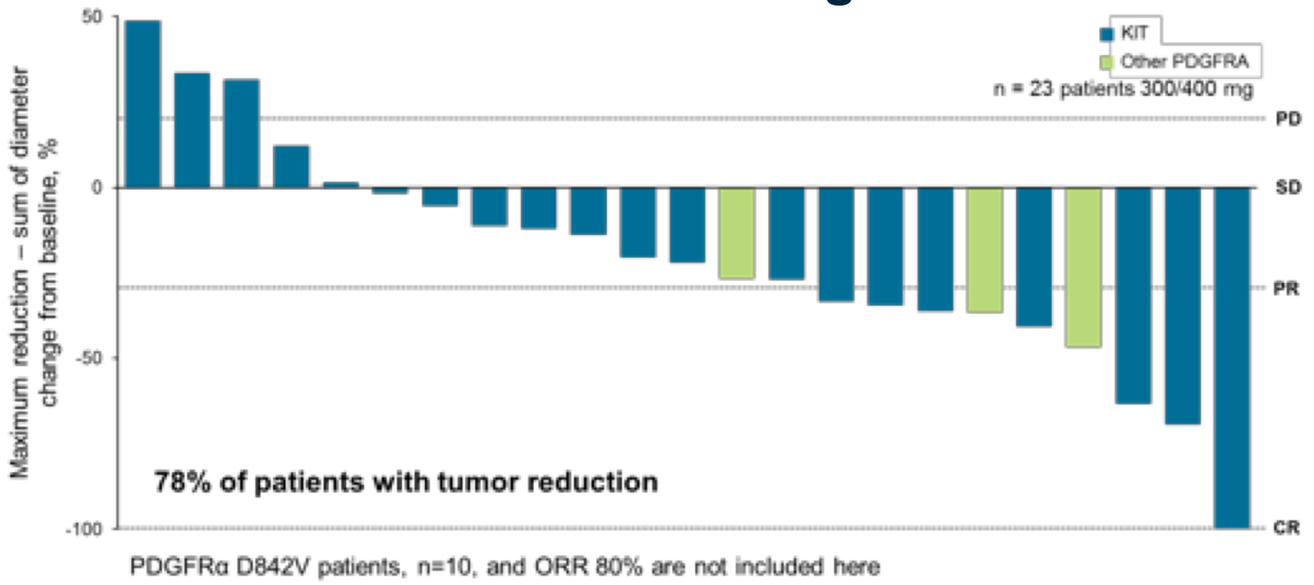
Plan to present detailed registration data in Q2 2019

blueprint MEDICINES

* 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 4L GIST.
** Avapritinib granted Breakthrough Therapy Designation for the treatment of unresectable or metastatic PDGFRα D842V-driven GIST.
Data previously reported in January 2019. Data cutoff: November 16, 2018. mDOR, median duration of response; ORR, objective response rate; QD, once daily.

Preliminary Phase 1 data in 3L/4L regorafenib-naïve GIST de-risk ongoing confirmatory Phase 3 VOYAGER trial

Preliminary 26% ORR for avapritinib[1] versus 5% ORR for regorafenib[2]



VOYAGER

3L/4L GIST R, 1:1

- avapritinib
- regorafenib

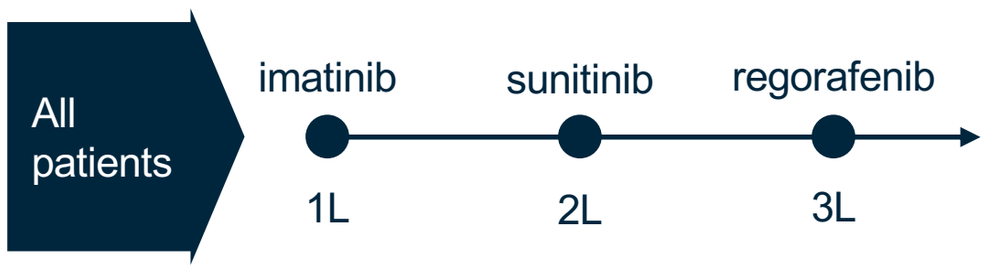
Primary endpoint: PFS

Expect to complete VOYAGER trial enrollment in 2H 2019

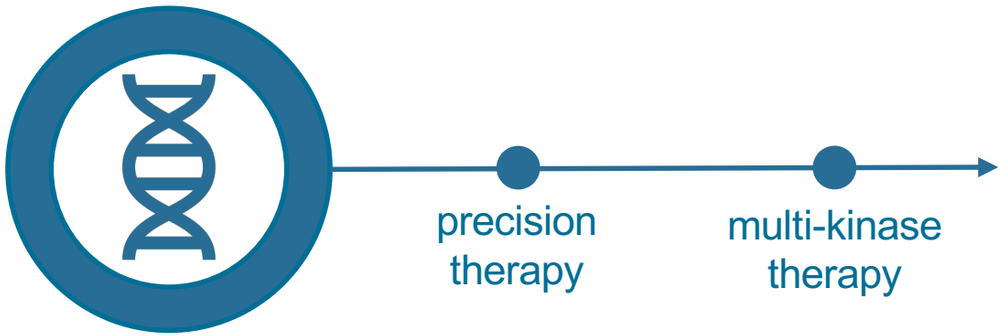
[1] Data previously presented in November 2018 at the CTOS Annual Meeting. Data cutoff: October 15, 2018.
[2] Regorafenib data in FDA-approved product insert.
R, randomized.

Planned COMPASS-2L precision medicine trial in 2L GIST recognizes the ongoing transformation of the GIST treatment paradigm

Treatment in standard sequence



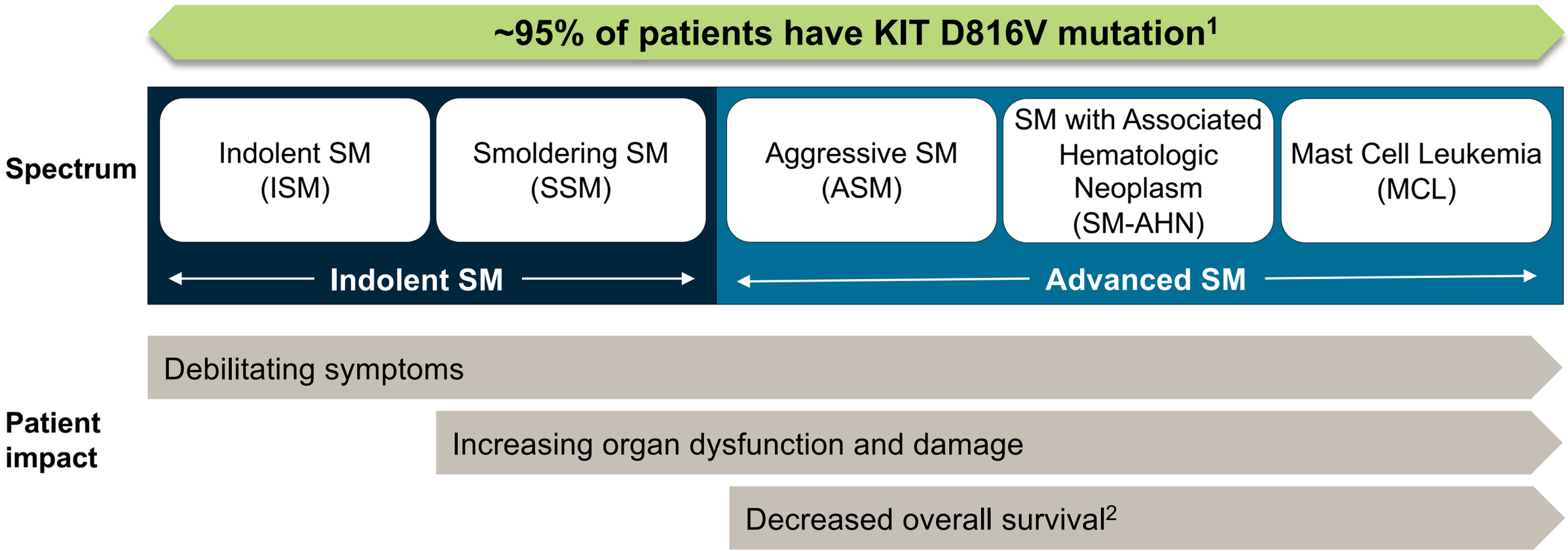
Initial treatment and sequence tailored to each patient's molecular profile



Goal: maximize opportunity for durable response / disease control

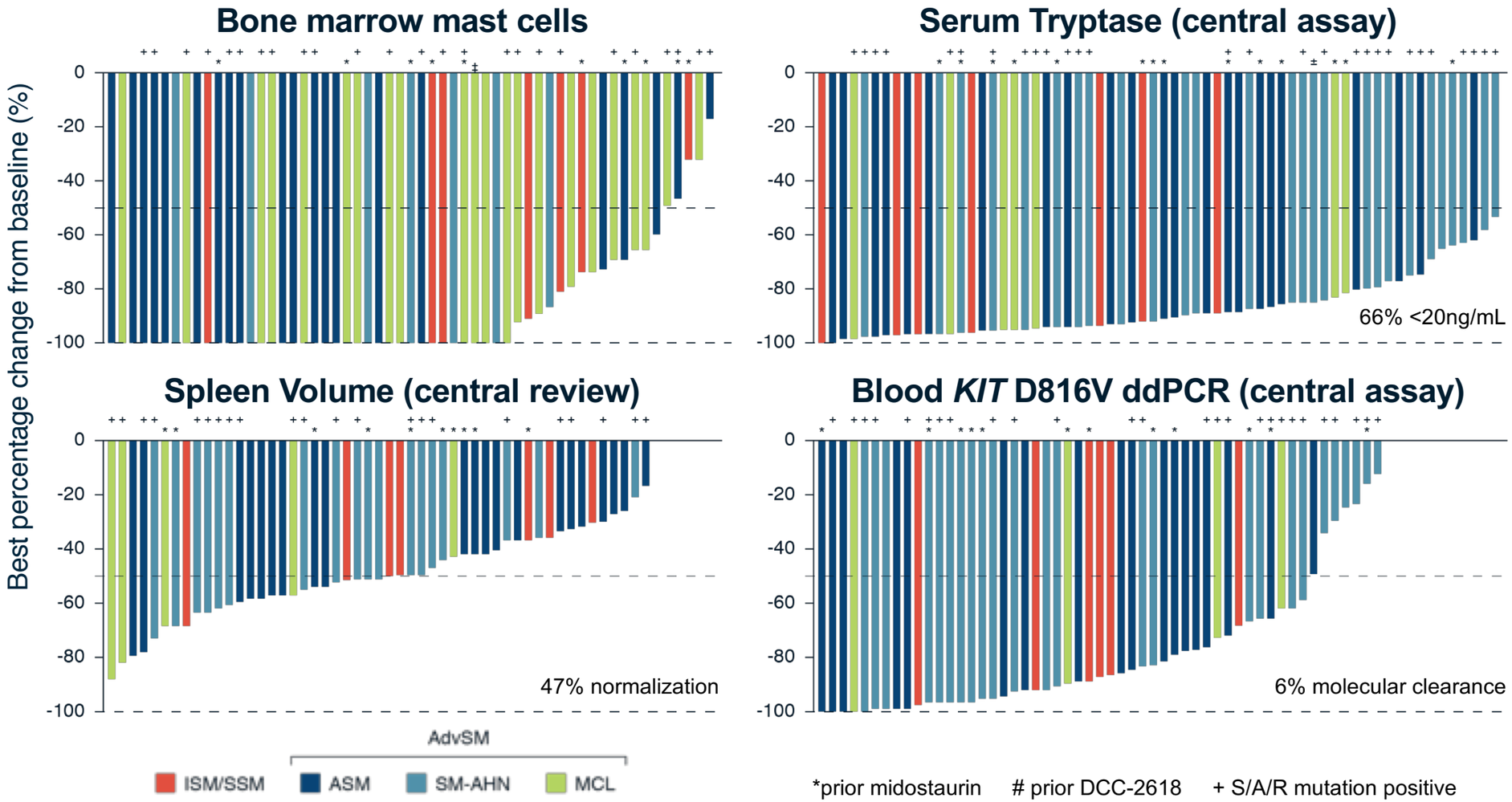
TODAY Increased understanding of GIST molecular profile & mutational sensitivity of current / emerging treatments **TOMORROW**

Avapritinib is the only highly selective KIT D816V inhibitor in development for systemic mastocytosis



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

Decline in mast cell burden in all evaluable patients across all subtypes, regardless of prior therapy or co-mutation status

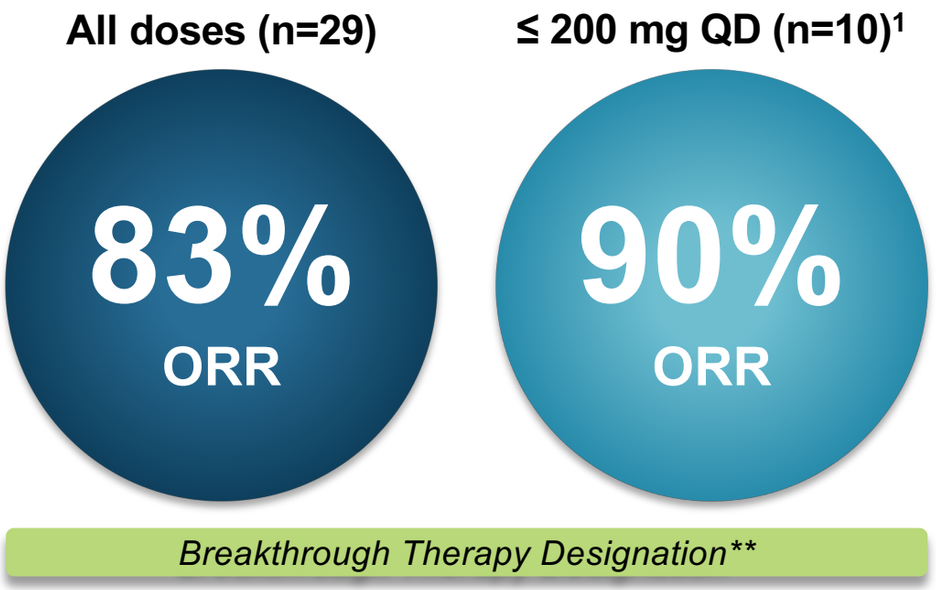


*prior midostaurin # prior DCC-2618 + S/A/R mutation positive

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

Clinical responses in advanced SM are durable and deepen over time

Best response per IWG-MRT-ECNM criteria*



Prolonged duration of response

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

Responses deepen over time

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

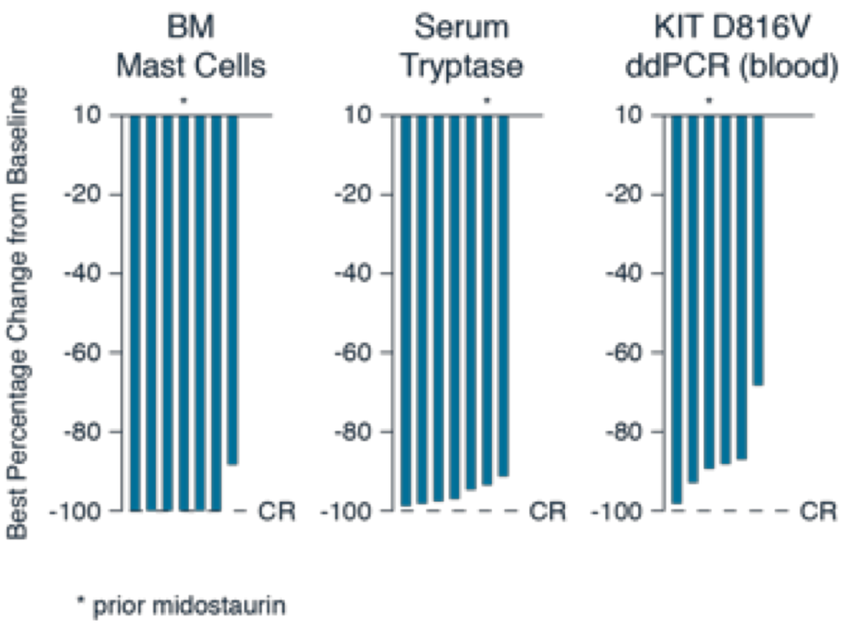
Safety (n=67)

- Avapritinib was 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, only 4% of patients discontinued treatment due to treatment-related AEs

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

Preliminary Phase 1 data highlight the potential of avapritinib in indolent SM

Evaluable indolent and smoldering SM patients in Phase 1 EXPLORER trial



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

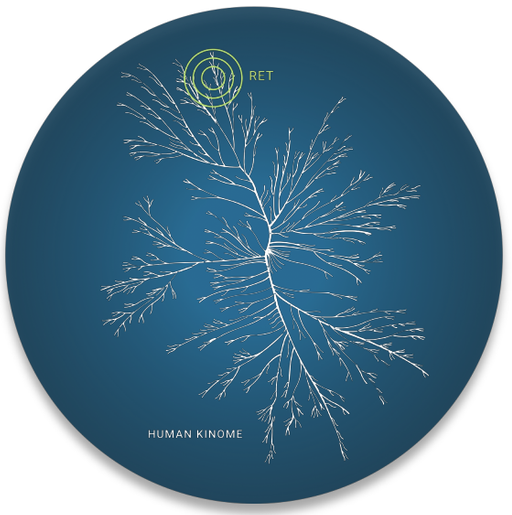
placebo

Open-label extension

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

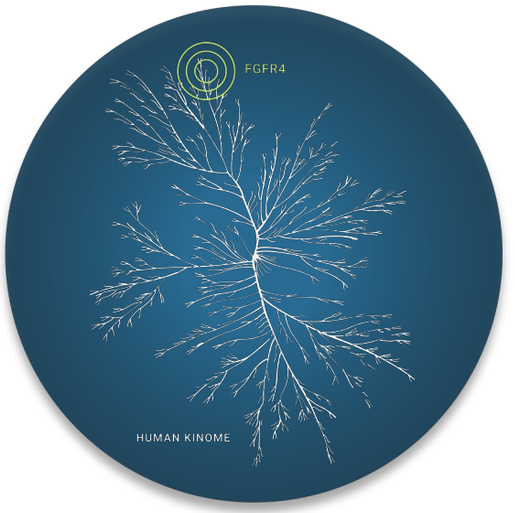
Data previously presented in December 2018 at the ASH Annual Meeting. Data cutoff: September 30, 2018.
BM, bone marrow; R, randomized; RP2D, recommended Phase 2 dose.

Growing portfolio of highly selective investigational kinase medicines



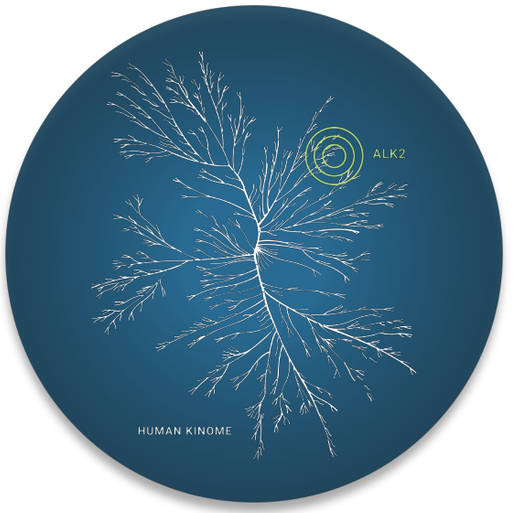
BLU-667
RET inhibitor

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



BLU-554
FGFR4 inhibitor

Hepatocellular carcinoma



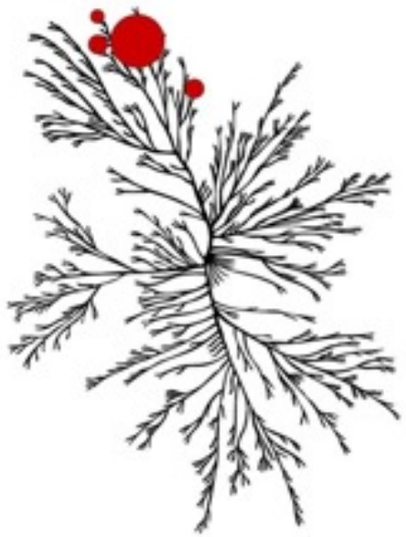
BLU-782
ALK2 inhibitor

Fibrodysplasia ossificans progressiva

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.

BLU-667 is designed to treat RET-altered cancers

High kinome selectivity for RET[1,2]



More potent and selective than multi-kinase inhibitors[1,2]

	Wild-type RET	RET V804L Gatekeeper resistance	RET V804M Gatekeeper resistance	RET M918T Mutation	CCDC6-RET Fusion	VEGFR2 Anti-target
BLU-667	0.4	0.3	0.4	0.4	0.4	35
Cabozantinib	11	45	162	8	34	2
Vandetinib	4	3597	726	7	20	4

- BLU-667 is 88-fold more selective for RET than VEGFR2
- BLU-667 is 20-fold more selective for RET than JAK1

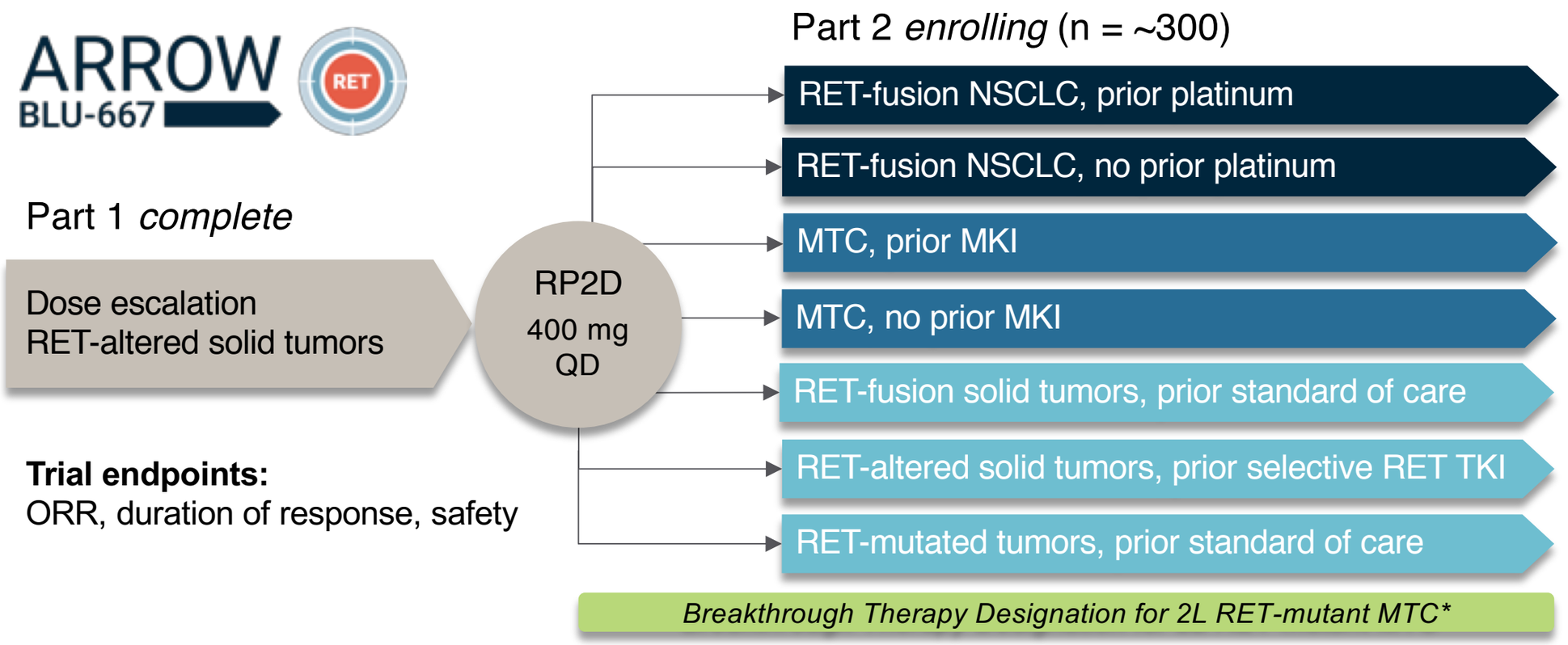
RET opportunity in major markets

~10,000 NSCLC patients[3]	~800 MTC patients[3]	Low variable frequency across multiple solid tumors

IC_{50}, half maximal inhibitory concentration. Kinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (CSTI) (www.cellsignal.com). The foregoing website is maintained by CSTI, and Blueprint Medicines is not responsible for its content.

[1] Data previously presented in April 2018 at AACR Annual Meeting. Data cutoff: April 6, 2018. [2] Subbiah V et al. *Cancer Discov.* 2018;8(7):836-849. [3] Epidemiology based on estimated incidence for RET-driven NSCLC (across treatment lines) and estimated prevalence for RET-driven MTC in major markets (US, France, Germany, Italy, Spain, the United Kingdom and Japan).

Plan to present updated ARROW trial data in 2Q 2019

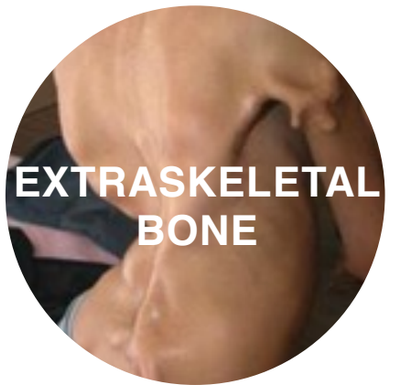


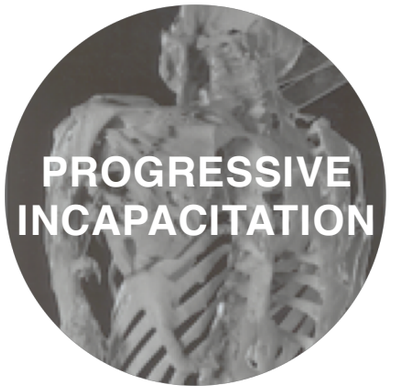
Expect to complete enrollment of 2L RET-fusion NSCLC and 2L RET-mutant MTC cohorts in Q2 2019, in support of planned NDA submission in 1H 2020

MKI, multi-kinase inhibitor; TKI, tyrosine kinase inhibitor
* BLU-667 granted Breakthrough Therapy Designation for the treatment of RET-mutation-positive MTC that requires systemic treatment and for which there are no acceptable alternative treatments.

BLU-782 is designed to target mutant ALK2, the underlying cause of fibrodysplasia ossificans progressiva

- Causes abnormal transformation of skeletal muscle, ligaments and tendons into bone
- Beginning in childhood, disease manifestations include painful disease flare-ups, locking of joints, progressive loss of mobility and respiratory dysfunction
- Premature death typically occurs in middle age due to cardiorespiratory complications
- There are no approved therapies

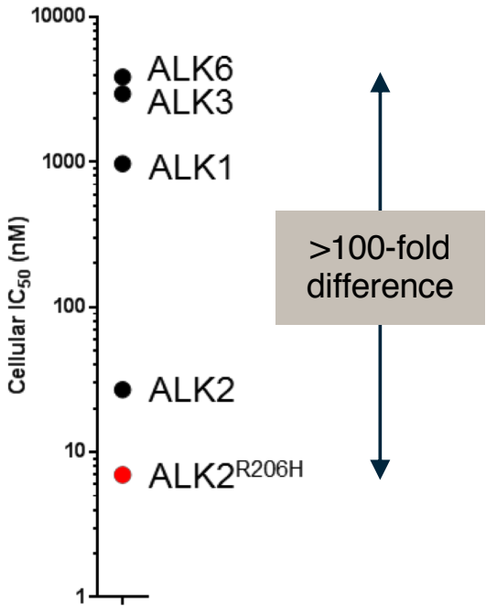




Phase 1 trial of BLU-782 in healthy volunteers is ongoing

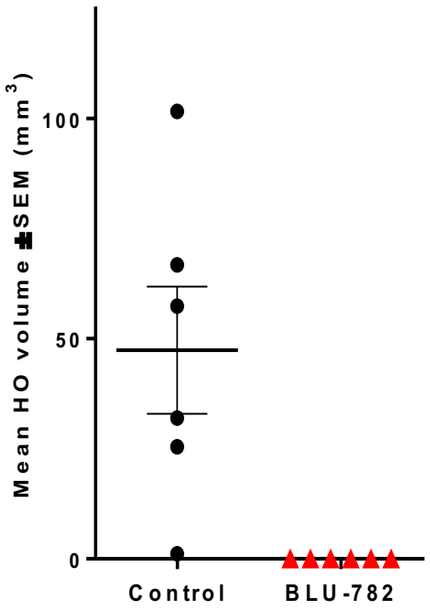
Foundational preclinical data support plans for clinical development of BLU-782 in FOP

Highly selective for mutant ALK2



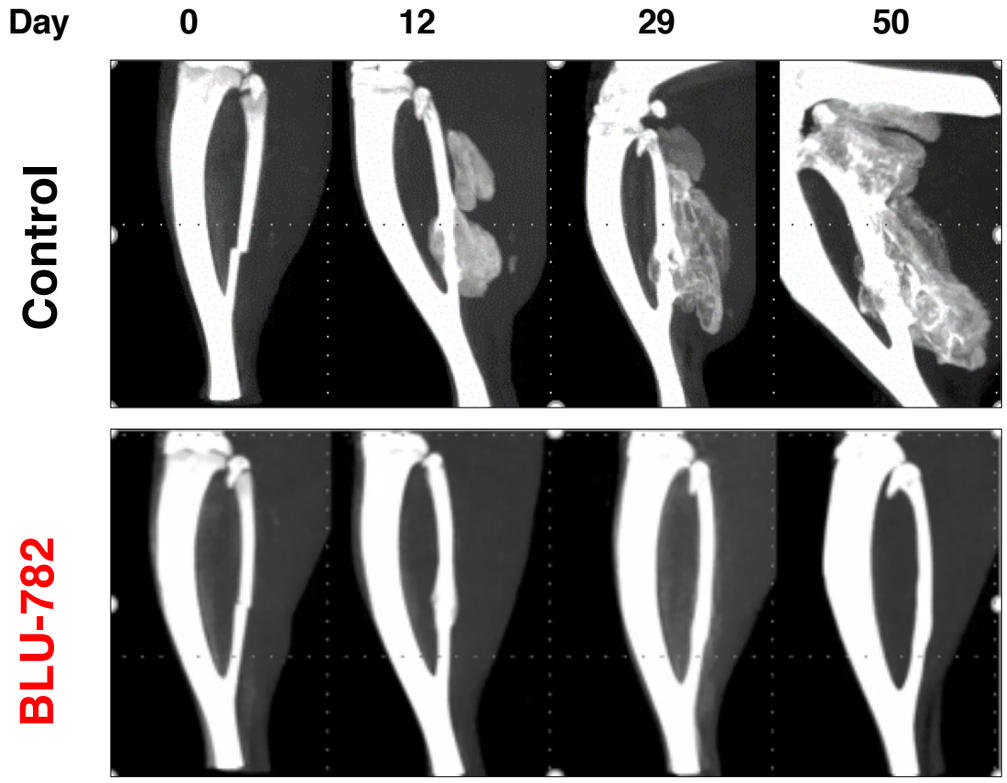
Cellular assay

Prevents injury-induced HO*



Micro CT at Day 17

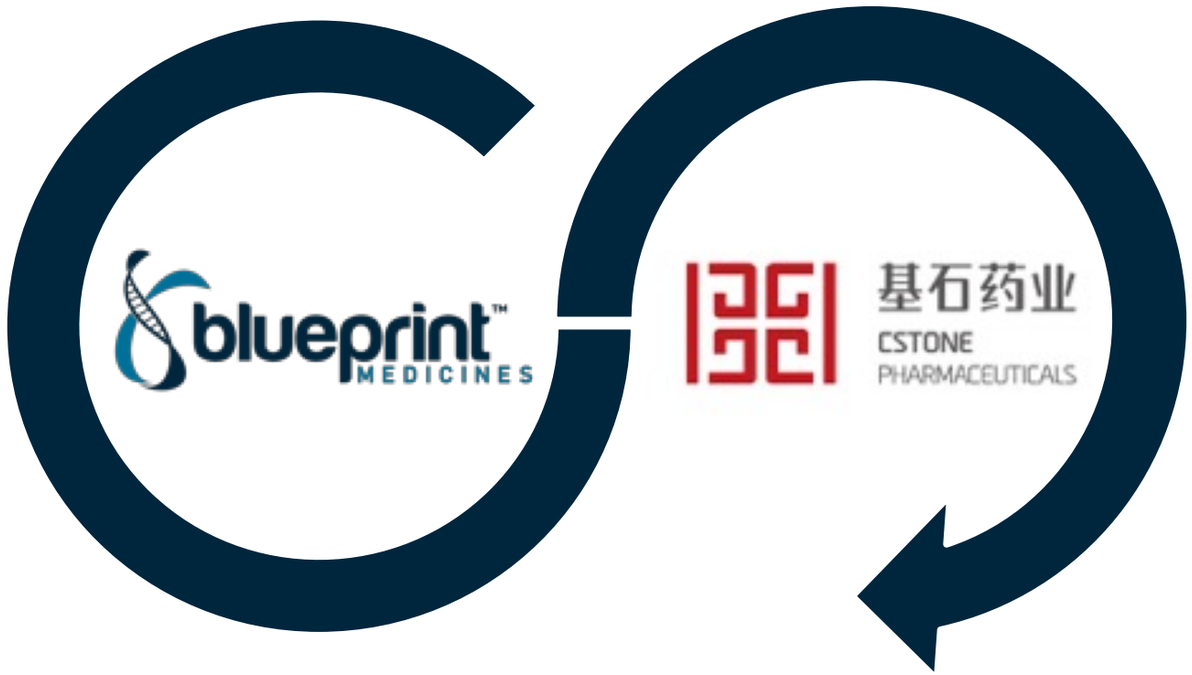
Prevents surgery-induced HO*



Data previously presented at ASBMR Annual Meeting in September 2018.
* Injury- and surgery-induced HO studies conducted in an ALK2 R2016H mouse model.
CT, computed tomography; HO, heterotopic ossification.

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]

Plan to initiate BLU-554 monotherapy and combination trials in China by mid-2019 and in 2H 2019, respectively

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

Strong financial position entering 2019

Balance Sheet *(unaudited)*	**FY '18**	**FY '17**
Cash, Cash Equivalents and Investments	$494.0M	$673.4M

Statement of Operations *(unaudited)*	**Q4 '18**	**Q4 '17**	**FY '18**	**FY '17**
Collaboration Revenue	$1.0M	$1.6M	$44.5M	$21.4M
Research & Development Expenses	$70.5M	$43.6M	$243.6M	$144.7M
General & Administrative Expenses	$13.6M	$8.1M	$47.9M	$28.0M
Net Loss	$(80.3)M	$(49.0)M	$(236.6)M	$(148.1)M

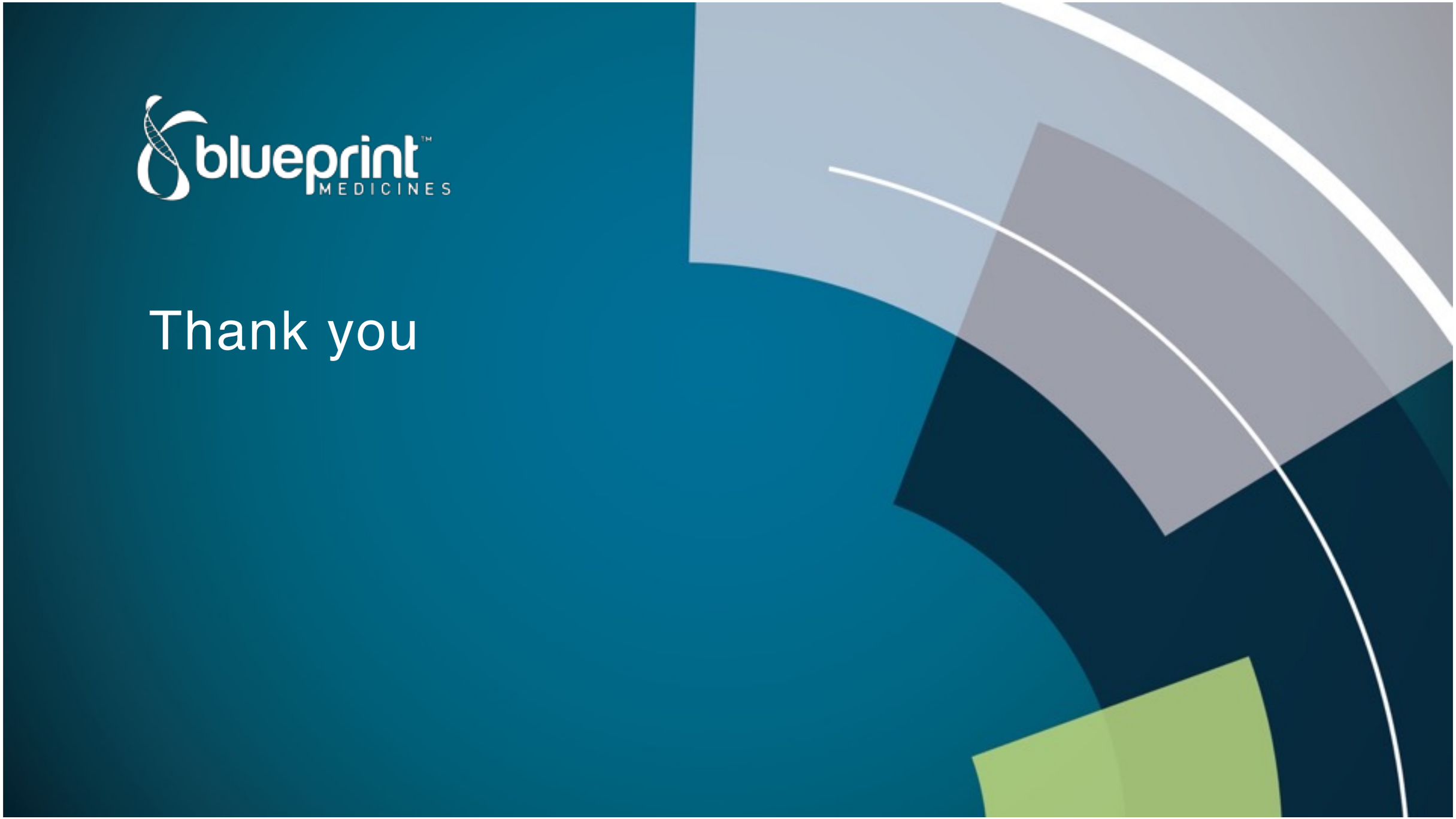
Based on current operating plans, expect existing cash balance will fund operations into the 2H of 2020*

blueprint MEDICINES

* Excludes any potential option fees and milestone payments under the Roche and CStone collaborations

Summary of anticipated corporate milestones for 2019-2020

Program	Milestone	Anticipated Timing
Avapritinib – GIST	Submit NDA for PDGFRA Exon 18 mutant GIST and 4L GIST	Q2 2019
	Present data from Phase 1 NAVIGATOR trial supporting planned NDA for PDGFRA Exon 18 mutant GIST and 4L GIST	Q2 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	Q2 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	2020
BLU-667 – RET	Present updated data from Phase 1 ARROW trial in RET-altered NSCLC, MTC and other advanced solid tumors	Q2 2019
	Complete enrollment of previously treated RET-altered NSCLC and MTC cohorts in Phase 1 ARROW trial	Q2 2019
	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 2L RET-fusion NSCLC and 2L RET-mutant MTC	1H 2020
BLU-554 – HCC	Initiate enrollment in China in ongoing global Phase 1 trial of BLU-554 under collaboration with CStone Pharmaceuticals	Mid-2019
	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 1 trial in healthy volunteers	Q1 2019
	Initiate Phase 2 trial in patients with FOP	1H 2020
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


blueprint™
MEDICINES
Thank you