PRECISION THAT MOVES™

Staying one step ahead of disease

August 10, 2021

R.S., living with
systemic mastocytosis

Forward-looking statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. The words "aim," "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 regarding plans, strategies, timelines and expectations for the current or future approved drugs and drug candidates of Blueprint Medicines Corporation (the "Company"), including timelines for marketing applications and approvals, the initiation of clinical trials or the results of ongoing and planned clinical trials; the Company's plans, strategies and timelines to nominate development candidates; plans and timelines for additional marketing applications for avapritinib and pralsetinib and, if approved, commercializing avapritinib and pralsetinib in additional geographies or for additional indications; the potential benefits of any of the Company's current or future approved drugs or drug candidates in treating patients; and the Company's financial performance, strategy, 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 impact of the COVID-19 pandemic to the Company's business, operations, strategy, goals and anticipated milestones, including the Company's ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved drugs, and launching, marketing and selling current or future approved drugs; the Company's ability and plans in establishing a commercial infrastructure, and successfully launching, marketing and selling current or future approved products; the Company's ability to successfully expand the approved indications for AYVAKIT™/AYVAKYT® (avapritinib) and GAVRETO™(pralsetinib) or obtain marketing approval for AYVAKIT/AYVAKYT in additional geographies in the future; the delay of any current or planned clinical trials or the development of the Company's drug candidates or the licensed drug candidate; 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 or marketing applications; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT, GAVRETO or any drug candidates it is developing; the Company's ability to develop and commercialize companion diagnostic tests for any of the Company's current or future approved drugs or drug candidates; and the success of the Company's current and future collaborations, partnerships and licenses. These and other risks and uncertainties are described in greater detail under "Risk Factors" in the Company's filings with the Securities and Exchange Commission ("SEC"), including its most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q, and any other filings it 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 its 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.

2011

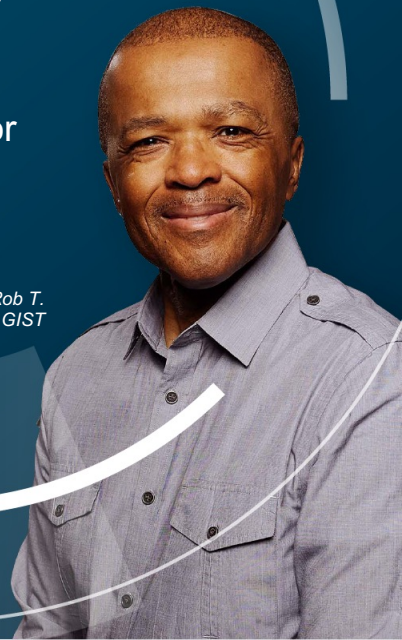
Hopeful foundation

A new precision therapy platform

2021

Hopeful reality

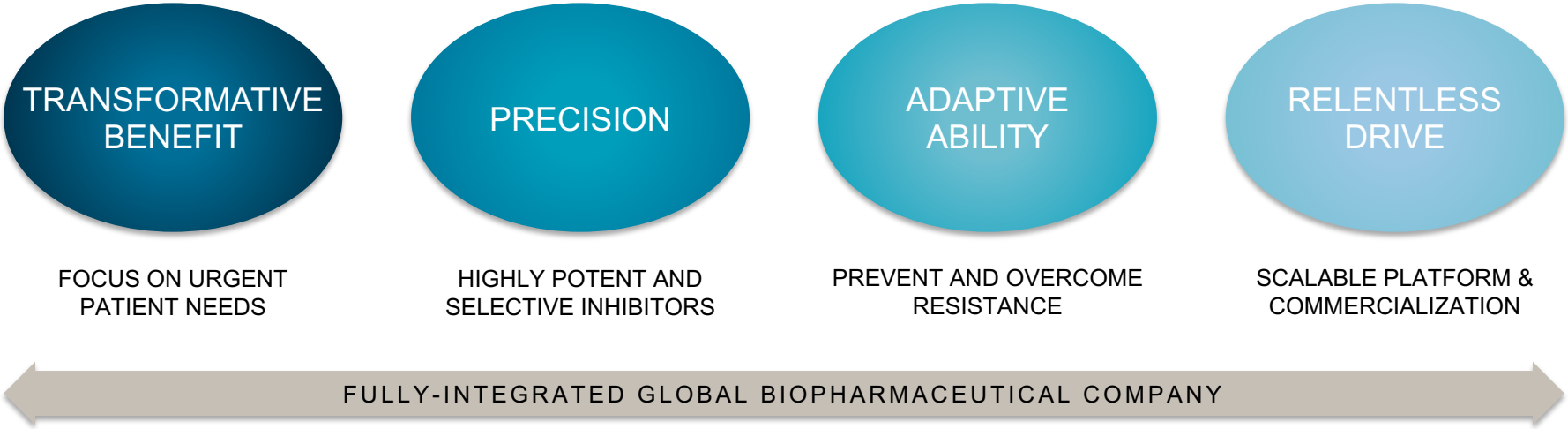
More than 2,500 patients treated with an approved or investigational Blueprint Medicines therapy



Rob T.
Living with GIST

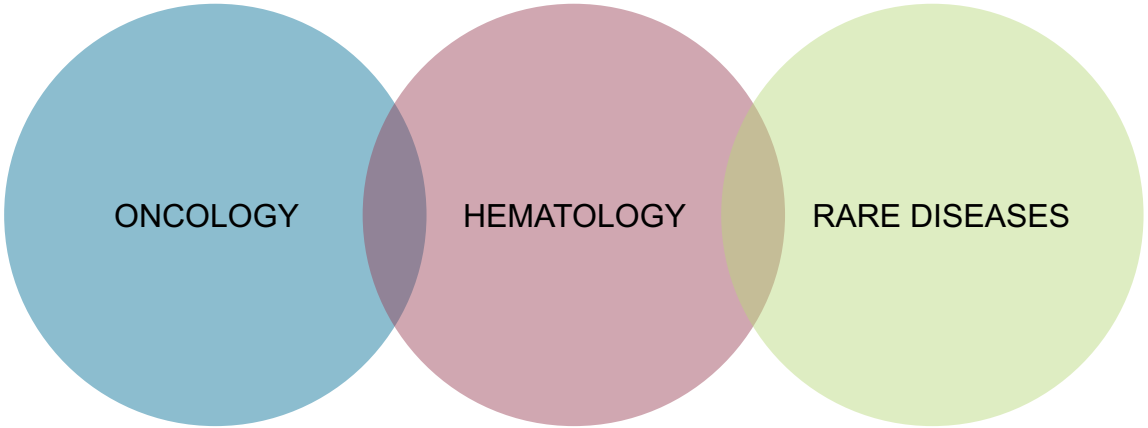
Blueprint Medicines' core mission and foundational principles

We aim to make real the promise of precision therapy to improve and extend life for as many people with cancer and hematologic disorders as possible



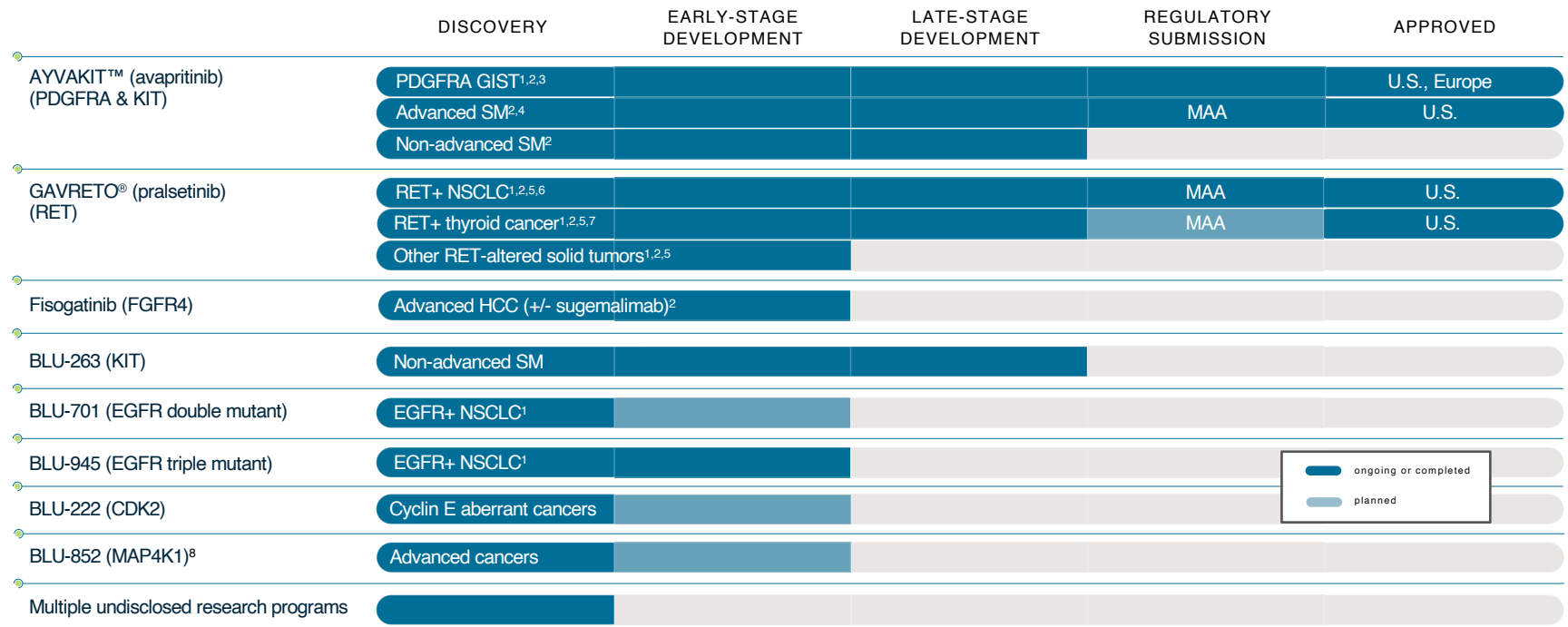
A leader in precision oncology and hematology

PORTFOLIO AREAS OF FOCUS



THERAPEUTIC AREA LEADERSHIP

- SYSTEMIC MASTOCYTOSIS
- LUNG CANCER



1. Unresectable or metastatic disease. 2. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan. 3. Approved in the U.S. for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. Received conditional marketing authorization in Europe under the brand name AYVAKYT® for the treatment of adults with unresectable or metastatic GIST harboring the PDGFRA D842V mutation. 4. Approved in the U.S. for the treatment of adults with advanced SM, including aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia. 5. In collaboration with Roche. Blueprint Medicines and Roche have co-exclusive rights to develop and commercialize pralsetinib in the U.S., and Roche has exclusive rights to develop and commercialize pralsetinib outside the U.S., excluding the CStone territory. 6. Received accelerated approval in the U.S. for the treatment of adults with metastatic RET fusion-positive NSCLC. Continued approval may be contingent on a confirmatory trial. The proposed indication for the MAA is locally advanced or metastatic RET fusion-positive NSCLC previously treated with platinum-based chemotherapy. 7. Received accelerated approval in the U.S. for the treatment of patients with advanced or metastatic RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer. Continued approval may be contingent on confirmatory trials. 8. In collaboration with Roche. Blueprint Medicines and Roche are conducting activities for up to two programs under the collaboration, including the program targeting MAP4K1. For one of the programs, Blueprint Medicines has U.S. commercial rights and Roche has ex-U.S. commercialization rights. For one of the programs, Roche has worldwide commercialization rights. GIST, gastrointestinal stromal tumors; HCC, hepatocellular carcinoma; MAA, marketing authorization application; NDA, new drug application; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

Updated as of July 29, 2021

2021 roadmap for precision medicine leadership

Accelerate global adoption of AYVAKIT and GAVRETO

Advance a new wave of therapeutic candidates toward clinical proof-of-concept

Further expand the company's precision therapy pipeline

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Accelerate global adoption of AYVAKIT and GAVRETO

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Our first decade of precision therapy innovation

AYVAKIT™ avapritinib | tablets

GAVRETO® pralsetinib | 100mg capsules

- First to achieve FDA approval of two internally discovered medicines within 10 years
- 9 approved or investigational precision therapies[1], plus multiple additional undisclosed research programs
- 5 FDA breakthrough therapy designations
- Global commercial footprint in the U.S. and Europe
- Multiple transformative collaborations
- Strong financial position to further accelerate innovation

AYVAKIT APPROVAL IN ADVANCED SM IS OUR FIFTH[2] APPROVAL IN THE PAST 18 MONTHS

1. Includes AYVAKIT, GAVRETO, fisogatinib, BLU-263, BLU-701, BLU-945, BLU-852, BLU-222 and BLU-782 (out-licensed to Ipsen). 2. Includes U.S. and Europe. FDA, U.S. Food and Drug Administration.

AYVAKIT update: foundation established for transformative growth

AYVAKIT™
avapritinib | tablets

- Now approved for advanced systemic mastocytosis and certain unresectable or metastatic PDGFRA GIST
- 2Q 2021 net product sales: $8.5M

LAUNCH PROGRESS

- Received FDA approval for and launched in advanced SM in U.S. in mid-June 2021
- Strong initial adoption across a broad set of prescribers, including mix of academic and community centers
- Added to NCCN guidelines as a preferred treatment regimen for advanced SM[1]
- Early indicators of robust patient access

PRIORITIES AND AREAS OF GROWTH

- Accelerating U.S. launch in advanced SM
- MAA for advanced SM under review by EMA
- Registrational PIONEER trial data in non-advanced SM expected in mid-2022

1. Added to NCCN guidelines as a category 2A preferred recommendation. PDGFRA, platelet-derived growth factor receptor alpha; GIST, gastrointestinal stromal tumors; FDA, U.S. Food and Drug Administration; SM, systemic mastocytosis; NCCN, National Comprehensive Cancer Network; MAA, marketing authorization application; EMA, European Medicines Agency.

GAVRETO update: expanding global launch through partnerships

GAVRETO®
pralsetinib | 100mg capsules

- Approved for certain advanced or metastatic RET-altered NSCLC, MTC and other thyroid cancers
- 2Q 2021 net product sales: $2.9M

LAUNCH PROGRESS

- Increased share of new patient starts in the U.S. to >40%
- First selective RET inhibitor approved in China
- Updated ARROW trial data in treatment-naïve lung cancer presented at ASCO
- Lung and thyroid cancer registration datasets published in Lancet Oncology and Lancet Diabetes and Endocrinology

PRIORITIES AND AREAS OF GROWTH

- RET patient identification through multi-disciplinary education including actionable biomarker testing
- Advancing global registration efforts through Roche and CStone partnerships

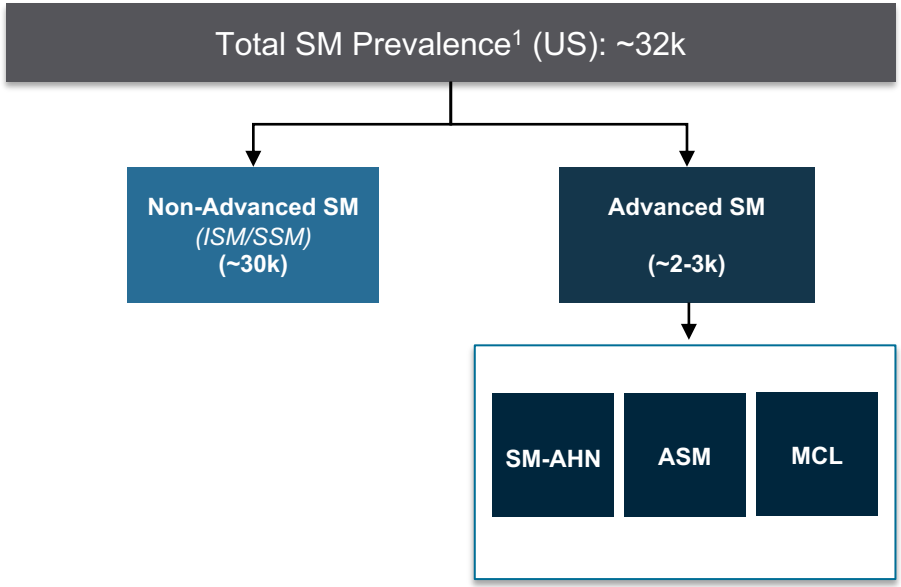
blueprint™ MEDICINES

NSCLC, non-small cell lung cancer; MTC, medullary thyroid cancer; ASCO, American Society of Clinical Oncology; RET, rearranged during transfection.

Significant initial target patient population with additional growth potential

Major markets include U.S., France, Germany, Italy, Spain, the United Kingdom and Japan. 1. Cohen S et al Br J Haematol (2014) 166(4):521-8 and World Bank Population estimates.

Advanced SM is estimated to represent ~5-10% of the total SM opportunity

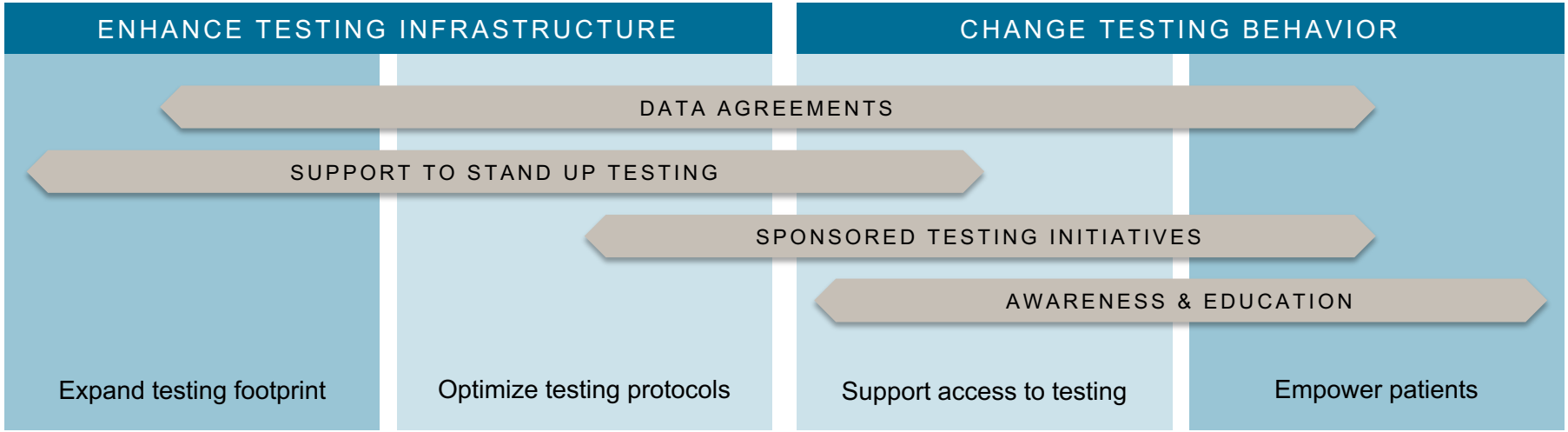


- Majority of advanced SM target population is diagnosed
- Initial focus on top potential treatment sites and prescribers
  - ~70 centers of excellence treat ~50% of advanced SM patients[2]

1. Estimated SM prevalence and patient subtypes based on internal claims analysis and epidemiology reported in S.S Cohen et al. 2014 and Orphanet.
2. Information on key SM centers of excellence identified based on depth of experience managing SM patients, trial site participation, disease area thought leadership and potential commercial opportunity, if approved.

Pursuing a range of testing initiatives to facilitate SM patient identification

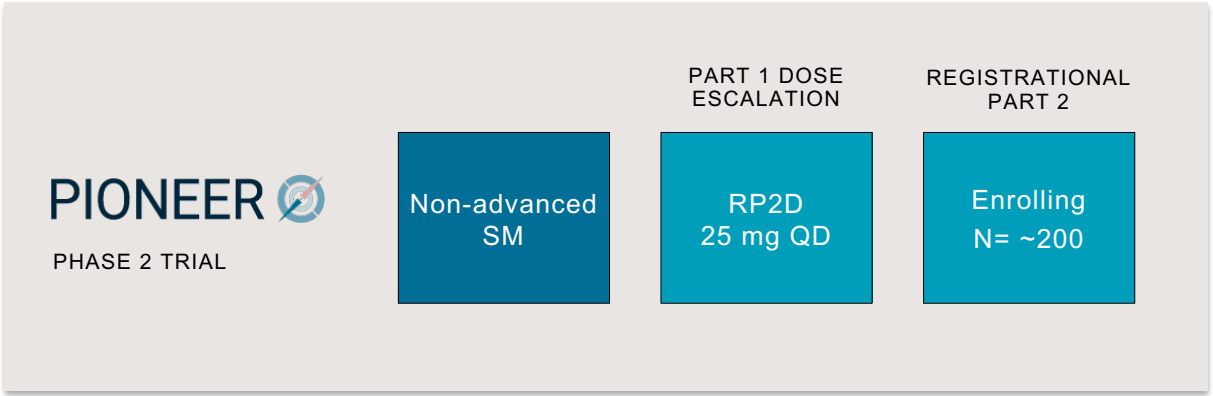
DATA SHOW HIGHLY SENSITIVE ddPCR TESTING DETECTS KIT D816V IN ~95% OF PATIENTS[1]



Anticipate highly sensitive ddPCR KIT D816V testing to be widely available in 2021 at laboratories currently covering ~80% of SM patients in U.S.[2]

1. Data in patients with non-advanced SM presented at the American Society of Hematology Annual Meeting in December 2020. 2. Based on internal market research.

Registrational Part 2 of PIONEER trial top-line data expected in mid-2022



PRIMARY ENDPOINT FOR APPROVAL:

CHANGE IN ISM-SAF TOTAL SYMPTOM SCORE

PIONEER REGISTRATION-ENABLING PART 2

Design: Randomized, double-blind, placebo-controlled treatment period, followed by open-label expansion

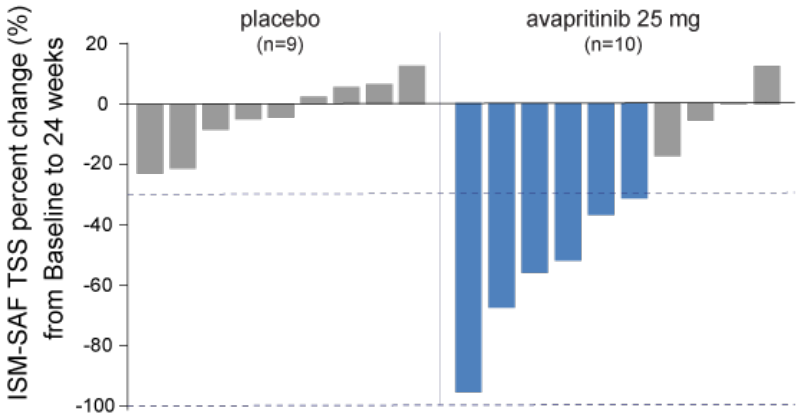
Key endpoints: Response rate defined as ≥30% reduction in ISM-SAF total symptom score (primary), measures of mast cell burden, quality of life, concomitant medications

Duration: 24 weeks

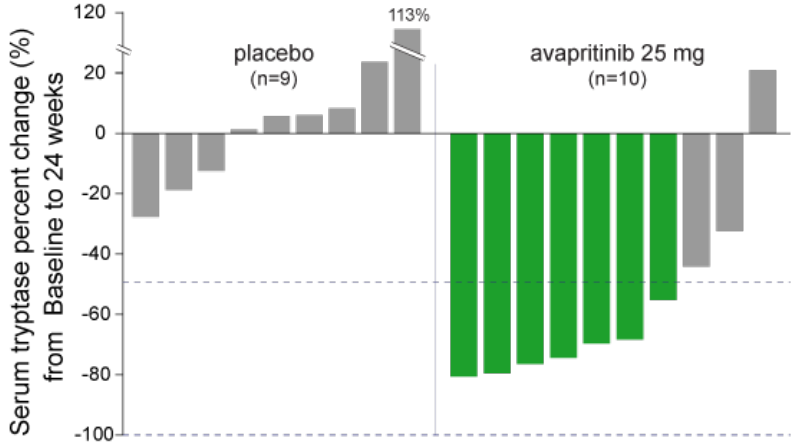
ISM, indolent system mastocytosis; ISM-SAF, indolent systemic mastocytosis – symptom assessment form; RP2D, recommended phase 2 dose.

PIONEER Part 1 data showed AYVAKIT 25 mg QD reduces symptoms and mast cell burden in non-advanced SM

Part 2 primary endpoint
≥30% reduction in ISM-SAF Total Symptom Score at 24 weeks



Part 2 first key secondary endpoint
≥50% tryptase reduction at 24 weeks*



Response rate:	**0%**	**60%**	**0%**	**70%**

Presented at EAACI Virtual 2020 Congress in June 2020. Data cutoff: March 31, 2020. *24 weeks or last assessment before, if 24 weeks not available.
EAACI, European Academy of Allergy and Clinical Immunology.

Safety results for AYVAKIT 25mg QD are similar to placebo at 16 weeks[1]

AE in >15% of placebo or avapritinib arms	Placebo n=9		avapritinib 25 mg n=10	
Preferred term				
% of subjects with ≥1 AE	any grade	grade 3	any grade	grade 3
	89	**22**	**100**	**0**
Nausea	22	0	10	0
Dizziness	22	0	30	0
Headache	11	0	30	0
Diarrhea	11	0	0	0
Fatigue	11	0	40	0
Face edema	0	0	10	0
Peripheral edema	0	0	10	0
Periorbital edema	0	0	0	0
Bone Pain	22	0	0	0

AVAPRITINIB 25 MG QD

- **No patients had serious AEs**
  - 2 patients treated with placebo had serious AEs, 1 with psychogenic seizure and 1 with diffuse cutaneous mastocytosis
- **No patients had dose modifications**
- **No patients discontinued due to AEs**

FOLLOW UP AT 24 WEEKS SHOWED NO ≥GRADE 3 AES OR DISCONTINUATIONS DUE TO AES FOR 25 MG QD[2]

1. Data presented in March 2020 at AAAAI annual meeting. Data cutoff: December 27, 2019. 2. Data cutoff: March 31, 2020.

2021 roadmap for precision medicine leadership

Accelerate global adoption of AYVAKIT and GAVRETO

Advance a new wave of therapeutic candidates toward clinical proof-of-concept

Further expand the company's precision therapy pipeline

Results from a Phase 1 trial of BLU-263 in healthy volunteers

BLU-263
NEXT-GENERATION KIT INHIBITOR

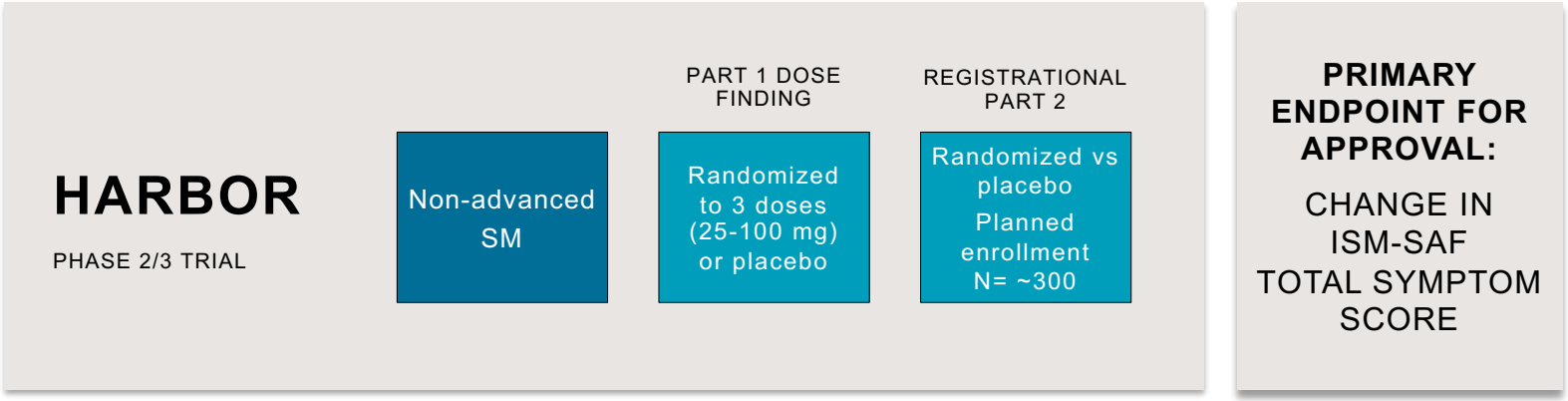
- BLU-263 was generally well-tolerated at all doses tested in healthy volunteers
- Pharmacokinetics were linear and dose-dependent
- Half-life supports once-daily dosing
- Initiated Phase 2/3 HARBOR trial in non-advanced SM, at doses ranging 25-100 mg QD, in Q2 2021

Treatment-related AEs, N of subjects	Single ascending dose cohorts	
	All other doses N=24	200 mg N=6
Any TRAE	0	1
Upper abdominal pain	0	1
Decreased appetite	0	1
Somnolence	0	0
Headache	0	0

Treatment-related AEs, N of subjects	Multiple ascending dose cohorts		
	25 mg N=6	50 mg N=6	100 mg N=6
Any TRAE	1	0	0
Upper abdominal pain	1	0	0
Fatigue	1	0	0
Chapped lips	1	0	0
Nausea	1	0	0
Headache	1	0	0

Data presented at AACR 2021 Annual Meeting. Data cut-off: November 9, 2020. AE, adverse event; TRAE, treatment-related AE.

HARBOR trial of BLU-263 in non-advanced SM initiated in Q2 2021



HARBOR PARTS 1 AND 2

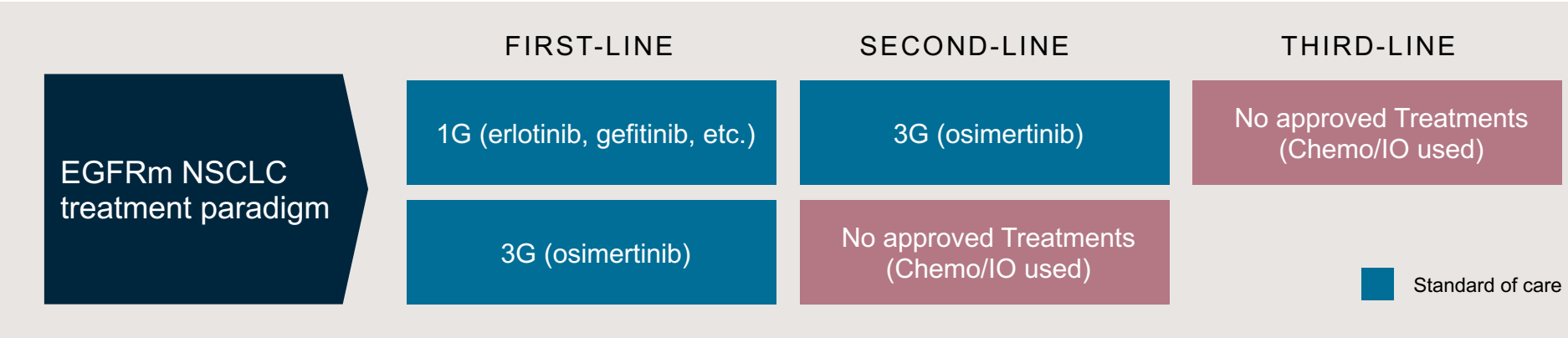
Design: Randomized, double-blind, placebo-controlled treatment period, followed by open-label expansion

Key endpoints: Response rate defined as ≥30% reduction in ISM-SAF total symptom score (primary), measures of mast cell burden, quality of life, concomitant medications

Study includes an exploratory arm in monoclonal mast cell activation syndrome

ISM, indolent system mastocytosis; ISM-SAF, indolent systemic mastocytosis – symptom assessment form; RP2D, recommended phase 2 dose.

Significant patient needs remain in EGFRm NSCLC across all lines of therapies



- Treatment resistance emerges over time which represents a significant barrier to durable benefit
- Chemotherapy +/- IO are the main treatment options post-osimertinib[1]
- CNS is a common site of metastases in EGFR driven NSCLC that needs to be targeted[2]
- **To improve durability and overall treatment outcome, we need effective, highly tolerated, brain-penetrant treatment options that target the most common on-target mutations early in initial therapy**

1. Piper-Vallillo, et al. Emerging treatment paradigms for EGFR-mutant lung cancers progressing on osimertinib. Journal of Clinical Oncology, 2020. 2. Remon and Besse. Brain metastases in oncogene-addicted NSCLC patients: incidence and treatment. Frontiers in Oncology, 2018. CNS, central nervous system; 1G, first-generation; 3G, third-generation; Chemo/IO, chemotherapy/immunotherapy.

BLU-701: potential best-in-class coverage of activating EGFR mutations, plus C797S osimertinib-resistant mutants

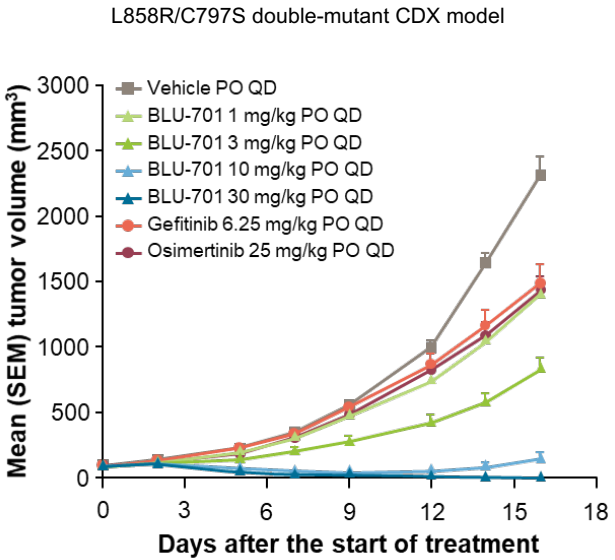
POTENCY ON ACTIVATING & RESISTANCE MUTANTS[1]

	BLU-701	gefitinib	osimertinib
ex19del	**3.3**	4.6	5.0
L858R	**3.3**	4.2	10.3
ex19del/C797S	**1.8**	6.1	>8000
L858R/C797S	**3.3**	3.8	>7000

WILD-TYPE SELECTIVITY[2]

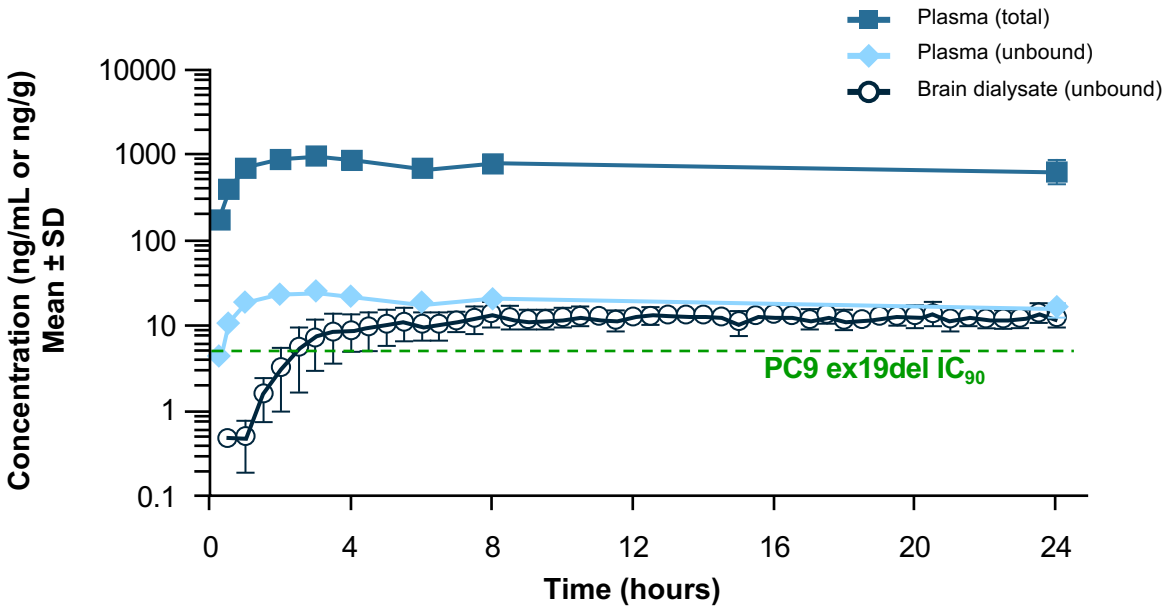
Wild-type EGFR	**107.3**	16.6	113.6

SINGLE AGENT ANTI-TUMOR ACTIVITY



Data presented at AACR 2021 Annual Meeting. 1. Cellular inhibition IC_{50} (nM) in Ba/F3 cell lines. 2. Cellular inhibition IC_{50} in A431 (wild-type EGFR) cell line. Wild-type EGFR selectivity shading: green = >50 nM; yellow = >10 nM, ≤50 nM. PO, oral administration. CDX, cell-line derived xenograft.

BLU-701 plasma and brain concentrations are comparable in preclinical models, suggesting significant brain penetration



Compound	IV infusion $Kp_{u,u}$ (C_{ss})[a]
BLU-701	0.98
Gefitinib	0.11
Osimertinib	0.30

BLU-701 30 MG/KG ACHIEVED CONCENTRATIONS ABOVE IC90 IN PLASMA AND BRAIN DIALYSATE

Data presented at AACR 2021 Annual Meeting.

BLU-945: potential first-in-class triple-mutant EGFR inhibitor, with exceptional wild-type EGFR selectivity to enable combinations

POTENCY ON RESISTANCE MUTANTS[1]

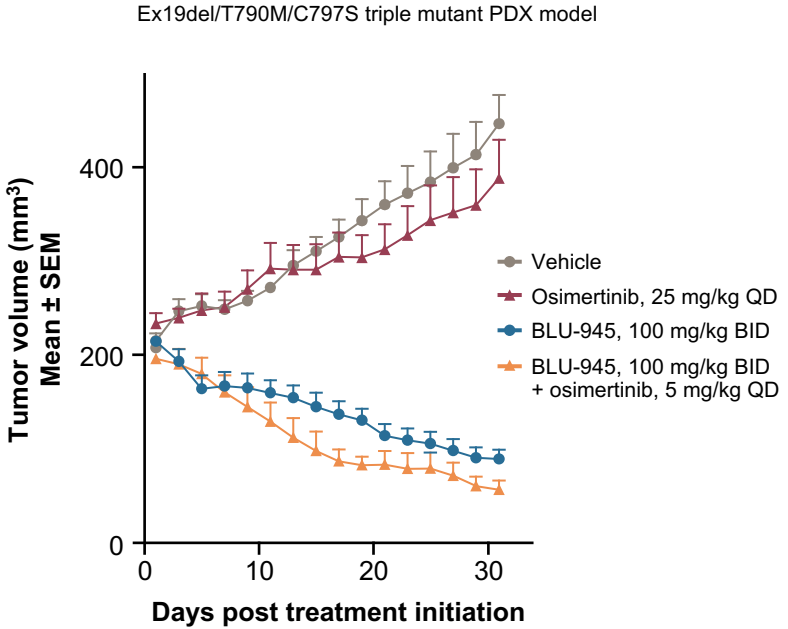
	BLU-945	gefitinib	osimertinib
L858R/T790M	**1.2**	4679.8	4.7
ex19del/T790M/C797S	**4.4**	4864.7	>10000
L858R/T790M/C797S	**2.9**	6707.7	7754.6

WILD-TYPE SELECTIVITY[2]

Wild-type EGFR	**544.4**	16.5	115.9

- BLU-945 demonstrated robust CNS activity in preclinical models

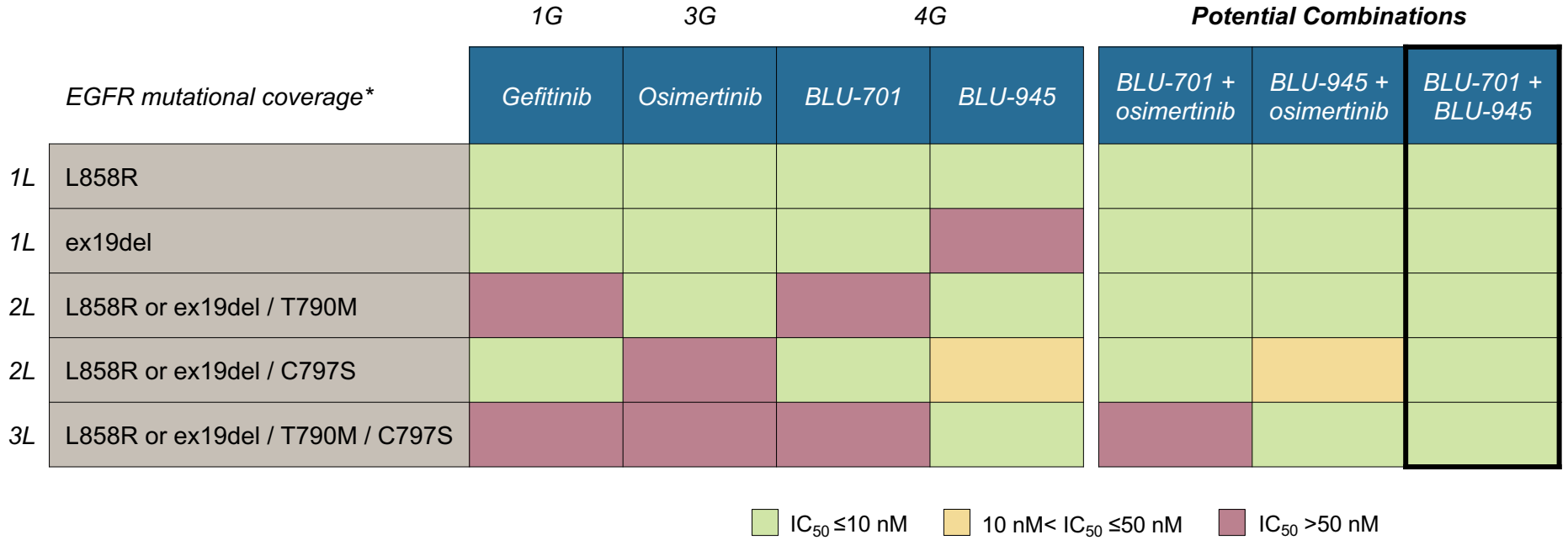
ANTI-TUMOR ACTIVITY ALONE AND IN COMBINATION WITH OSIMERTINIB



Data presented at AACR 2021 Annual Meeting. 1. Cellular inhibition IC_{50} (nM) in NCI-H1975 (EGFR double mutant) and Ba/F3 (EGFR triple mutant) cell lines. 2. Cellular inhibition IC_{50} in A431 (wild-type EGFR) cell line. Wild-type EGFR selectivity shading: green = >50 nM; yellow = >10 nM, ≤50 nM. PDX, patient-derived xenograft.

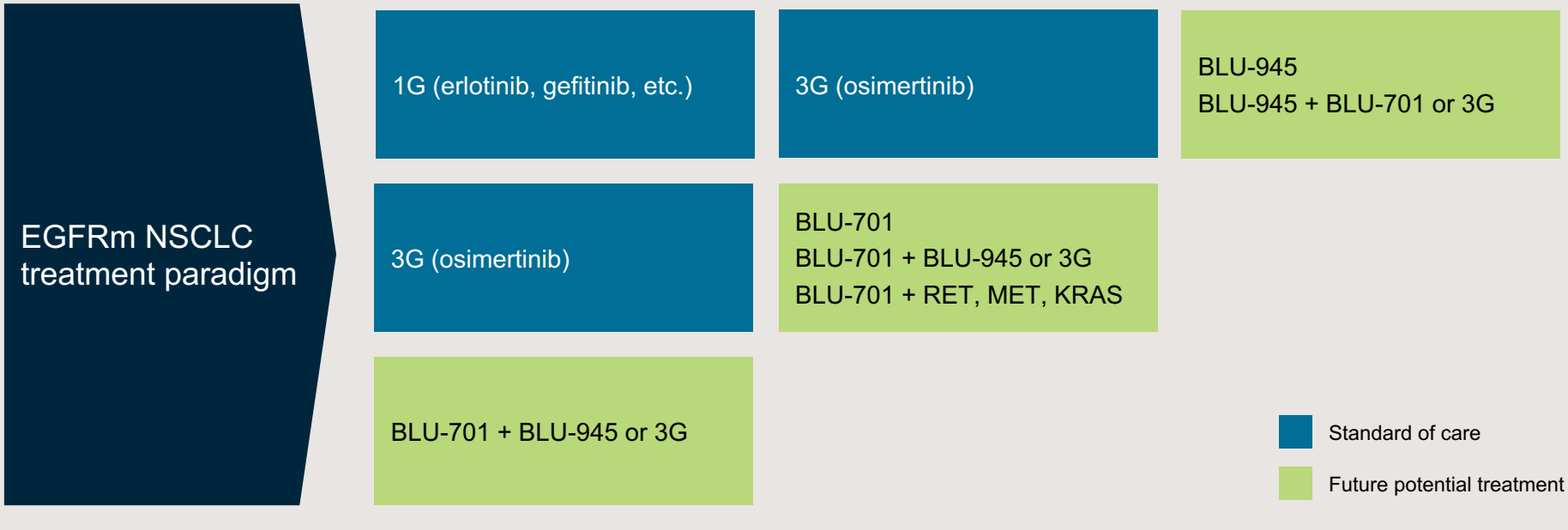
BLU-701 and BLU-945 provide comprehensive EGFR mutational coverage

T790M & C797S: MOST COMMON ON-TARGET RESISTANCE TO 1G AND 3G, RESPECTIVELY

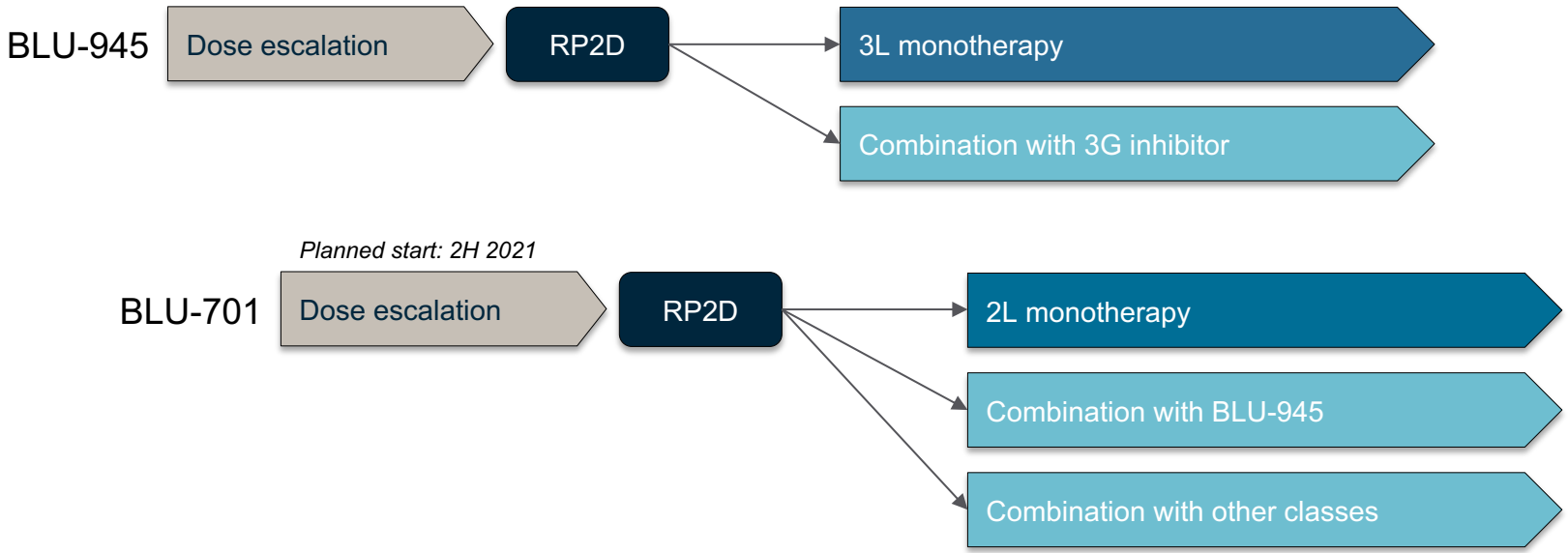


* Based on biochemical IC_{50}. 1L, first line; 2L, second line; 3L, third line; 4G, fourth generation.

We aim to transform EGFRm NSCLC treatment with 4G inhibitors that overcome or prevent on-target resistance across treatment lines



Plan to rapidly develop BLU-945 and BLU-701 monotherapy and combination regimens



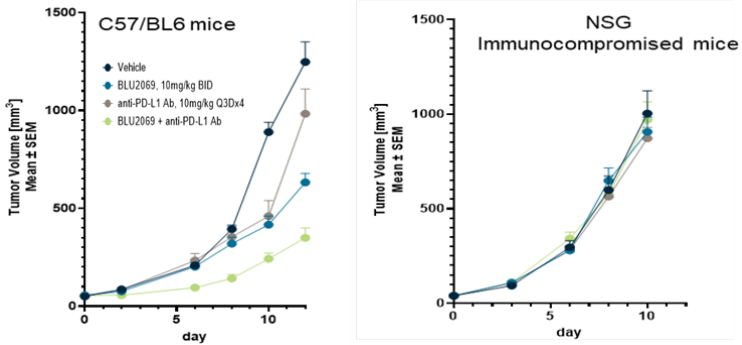
BLU-945 PHASE 1/2 TRIAL INITIATED IN Q2 2021

2L, second line; 3L, third line; 3G, third generation; IND, investigational new drug application; RP2D, recommended Part 2 dose.

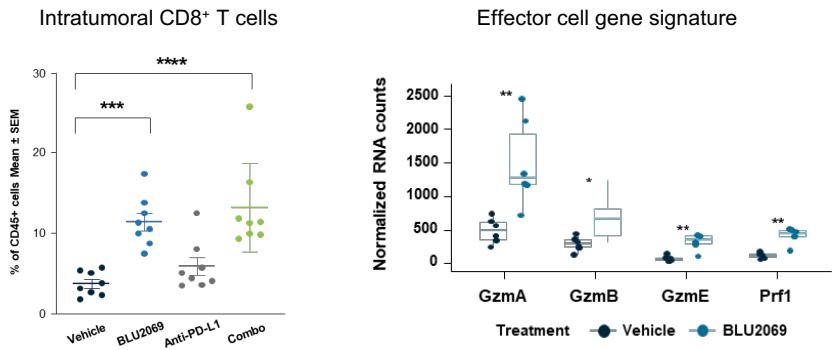
BLU-852, the first development candidate nominated under our cancer immunotherapy collaboration with Roche, has best-in-class potential

	Enzyme activities IC_{50} (nM)			Cell activity IC_{50} or EC_{50} (nM)		Whole Blood activity IC_{50} or EC_{50} (nM)		Selectivity
Compound	MAP4K1	LCK	MAP4K4	pSLP76*	IL-2†	pSLP76*	IL-2†	% kinome >100x
BLU2069	0.17	19	45	29	16	615	517	95%
BLU6348	0.13	78	73	27	11	1033	1194	96%
BLU-852	0.11	502	1196	40	11	851	1240	97%

ANTI-TUMOR ACTIVITY IN AN MCA-205 SARCOMA MODEL



INCREASED CD8 T CELL FREQUENCY & ACTIVATION



Data presented at AACR 2021 Annual Meeting. * IC_{50} values. † EC_{50} values. EC_{50}, half-maximal effective concentration; IC_{50}, half-maximal inhibitory concentration; nM, nanomolar.

Multiple pipeline programs advancing to clinical data inflection points

Program	Target	Therapeutic area focus	Trial	Status
AYVAKIT	KIT D816V	Non-advanced SM	PIONEER Phase 2	Topline data expected mid-2022
BLU-263	KIT D816V	Non-advanced SM	HARBOR Phase 2/3	Trial initiated in Q2 2021
BLU-945	EGFR triple mutant	EGFRm NSCLC	Phase 1/2	Trial initiated in Q2 2021
BLU-701	EGFR double mutant	EGFRm NSCLC	Phase 1	Planned initiation in 2H 2021
BLU-222	CDK2	Cyclin E aberrant cancers	Phase 1	Planned initiation in 1H 2022
BLU-852*	MAP4K1	Cancer immunotherapy	Phase 1	Planned initiation in 2022

KIT, KIT proto-oncogene receptor kinase; MAP4K1, hematopoietic progenitor kinase 1.
*In collaboration with Roche. For one of the programs, Blueprint Medicines has U.S. commercial rights and Roche has ex-U.S. commercialization rights. For one of the programs, Roche has worldwide commercialization rights.

2021 roadmap for precision medicine leadership

Accelerate global adoption of AYVAKIT and GAVRETO

Advance a new wave of therapeutic candidates toward clinical proof-of-concept

Further expand the company's precision therapy pipeline

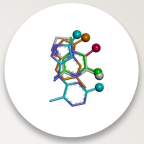
Constant expansion of highly productive research platform

WORLD-CLASS EXPERTISE IN CATALYTIC KINASE INHIBITION

MOLECULAR TARGETING

Deep biological insights across core areas of focus

Vast genomic datasets and computational power



THERAPEUTIC DESIGN

Proprietary library of fully annotated compounds

Sophisticated structure-based design capability

PLANNED FUTURE

EXPANDED INTERNAL CAPABILITY ACROSS ADDITIONAL PRECISION THERAPY MODALITIES

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POTENTIAL COMPLEMENTARY EXTERNAL INNOVATION

Poised for transformative growth, with a strong financial position and a diversified revenue stream

Statement of Operations (unaudited)	Three Months Ended 6/30/2021	Three Months Ended 6/30/2020	Six Months Ended 6/30/2021	Six Months Ended 6/30/2020
Total revenue	$27.3M	$8.3M	$48.9M	$14.5M
Collaboration revenue	$15.9M	$2.7M	$28.5M	$5.4M
Net product sales	$11.4M	$5.7M	$20.4M	$9.1M
Cost of sales	$6.5M	$0.1M	$6.6M	$0.2M
Research & development expense[1]	$80.0M	$91.1M	$159.7M	$175.2M
Selling, general & admin expense[2]	$49.3M	$42.2M	$91.3M	$77.8M
Net loss	$(108.4)M	$(123.5)M	$(208.2)M	$(234.4)M

Balance Sheet (unaudited)	6/30/2021	12/31/2020
Cash, cash equivalents and investments	$1,380.1M	$1,549.7M

1. Includes stock-based compensation expense of $10.5M and $8.7M in the three months ended 6/30/21 and 6/30/20, respectively, and $19.4M and $16.5M in the six months ended 6/30/21 and 6/30/20, respectively. 2. Includes stock-based compensation expense of $13.8M and $10.8M in the three months ended 6/30/21 and 6/30/20, respectively, and $25.6M and $19.9M in the six months ended 6/30/21 and 6/30/20.