Pioneering the Science of Time

COMPANY OVERVIEW

APRIL 14, 2022

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, express or implied 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 the initiation of clinical trials and trial cohorts, the results of ongoing and planned clinical trials, data publications, marketing applications and approvals; the anticipated benefits of the Company's ISM Symptom Assessment Form; expectations related to the expansion of the Company's research platform; the Company's plans, strategies and timelines to increase output from its discovery engine and to nominate development the anticipated benefits of the preclinical profiles of the Company's drug candidates; the Company's plans, strategies and timelines for the development of the Company's drug candidates as monotherapies and combination with other agents; anticipated indications for the Company's drug candidates; plans and timelines for additional marketing applications for avapritinib and pralsetinib and, if approved, commercialization of avapritinib and pralsetinib in additional indications or in additional geographies; 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. If such expectations, assumptions, estimates and projections do not fully materialize or prove incorrect, the events or circumstances referred to in the forward-looking statements may not occur. 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 timing and results of preclinical and clinical studies for the Company's drug candidates, which may not support further development of such drug candidates either as monotherapies or in combination with other agents or may impact the anticipated timing of data or regulatory submissions; 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; the Company's ability to successfully expand its operations and scientific platform and the costs thereof; the Company's ability to realize the benefits of its executive leadership transition plan; 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. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

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.

Blueprint Medicines is a global leader in precision therapy

AYVAKIT® avapritinib | tablets

GAVRETO® pralsetinib | 100mg capsules

Ongoing global collaboration with Roche and Genentech for the development and commercialization of GAVRETO

OUR FIRST DECADE OF ACHIEVEMENT

2 internally discovered medicines

FDA & EMA approved across **5** indications

within **10** years, and with

5 breakthrough therapy designations

BROAD AND GROWING PORTFOLIO WITH 10 PRECISION THERAPIES IN DEVELOPMENT

AYVAKIT is approved for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, and adult patients with advanced SM, including aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia. GAVRETO is approved for the treatment of adult patients with RET-fusion positive NSCLC, adult and pediatric patients with advanced or metastatic RET-mutant medullary thyroid cancer who require systemic therapy and adult, and pediatric patients with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory. FDA, U.S. Food and Drug Administration; GIST, gastrointestinal stromal tumor; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

Not for promotional use.

Our path to potential transformative growth and an independent financial profile

YEAR END 2021

- AYVAKIT/AYVAKYT and GAVRETO approved with ongoing global expansion
- A leading precision therapy research platform
- Strong financial position with ~$1B cash and cash equivalents

NEAR-TERM PLANS • 2022-2023

- Constellation of clinical data catalysts across strategic therapeutic areas
- AYVAKIT launch in non-advanced systemic mastocytosis
- Continued product revenue growth plus collaboration milestones and royalties

FUTURE GOALS • 2024-2025+

- Broad portfolio of marketed medicines in precision oncology and hematology
- Diversified research platform with unparalleled productivity
- Independent financial profile

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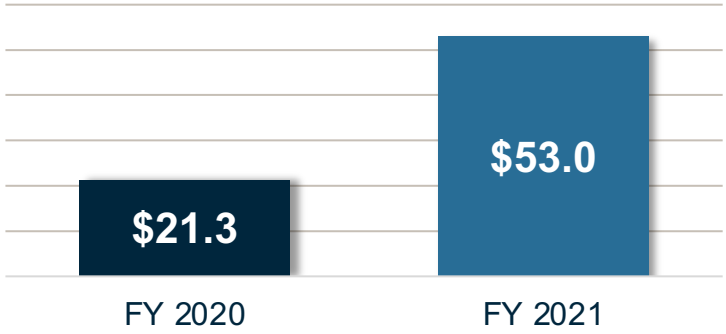
AYVAKIT update: full-year and Q4 2021 performance

AYVAKIT® avapritinib | tablets

GLOBAL NET REVENUES ($, MILLIONS)



ACHIEVED $20.0M NET REVENUES IN Q4 2021

Q4 2021 PERFORMANCE METRICS[1]

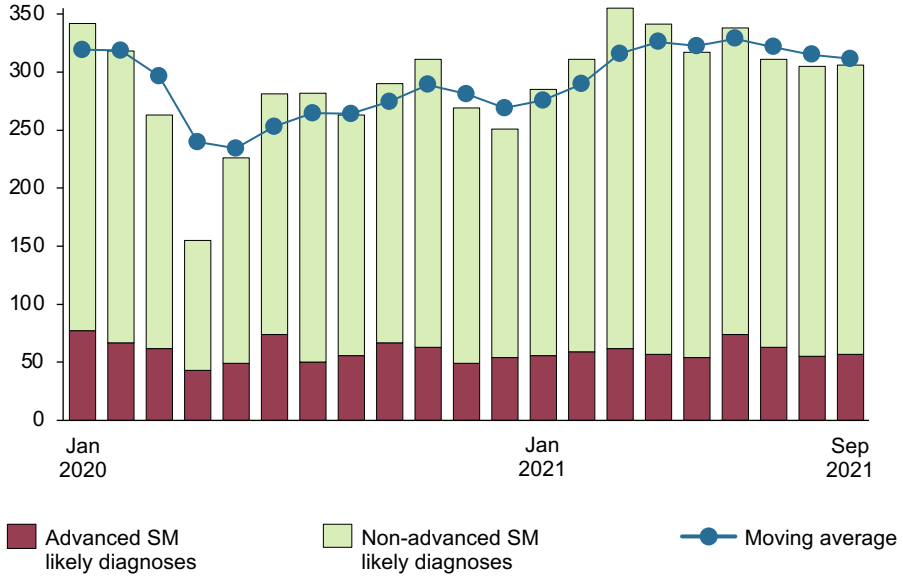
- **~55%** QoQ revenue growth for advanced SM
- **~80** new prescribers or accounts
- **~45%** of volume driven by community practices
- **~20%** of patients newly diagnosed in 2021

ANTICIPATE $115 TO $130 MILLION IN AYVAKIT NET PRODUCT REVENUES IN 2022

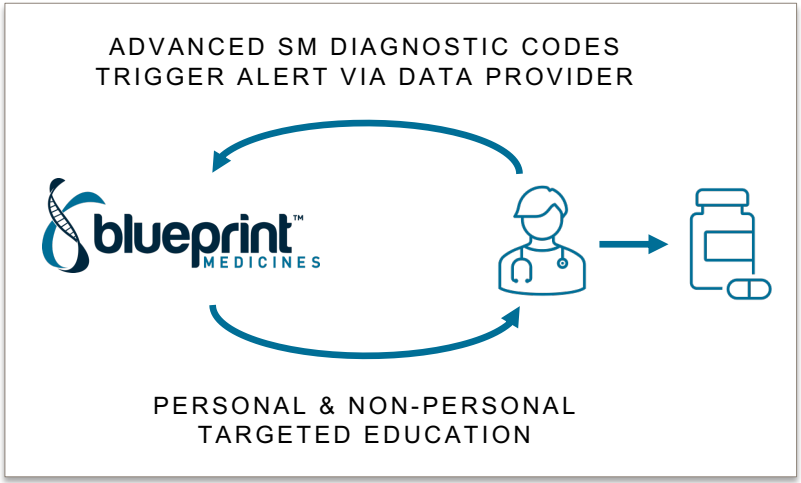
1. Reported data represent estimations. QoQ, quarter over quarter.

Using innovative data-driven approaches to optimize engagement

OBSERVED MONTHLY SM DIAGNOSES IN U.S.[1]



REAL-TIME PROVIDER ENGAGEMENT FOR ADVANCED SM[2]



1. Based on analyses of available U.S. claims data. 2. Healthcare provider targeting exclusively focused on AYVAKIT's FDA approved indication for advanced SM.

Not for promotional use.

We're primed to bring the promise of precision therapy to broad populations

Upcoming wave of clinical data milestones has the potential to dramatically expand our impact

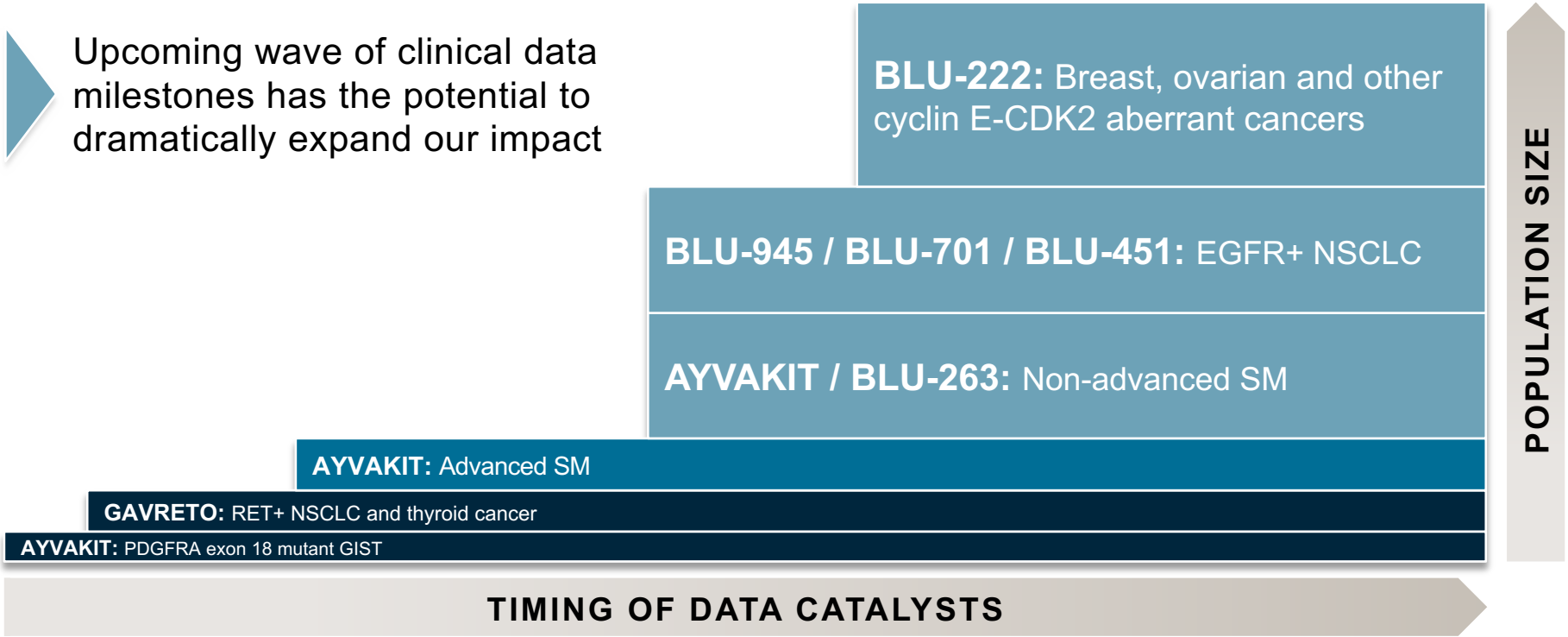


Figure is illustrative. GIST, gastrointestinal stromal tumors; NSCLC, non-small cell lung cancer.

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FUTURE GOALS • 2024-2025+

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SYSTEMIC MASTOCYTOSIS

STRATEGIC THERAPEUTIC AREA

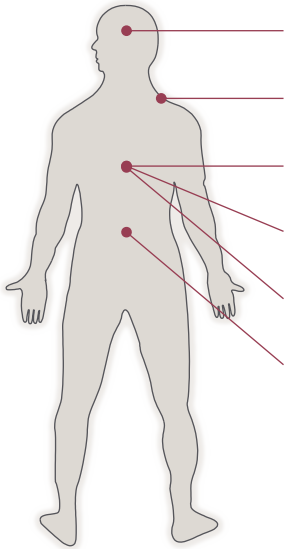
Pioneering the Science of Time

Every day, we seek to transform science into more time for life. Time to be with families, time to be productive community members, time to feel the small moments of joy that shape our lives.

blueprint MEDICINES

Systemic mastocytosis, a rare mast cell disease with high medical need

SYSTEMIC MASTOCYTOSIS SYMPTOMS



- Brain fog
- Pruritis, flushing and pigmented skin lesions
- Life-threatening organ infiltration and damage
- Unpredictable, life-threatening anaphylaxis
- Debilitating fatigue
- GI upset with vomiting, diarrhea and nausea

95% of SM cases driven by the KIT D816V mutation

ADVANCED SM[1]

6 months to 3.5 years median overall survival based on disease subtype

NON-ADVANCED SM[2]

30% had ≥1 emergency room visit in prior year

51% take ≥3 prescription medicines for SM

65% reported SM impacted their ability to work

90% feel SM controls their life to some extent

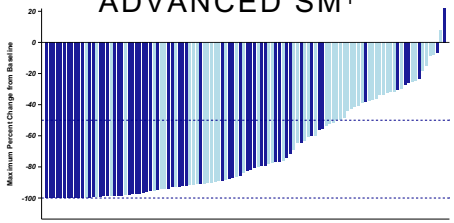
Worse physical functioning and mental health reported than patients with colorectal or lung cancer

1. Sperr WR, et al. Lancet Haematol, 2019. 2. Data from the TouchStone Survey presented at American Society of Hematology annual meeting in December 2020.

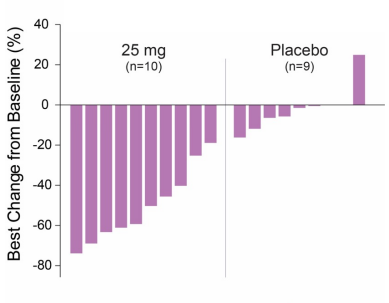
Avapritinib is a clinically validated, highly potent inhibitor of KIT D816V

REDUCED MAST CELL BURDEN

ADVANCED SM[1]

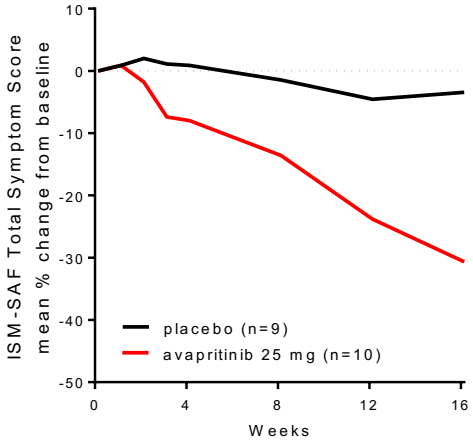


NON-ADVANCED SM[2]



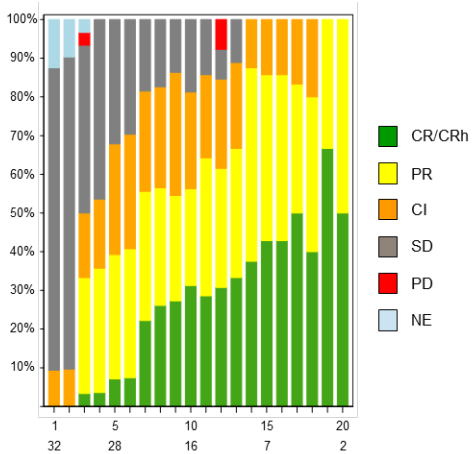
IMPROVED DISEASE SYMPTOMS

NON-ADVANCED SM[2]



INDUCED DEEP AND DURABLE RESPONSES

ADVANCED SM[1]



Safety data support evaluation of chronic treatment

1. Top-line EXPLORER and PATHFINDER data reported in September 2020. Data cutoff: May 27, 2020 for EXPLORER and June 23, 2020 for PATHFINDER, with response assessments per central review completed in September 2020. 2. Data reported at AAAAI Annual Meeting in March 2020. Data cutoff: December 27, 2019.

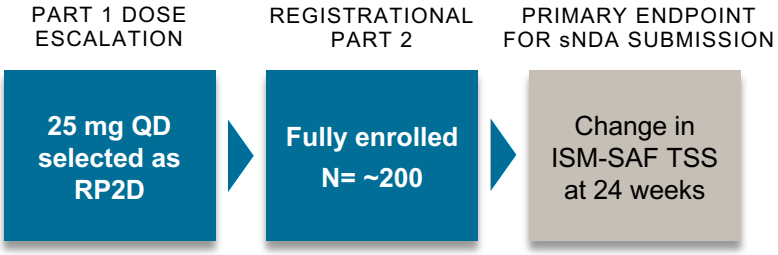
Broad clinical strategy designed to address the spectrum of medical need in non-advanced SM

Avapritinib

- FDA breakthrough therapy designation granted for moderate to severe indolent SM

PIONEER

Phase 2 trial in non-advanced SM



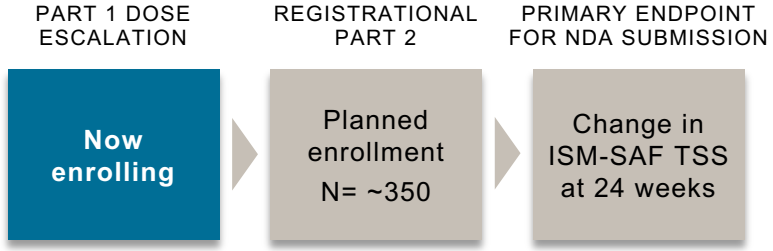
Plan to report top-line registration-enabling Part 2 data in mid-2022

BLU-263

- Next-generation KIT D816V inhibitor
- Opportunity to reach a broader population of patients with SM, based on potential for optimized risk-benefit profile

HARBOR

Phase 2/3 trial in non-advanced SM



Plan to present data in 2H 2022

ISM-SAF, indolent SM symptom assessment form; RP2D, recommended part 2 dose; TSS, total symptom score.

ISM-SAF is a patient-reported outcomes tool developed with input from SM patients, disease experts and global regulatory authorities

ISM-Symptom Assessment Form

- Clinical benefit measure and primary endpoint for PIONEER trial
- Designed with input from disease experts, patients and regulatory authorities to support regulatory approval[1]
- ISM-SAF produced reliable, construct-valid, sensitive scores when administered in PIONEER Part 1 to patients with indolent SM[2]

Symptom	Domains	Score
Abdominal pain	GI (0 – 30)	Scored 0 – 10 daily (24-hour recall) on a handheld device 0 is no symptoms 10 is worst Analyzed as a 14-day moving average
Diarrhea		
Nausea		
Spots	Skin (0 – 30)	
Itching		
Flushing		
Brain Fog	Neurocognitive (0 – 30)	
Headache		
Dizziness		
Bone pain		
Fatigue		

Total Symptom Score (0-110)

1. Taylor, et al. Orphanet J Rare Dis, 2021. 2. Padilla, et al. Orphanet J Rare Dis, 2021. GI, gastrointestinal.

ISM-SAF TSS correlates with symptom and quality of life measures

CLINICALLY IMPORTANT TSS OUTCOMES

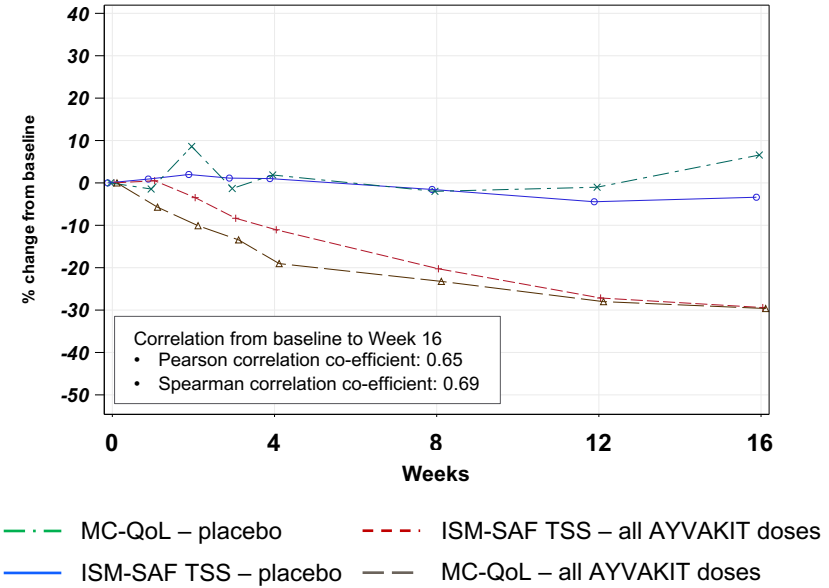
~30% reduction in ISM-SAF TSS

- 30% reduction in TSS is correlated with 1 to 2-point change on PGIS symptom questionnaire[1]
- 2-point reduction on PGIS is associated with change from severe to mild symptoms[2]

~30% difference in ORR versus placebo

- Registration-enabling symptom assessment tools have shown ORR differences of ~15-40% versus placebo (e.g., linaclotide, ruxolitinib)[2]

PIONEER PART 1 DATA SHOW TSS CORRELATES WITH MC-QOL[3]



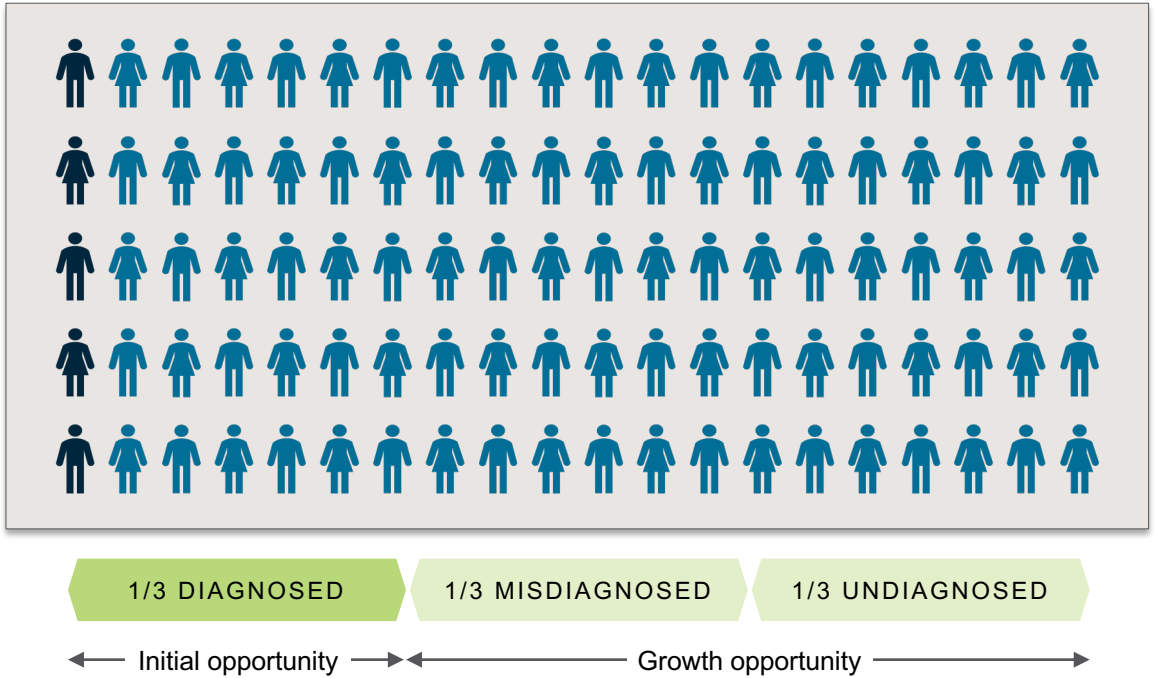
1. Padilla, et al. Orphanet J Rare Dis, 2021. 2. Linaclotide and ruxolitinib prescribing information. 3. Data reported at AAAAI annual meeting in March 2020. Data cutoff: December 27, 2019. PGIS, Patient Global Impression of Symptom Severity; ORR, overall response rate.

Significant initial target SM patient population, with high growth potential

75,000 SM PATIENTS IN MAJOR MARKETS

5-10%
ADVANCED SM

90-95%
NON-ADVANCED SM



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

We're executing a comprehensive plan to accelerate SM patient identification

RAISE AWARENESS VIA EDUCATION

- Multiple ongoing healthcare provider and patient education programs designed to unmask signs and symptoms of disease

SUPPORT ACCESS TO TESTING

- Sponsored no-charge KIT D816V testing program with LabCorp Oncology now available for patients with suspected SM

GENERATE EVIDENCE

- PROSPECTOR screening study initiated to assess KIT D816V prevalence in patients with evidence of mast cell activation

ENHANCE TESTING INFRASTRUCTURE

- Highly sensitive blood-based KIT D816V testing is recommended and available at laboratories covering >80% of SM patients
- Ongoing community engagement to generate testing and treatment algorithms

LUNG CANCER

STRATEGIC THERAPEUTIC AREA

Precision that Moves

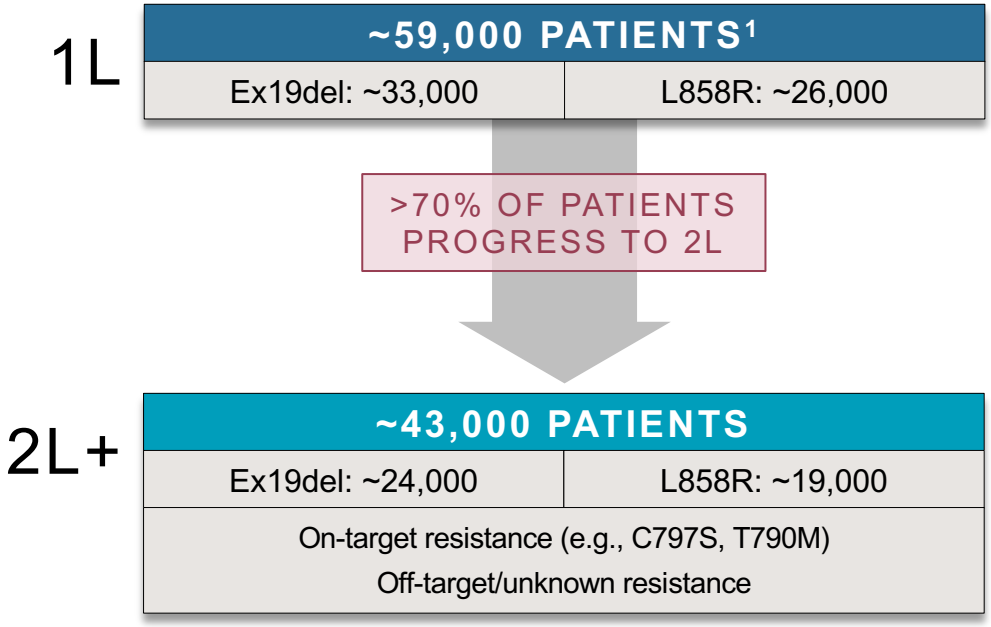
We help patients stay one step ahead with therapies that adapt to disease evolution. This includes solving for treatment resistance and intractable sites of progression, as well as pioneering innovative combinations to prolong benefit.

Diane L.
Lung cancer patient

blueprint MEDICINES

Increasing tumor resistance and complexity drives disease progression, with no approved therapies after 1L standard of care osimertinib

EGFR-MUTANT NSCLC
ESTIMATED INCIDENT PATIENTS PER YEAR



CHALLENGES

- Lower OS and PFS in patients with L858R activating mutation
- On- and off-target resistance increasingly emerges
- CNS is a common site of disease progression

Approximate patient numbers covering major markets – US, EU4, UK, and Japan. 1. Excludes rare mutations including exon 20 insertions. Internal estimates adapted from Ramalingam, et al. NEJM, 2020; Decision Resources Group: NSCLC Forecast and Epidemiology; and Harrison Seminars in Cancer Biology, 2020. Ex19del, exon 19 deletion mutations; CNS, central nervous system; OS, overall survival; PFS, progression free survival.

Opportunities for our next-generation EGFR precision therapies

EGFR-MUTANT NSCLC
ESTIMATED INCIDENT PATIENTS PER YEAR

1L

~59,000 PATIENTS[1]	
Ex19del: ~33,000	L858R: ~26,000

>70% OF PATIENTS PROGRESS TO 2L

2L+

~43,000 PATIENTS	
Ex19del: ~24,000	L858R: ~19,000
On-target resistance (e.g., C797S, T790M) Off-target/unknown resistance	

OPPORTUNITIES

- Enhance activity on L858R activating mutation
- Prevent or treat on-target resistance
- Treat off-target resistance with well-tolerated combos
- Prevent or treat brain mets with enhanced CNS penetration

Approximate patient numbers covering major markets – US, EU4, UK, and Japan. 1. Excludes rare mutations including exon 20 insertions. Internal estimates adapted from Ramalingam, et al. NEJM, 2020; Decision Resources Group: NSCLC Forecast and Epidemiology; and Harrison Seminars in Cancer Biology, 2020. CNS, central nervous system.

Our portfolio of EGFR therapies are purpose-built to address medical needs

TREATMENT GOALS

Effectively block the EGFR pathway

Establish 2L+ SOC with combinations that treat on- and off-target resistance

BLUEPRINT MEDICINES EGFR PORTFOLIO

BLU-945

- Potent EGFR mutation coverage:
  - LR and LR/CS
  - TM and TM/CS regardless of activating mutation
  - Potential for broader coverage at higher exposures
- Highly selective over wild-type EGFR

BLU-701

- Potent EGFR mutation coverage:
  - Ex19del and LR
  - CS regardless of activating mutation
- Highly CNS penetrant

BLU-451

- Potent inhibitor of all common Ex20ins
- Highly selective over wild-type EGFR
- CNS penetrant

CS, C797S resistance mutation; Ex20in, activating exon 20 insertion mutations; LR, L858R activating mutation; TM, T790M resistance mutation.

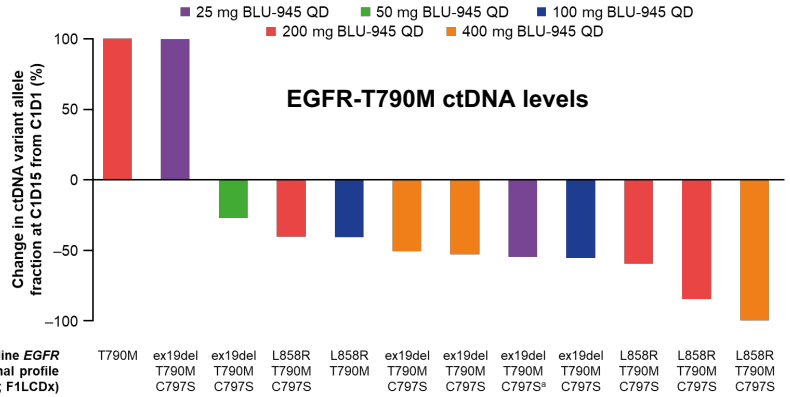
Early BLU-945 dose escalation data achieve clinical proof-of-concept

- Dose-dependent reductions in ctDNA allele fractions for EGFR resistance mutations targeted by BLU-945
- Increasing coverage of EGFR activating and resistance mutations at higher doses, based on pharmacokinetic data
- Dose-dependent antitumor activity, with reductions in target lesions observed at 200 mg QD and higher
- Generally well-tolerated, with no significant adverse events associated with wild-type EGFR inhibition

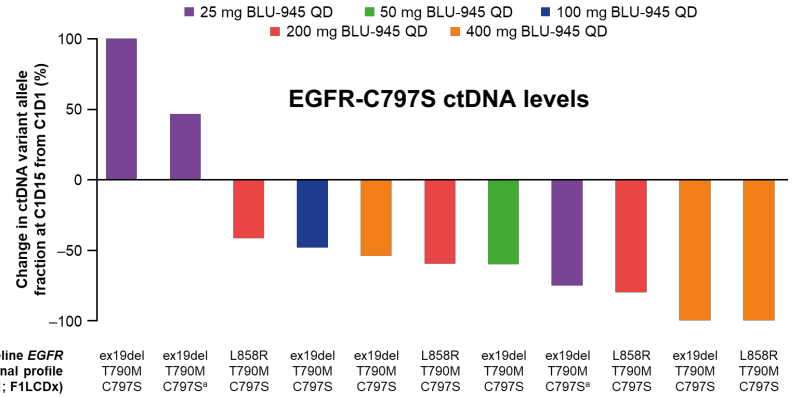
DATA SUPPORT INITIATION OF BROAD COMBINATION DEVELOPMENT STRATEGY

BLU-945 treatment led to dose-dependent reductions in ctDNA

83% OF EGFR-T790M VARIANT ALLELES REDUCED WITH TREATMENT



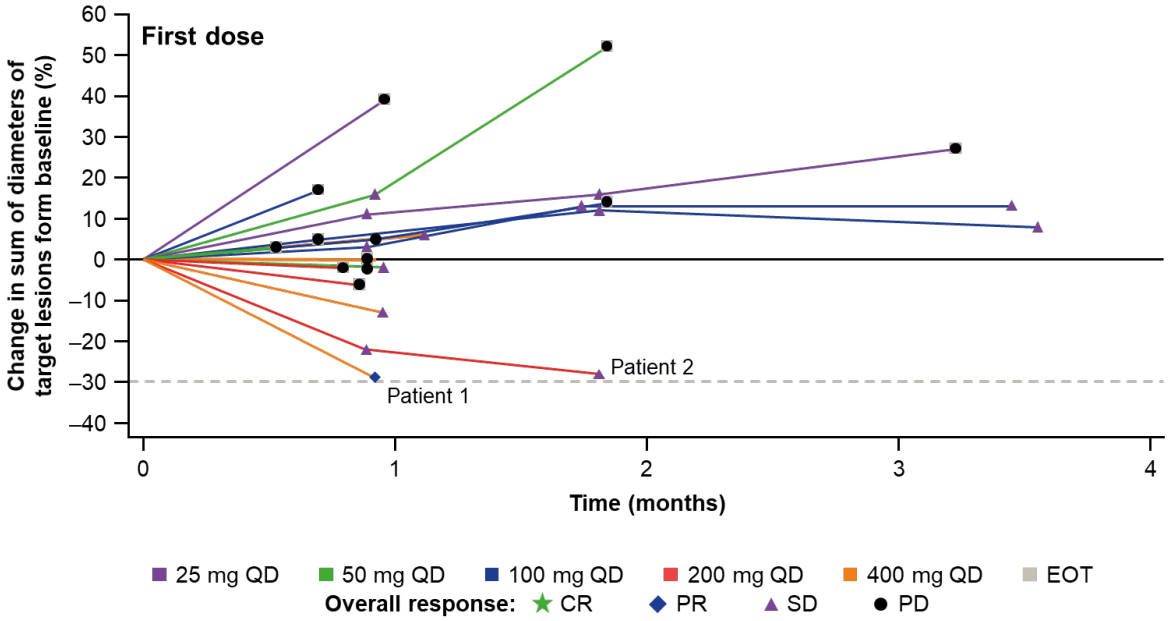
81% OF EGFR-C797S VARIANT ALLELES REDUCED WITH TREATMENT



- In the 400-mg cohort, all detectable T790M and C797S alleles showed reduction, including three that fell below the limit of detection (clearance)

Data presented at AACR in April 2022. [a]Patient had two different DNA mutations in C797S. Note: reductions in individual variant allele fractions as shown; therefore, patients with multiple mutations may be represented on both plots. All T790M and C797S allele fractions with available baseline and C1D15 data are shown. Increases of greater than 100% were truncated at 100%. C, Cycle; ctDNA, circulating tumor DNA; D, day; F1LCDx, FoundationOne Liquid CDx assay; QD, once daily.1. Ku BM et al. Oncology. 2022; Epub ahead of print. PMID: 35196661; 2 Ma L et al. Front Oncol. 2021;11:643199; 3. Fernandes MGO et al. Cells. 2021;10:1912. As of the data cut-off (March 9, 2022), 33 patients have been treated with BLU-945 at 25–400 mg once daily (QD) in the first 5 cohorts.

BLU-945 showed dose-dependent anti-tumor activity, with tumor shrinkage reported at doses ≥200 mg QD



- Unconfirmed PR reported in patient with ex19del/T790M/C797S treated at 400 mg QD
- Dose escalation from 100 to 200 mg QD led to stabilization of tumor growth in two patients

Data presented at AACR in April 2022.

[a]Patients with measurable target lesions at baseline with post-baseline scans (investigator assessed); [b]Data cut off, March 9, 2022; CR, complete remission; EOT, end of treatment; PD, progressive disease; PR, partial remission; QD, once daily; SD, stable disease. An unconfirmed PR is a PR in which tumor reduction ≥30% has occurred but has not yet been confirmed via a subsequent scan. As of the data cut-off (March 9, 2022), 33 patients have been treated with BLU-945 at 25–400 mg once daily (QD) in the first 5 cohorts.

BLU-945 was generally well-tolerated in the ongoing Phase 1 trial

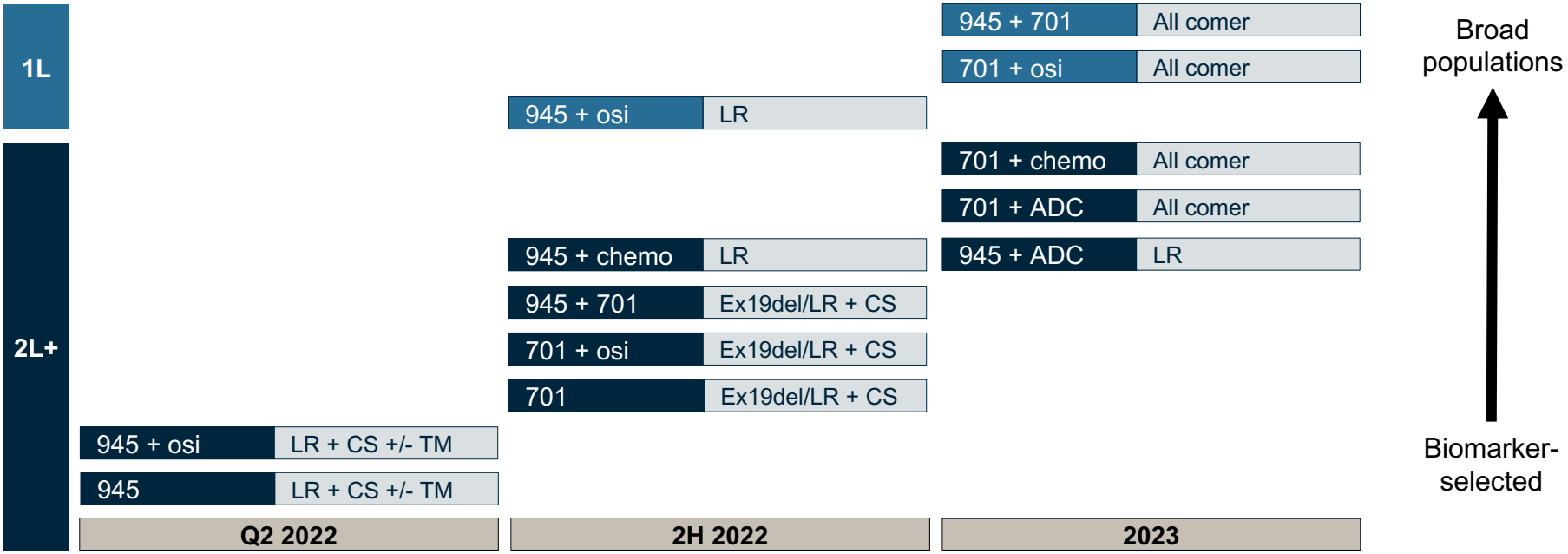
Most common AEs by preferred term in ≥10% of patients

AEs, regardless of causality, n (%)	All AEs N=33		Treatment-related AEs N=33	
	Any grade	Grade 3	Any grade	Grade 3
Nausea	10 (30)	2 (6)	7 (21)	1 (3)
Headache	6 (18)	2 (6)	1 (3)	0
Fatigue	6 (18)	0	5 (15)	0
Cough	5 (15)	0	1 (3)	0
Dyspnea	5 (15)	1 (3)	0	0
Vomiting	5 (15)	1 (3)	3 (9)	1 (3)
Hyponatremia	4 (12)	0	0	0
Dry Mouth	4 (12)	0	3 (9)	0
Anemia	4 (12)	1 (3)	0	0

- No Grade 4 or 5 AEs
- One DLT, grade 3 transaminitis, in 400 mg QD cohort
  - Improved with dose interruption; patient remains on therapy
- AEs associated with EGFR wild-type inhibition were minimal
- No interstitial lung disease or QTc prolongation
- 8 (24%) serious AEs, with 2 (6%) deemed to be related:
  - Grade 3 vomiting
  - Grade 3 transaminitis
- No treatment discontinuations due to AEs
- Dose escalation continues and the MTD has not yet been determined

Data presented at AACR in April 2022. AE, adverse event; DLT, dose-limiting toxicity; MTD, maximum tolerated dose. As of the data cut-off (March 9, 2022), 33 patients have been treated with BLU-945 at 25–400 mg once daily (QD) in the first 5 cohorts.

Phase 1/2 trials to rapidly generate data in broad populations, informing development and registration strategies



PLANNED INITIATION OF PHASE 1/2 SYMPHONY / HARMONY TRIAL COHORTS

BLU-451: a potential best-in-class EGFR exon 20 precision therapy

- **Potent inhibition** of all common EGFR exon 20 insertion variants
- **CNS penetrant** with robust activity in a preclinical intracranial model
- **Highly selective** over wild-type EGFR and off-target kinases
- **Oral administration**, with well-characterized preclinical pharmacology

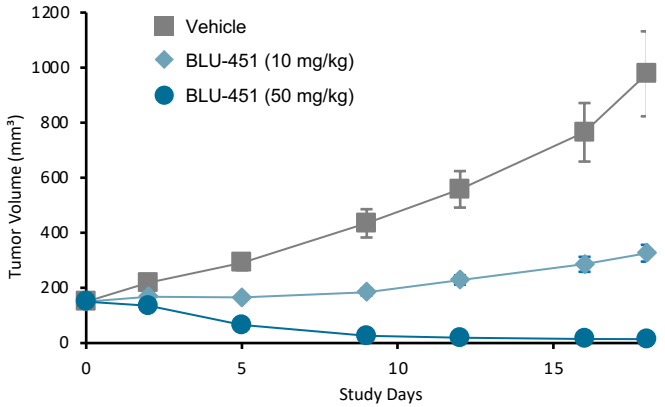
BLU-451 PRECLINICAL PROFILE HAS POTENTIAL TO TRANSLATE INTO IMPROVED SAFETY AND EFFICACY, INCLUDING IN PATIENTS WITH BRAIN METASTASES

Preclinical data show BLU-451 is highly selective, potent and CNS penetrant

HIGHLY SELECTIVE OVER WILD-TYPE EGFR (CELLULAR ACTIVITY IC50, NM)

	BLU-451
WT EGFR	1,630
EGFR Exon 20 insertion variants: SVD	53
EGFR Exon 20 insertion variants: ASV	78
EGFR Exon 20 insertion variants: NPH	75
EGFR Exon 20 insertion variants: FQEA	61
EGFR Exon 20 insertion variants: NPG	7

ROBUST ANTI-TUMOR ACTIVITY IN AN EGFR EXON 20 MODEL



HIGHLY CNS PENETRANT

PRECLINICAL DATA PRESENTED FOR BLU-451 AT AACR ANNUAL MEETING

Lengo Therapeutics data on file. WT EGFR lines comprise A431, H2073, and Ba/F3 WT EGFR cells. In vivo efficacy demonstrated in LU0387 PDX model.

ADDITIONAL PIPELINE PROGRAMS

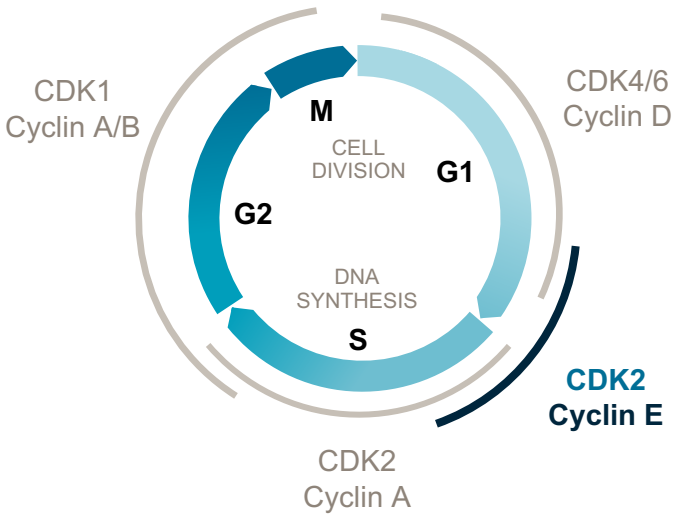
The Urgency of Now

We are constantly on the move, relentless in our determination to accelerate development of new therapies, expedite clinical trials and quickly bring approved medicines to patients worldwide.

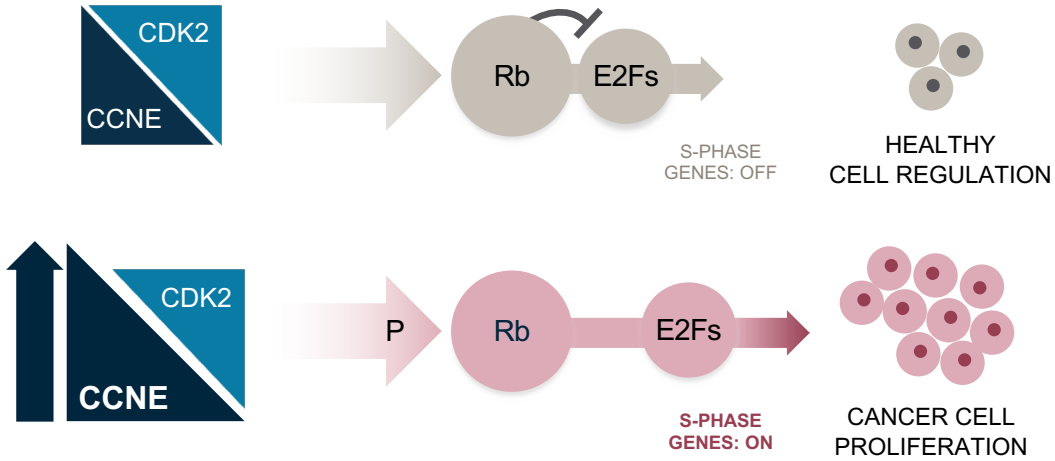
blueprint MEDICINES

CDK2 and CCNE1 are cell cycle regulators implicated in various CDK2-vulnerable cancers

CDK-CYCLIN COMPLEXES REGULATE THE CELL CYCLE



ABERRANT CYCLIN E (CCNE1) DRIVES PROLIFERATION

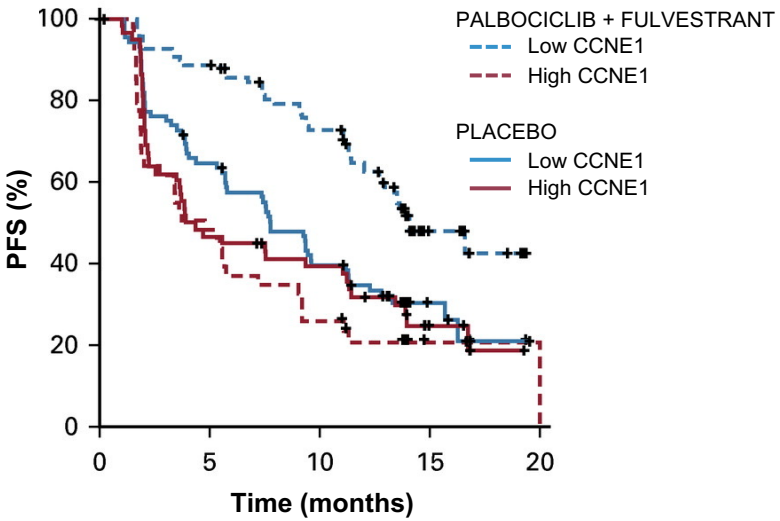


Aberrant CCNE hyperactivates CDK2, dysregulating Rb protein phosphorylation and E2F transcription factor activation of S-phase genes, resulting in cancer cell proliferation

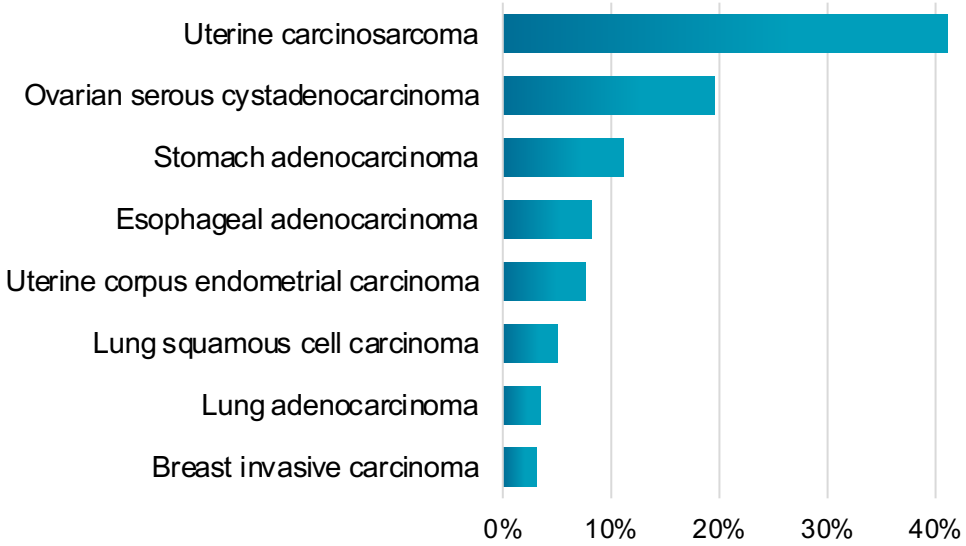
E2F, E2F transcription factor; P, phosphorylation; Rb, retinoblastoma protein.

Aberrant CCNE is a disease driver in multiple cancers

LOWER PFS IN PALBOCICLIB-TREATED HR+ BREAST CANCER WITH HIGH CCNE1[2]



REPRESENTATIVE TUMOR TYPES BY CCNE1 AMPLIFICATION FREQUENCY[1]



1. CCNE1 amplification frequency represented as percentage of total patient samples. Data from the National Cancer Institute's The Cancer Genome Atlas Program (www.cancer.gov/tcga).
2. Turner, et al. Cyclin E1 expression and palbociclib efficacy in previously treated hormone receptor-positive metastatic breast cancer. J Clin Oncol, 2019.

BLU-222 is a selective and potent CDK2 inhibitor

Kinome S(10)[a]
0.045

Enzyme activity IC_{50} (nM)[b]					
CDK2	CDK1	CDK4	CDK6	CDK7	CDK9
2.6	233.6	377.4	275.2	6941.2	6115.1

NanoBRET activity IC_{50} (nM)[c]					
CDK2	CDK1	CDK4	CDK6	CDK7	CDK9
17.7	452.3	5104.6	2621.7	6330.4	2697.7

Cellular activity IC_{50} (nM)[d]	
pRb T821 (CDK2 cell)	pLamin S22 (CDK1 cell)
4.2	380.2

BLU-222 EXHIBITS SINGLE-DIGIT NANOMOLAR POTENCY AND IS SELECTIVE FOR CDK2 OVER OTHER CDK FAMILY MEMBERS

Data presented at AACR 2022 Annual Meeting.
[a]Kinome S(10): fraction of kinases with <10 percentage of control at 3 uM among all the kinases tested, measured by KINOME scan platform against 468 kinases. [b]Enzyme activities IC_{50} were measured at 1 mM ATP using canonical CDK/Cyclin pairs: CDK2/Cyclin E1; CDK1/Cyclin B1; CDK4/Cyclin D1; CDK6/Cyclin D3; CDK7/Cyclin H1/MNAT1; CDK9/Cyclin T1. [c]HEK-293T cells were transfected with canonical CDK/cyclin pairs as in the enzyme assay and treated with compound and a tracer for 2 hours before measurements were taken. [d]pRb T821 protein was assessed in synchronized OVCAR-3 cells to reflect CDK2 cellular potency; pLamin S22 was assessed in asynchronous OVCAR-3 cells to reflect CDK1 cellular potency.
ATP, adenosine triphosphate; IC_{50}, half-maximal inhibitory concentration; pRB, phosphorylated retinoblastoma protein.

Phase 1/2 VELA trial of BLU-222 advancing toward clinical proof-of-concept

Vela

PHASE 1/2 TRIAL OF BLU-222
IN CDK2 VULNERABLE CANCERS

PHASE 1 DOSE ESCALATION
(NOW ENROLLING)

Multiple dose cohorts* → RP2D

**Includes monotherapy and combination regimens*

- Safety
- Preliminary clinical activity
- Patient selection strategy

PHASE 2 EXPANSION
(PLANNED)

- Combo with ER antagonist – ER+/HER2- breast
- Combo with CDK4/6i + ER antagonist – ER+/HER2- breast
- Monotherapy – CCNE1 tumors
- Combo with chemotherapy – CCNE1 tumors
- Monotherapy – multiple other CCNE1 tumors (basket cohort)

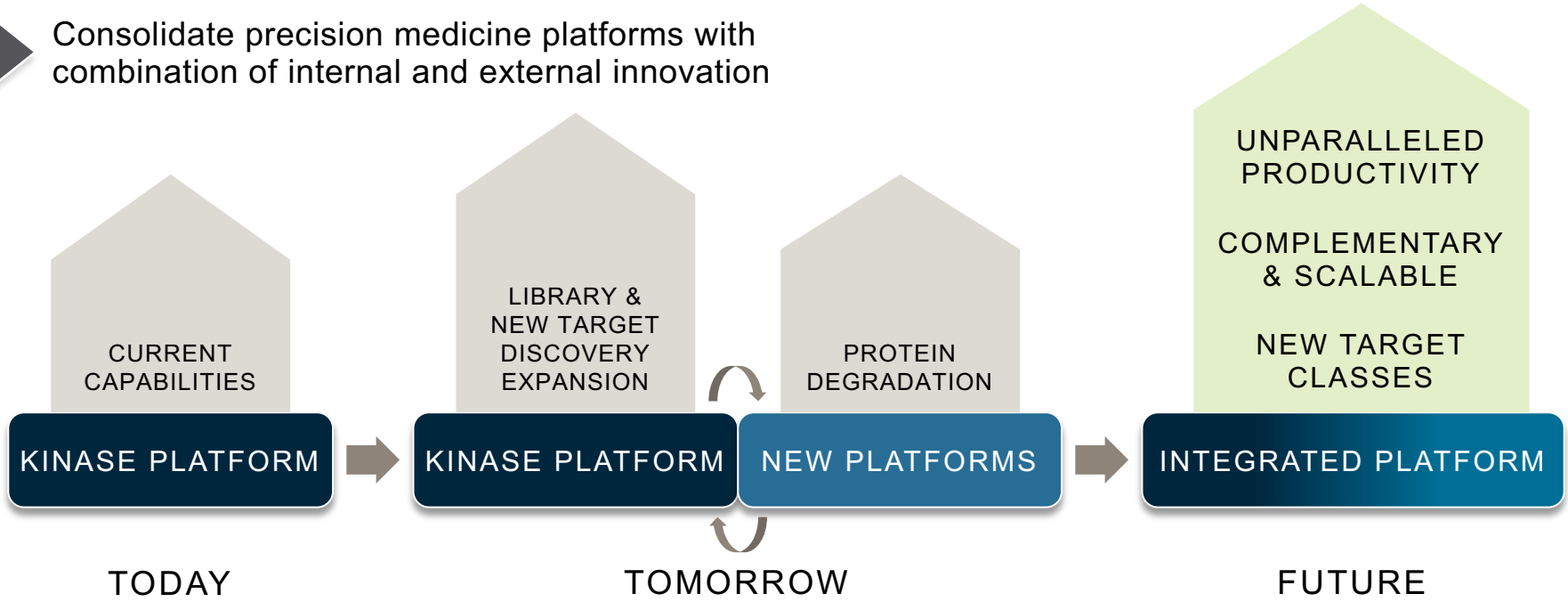
PHASE 1/2 VELA TRIAL OF BLU-222 INITIATED IN Q1 2022 AND FIRST PATIENT DOSED

blueprint™ MEDICINES

CCNE1, cyclin E; CDK4/6i, CDK4/6 inhibitor; ER, estrogen receptor.

Research platform expansion to drive innovation & expanded productivity

Consolidate precision medicine platforms with combination of internal and external innovation



EXPANSION AIMS TO DOUBLE THE HISTORIC OUTPUT OF OUR DISCOVERY ENGINE BY 2025

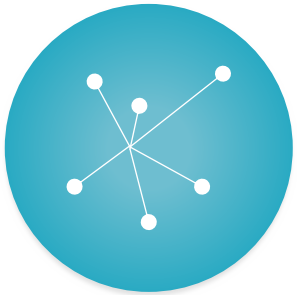
Significant progress across our portfolio will drive near-term news flow

Top-line PIONEER trial data in non-advanced SM with potential to significantly expand AYVAKIT label

MID-2022

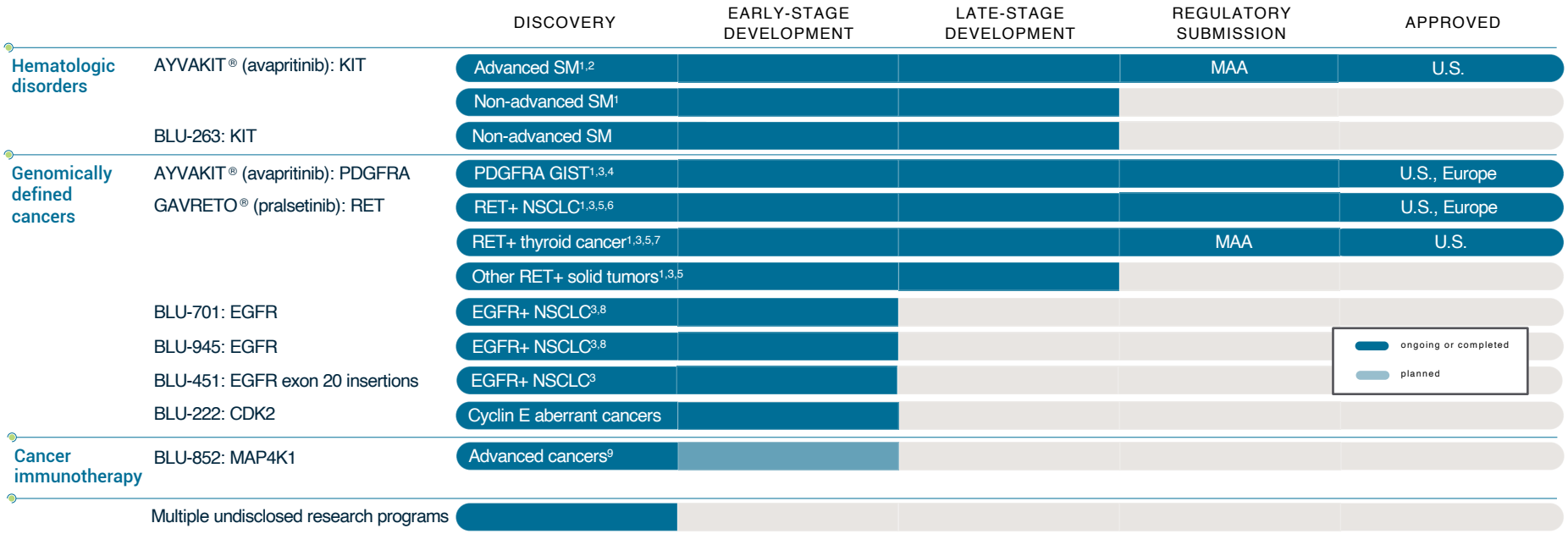
Multiple anticipated datasets for EGFR and CDK2 programs with potential to unlock broad patient opportunities

2H 2022 THRU 2023



Plan to unveil new research programs and vision for scientific platform expansion at R&D Day

2H 2022



1. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib, pralsetinib and fisogatinib in Mainland China, Hong Kong, Macau and Taiwan. 2. 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. Received a positive opinion from the European Medicines Agency's Committee for Medicinal Products for Human Use for the treatment of adult patients with aggressive SM, SM with an associated hematological neoplasm or mast cell leukemia, after at least one systemic therapy. 3. Unresectable or metastatic disease. 4. 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. 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. Received conditional marketing authorization in Europe for the treatment of adults with advanced RET fusion-positive NSCLC not previously treated with a RET inhibitor. 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. Zai Lab has exclusive rights to develop and commercialize BLU-701 and BLU-945 in Mainland China, Hong Kong, Macau and Taiwan. 9. 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; NSCLC, non-small cell lung cancer; SM, systemic mastocytosis.

Updated as of April 8, 2022.

Strong financial position bolstered by diversity of revenue & growing product revenue

Statement of Operations (unaudited)	Three Months Ended 12/31/2021	Three Months Ended 12/31/2020	FY Ended 12/31/2021	FY Ended 12/31/2020
Total revenue	$107.0M	$34.1M	$180.1M	$793.7M
Net product sales	$20.M	$6.7M	$57.7M	$22.1M
Collaboration revenue	$87.0M	$27.4M	$122.4M	$771.6M
Cost of sales	$7.5M	$0.1M	$17.9M	$0.4M
Collaboration loss sharing	$4.5M	--	$7.8M	--
Research & development expense[1,2]	$356.9M	$77.4M	$601.0M	$326.9M
Selling, general & admin expense[3]	$54.2M	$42.5M	$195.3M	$157.7M
Net income (loss)	$(318.7)M	$(85.7)M	$(644.1)M	$313.9M

Balance Sheet (unaudited)	12/31/2021	12/31/2020
Cash, cash equivalents and investments	$1,034.6M	$1,549.7M

ANTICIPATE $180 TO $200 MILLION IN TOTAL NET REVENUES IN 2022

1. Includes stock-based compensation expense of $10.0M and $8.5M in the three months ended 12/31/21 and 12/31/20, respectively, and $39.7M and $33.6M in the full year ended 12/31/21 and 12/31/20, respectively. 2. Includes a one-time charge of $260.0M to acquire in-process research and development compounds through the acquisition of Lengo Therapeutics. 3. Includes stock-based compensation expense of $12.7M and $11.0M in the three months ended 12/31/21 and 12/31/20, respectively, and $52.0 and $41.9M in the full year ended 12/31/21 and 12/31/20.

Our path to potential transformative growth and an independent financial profile

YEAR END 2021

- AYVAKIT/AYVAKYT and GAVRETO approved with ongoing global expansion
- A leading precision therapy research platform
- Strong financial position with ~$1B cash and cash equivalents

NEAR-TERM PLANS

- Constellation of clinical
  across strategic therape
- AYVAKIT launch in non
  systemic mastocytosis
- Continued product reve
  collaboration milestones

FUTURE GOALS • 2024-2025+

- Broad portfolio of marketed medicines in precision oncology and hematology
- Diversified research platform with unparalleled productivity
- Independent financial profile