precision at scale™

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Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, strategies, timelines and expectations for interactions with the U.S. Food and Drug Administration (FDA) and other regulatory authorities; statements regarding the benefits and expectations of AYVAKIT in treating patients with non-advanced systemic mastocytosis (SM); statements regarding the plans and potential benefits of AYVAKIT in treating patients with indolent SM; plans and timing for presenting detailed data from the SYMPHONY trial of BLU-945 in patients with advanced EGFR-mutant non-small cell lung cancer; statements regarding plans and expectations for the company's current or future approved drugs and drug candidates; 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.

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OUR MISSION

Make real the promise of precision therapy to extend and improve life for as many people as possible

Suki
patient with indolent systemic mastocytosis

Blueprint's strategy to achieve Precision at Scale by 2027

APPROACH

- Start with genetic drivers of disease
- Design highly potent and selective medicines
- Select the right patients
- Drive transformative outcomes with high POS

FOCUS

Mast cell disorders

Lung cancer

Breast cancer

ASPIRATION

blueprint™ 2027

POS, probability of success.

Blueprint has a compelling value proposition

1

FOUNDATION OF SUCCESS

Differentiated scientific platform, development and business execution

2

COMMERCIAL PORTFOLIO

Doubling product revenue in 2022

3

NEAR-TERM REVENUE GROWTH

Anticipated expansion into indolent SM, a ~15x larger patient opportunity

4

ROBUST CLINICAL PIPELINE

Diverse set of programs targeting compelling peak revenue opportunities

SM, systemic mastocytosis.

Blueprint's proven track record of R&D success

development candidates nominated

success rate from IND to clinical POC

breakthrough therapy designations

years from IND to first approval

approved medicines

FDA approved indications

FDA, Food and Drug Administration. IND, investigational new drug application. POC, proof-of-concept.

Our scientific platform is a competitive advantage

SELECTIVE
SMALL MOLECULE
PRECISION THERAPIES

DURABILITY

Potent target inhibition leading to rapid and deep responses

TOLERABILITY

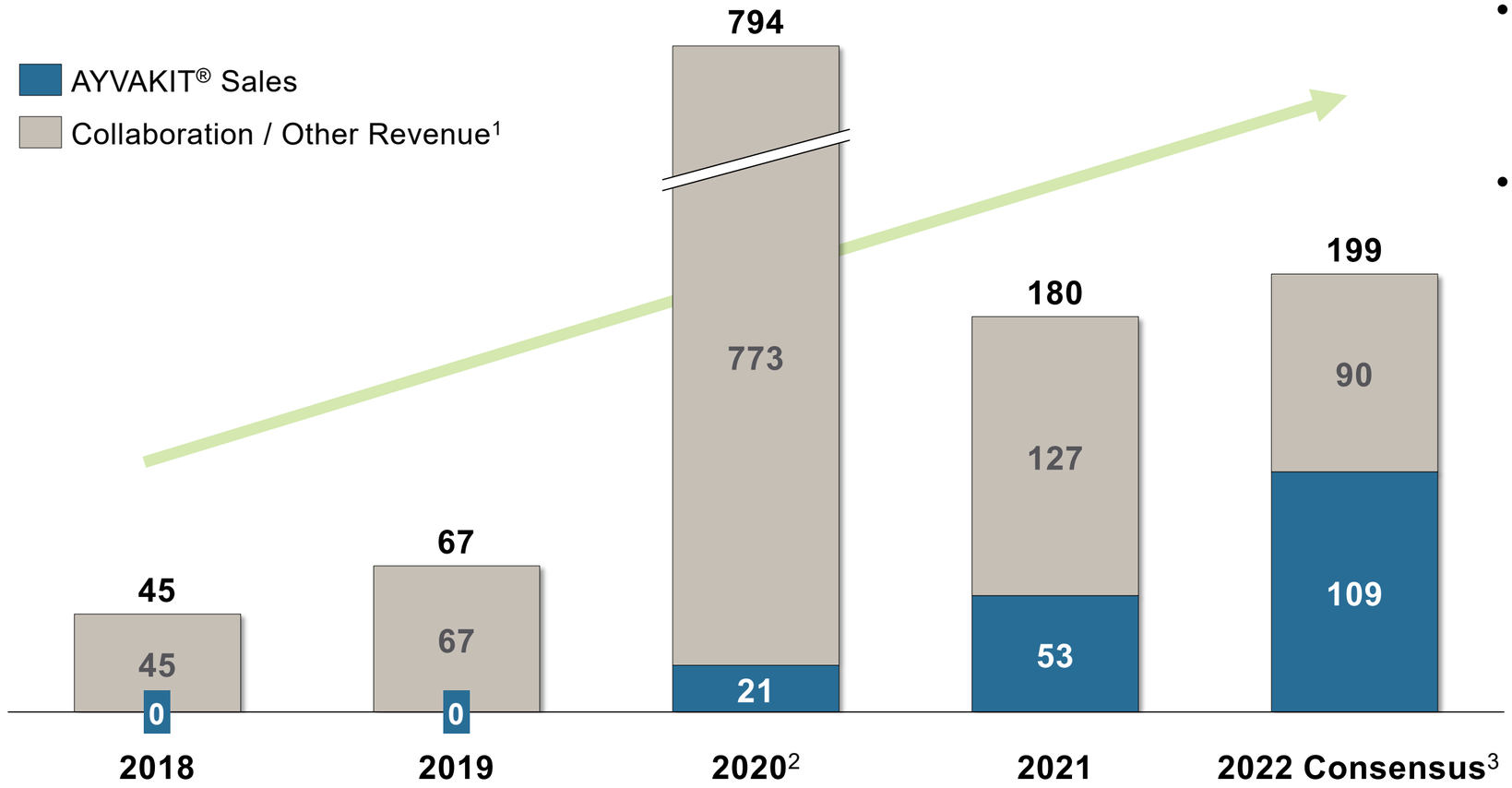
Limit side effects driven by off-target activity

COMBINABILITY

Combine therapies to shut down disease drivers and resistance

Consistent business execution resulting in balance sheet strength and diversity of revenue

BLUEPRINT MEDICINES NET REVENUE ($M)



- Entering 2023 with >$1B in cash
- On track to achieve high-end of 2022 total revenue guidance of $180M-$200M and AYVAKIT revenue guidance of $108M-$111M
- Strong product revenue growth anticipated over the next few years

Sources of Collaboration / Other Revenue

Roche Genentech · IPSEN Innovation for patient care · Roche · IDRx · zai Lab · 基石药业 CSTONE PHARMACEUTICALS

1 Includes Gavreto sales booked as revenue in 2020 and 2021. 2 Includes Roche collaboration payments. 3 2022 Ayvakit sales represents full year 2022 FactSet consensus as of 1/4/2023. 2022 Collaboration / Other Revenue represents 2022 FactSet consensus total revenue as of 1/4/2023 less 2022 Ayvakit sales.

Strong track record of business development enabling corporate strategy

>$1.1B of capital brought in to-date inclusive of upfront, milestones and royalties

FOP, fibrodysplasia ossificans progressiva. GIST, gastrointestinal stromal tumor. I/O, immunotherapy; WW, worldwide.

Strong foundation of enterprise capabilities and infrastructure

KNOWLEDGE & LEADERSHIP

Precision medicine and therapeutic area leadership

EXPERIENCED TEAM

Track record of bringing innovation from discovery to commercial

GLOBAL INFRASTRUCTURE

Established U.S. and EU operations, with global partner network

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Commercial portfolio of transformative medicines

AYVAKIT®
avapritinib | tablets

GAVRETO®
pralsetinib | 100 mg capsules

AYVAKIT is the first precision therapy to target the underlying cause of SM

AYVAKIT® avapritinib | tablets

~540 PATIENT YEARS OF SM CLINICAL DATA DEMONSTRATING

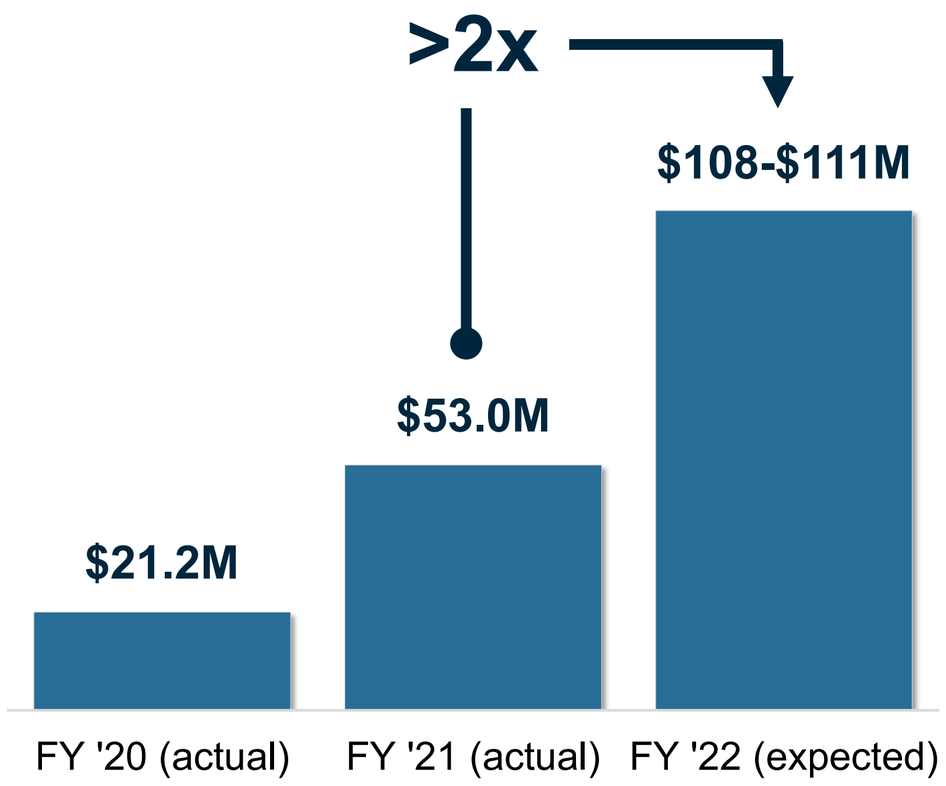
- Reduced mast cell burden
- Improved disease symptoms
- Improved quality of life
- Deep and durable clinical responses
- Positive benefit-risk profile
- One pill, once daily dosing

Currently FDA and EMA approved for advanced SM • sNDA submitted to FDA for indolent SM in Q4 2022

EMA, European Medicines Agency. sDNA, supplemental new drug application.

AYVAKIT is the standard of care for advanced SM in the U.S.

AYVAKIT NET REVENUE GROWTH



AVYAKIT is the preferred treatment for advanced SM

- ~75% of new patient starts / switches

Total number of patients on therapy continues to grow

- Anticipate continued growth with expansion of SM-AHN* treatment rate

Increasing healthcare provider experience

- >350 new U.S. accounts since launch

Favorable patient access achieved

- 100% coverage with rapid average time to fill of 4.9 days

* SM-AHN, SM with an associated hematologic neoplasm.

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Diverse set of programs targeting compelling peak revenue opportunities

Indolent SM opportunity is orders of magnitude larger than advanced SM

Among ~16,000 SM patients diagnosed and observable in U.S. claims data[1]

Treated patients with advanced SM

Treated patients with moderate to severe indolent SM

Estimated >$1.5B global peak revenue opportunity in SM[2]

1 U.S. claims data analyses on file. 2 Blueprint Medicines estimate.

Success of HAE disease modifying therapies highlight SM opportunity potential

HEREDITARY ANGIOEDEMA

- Rare disorder characterized by anaphylaxis, attacks of swelling
- Treated by allergist immunologists
- New specialty market established with the approval of disease modifying therapies
- Market is continuing to grow today, with >35% 3-year growth rate (2019-2021)

~7,500

patients diagnosed and treated in U.S.[1]

~$1.5B

sales of prophylactic therapies in 2021[2]

1 Based on Biocryst Pharmaceutical report on U.S. claims data analyses. 2 Based on company sales reports. HAE, hereditary angioedema.

Blueprint is positioned for success in indolent SM, a tractable specialty market

HIGH MEDICAL NEED

Debilitating symptoms, poor quality of life and high polypharmacy burden, with no available disease modifying therapy

MOTIVATED & IDENTIFIABLE PATIENTS

7,500 patients with moderate to severe ISM diagnosed, treated with polypharmacy and observable in U.S. claims data

PRESCRIBER CONCENTRATION

Top 350 allergist immunologists and hematologist oncologists actively manage ~1,500 patients

ESTABLISHED COMMERCIAL PRESENCE IN ADVANCED SM

Fully integrated team in the field today engaging with healthcare providers, payers and the patient community

Plan to initiate U.S. launch of AYVAKIT in indolent SM in the middle of 2023

ISM, indolent SM.

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Pipeline targeting prevalent diseases with high medical need

MAST CELL DISORDERS

AYVAKIT: KIT D816V

Elenestinib: KIT D816V[1]

Research: wild-type KIT

LUNG CANCER

GAVRETO: RET

BLU-945: EGFR

BLU-525: EGFR

BLU-451: EGFR exon 20

BREAST CANCER

BLU-222: CDK2

Multiple additional undisclosed research programs in areas of medical need

1 Elenestinib was formerly known as BLU-263.

Comprehensive and modular EGFR portfolio strategy

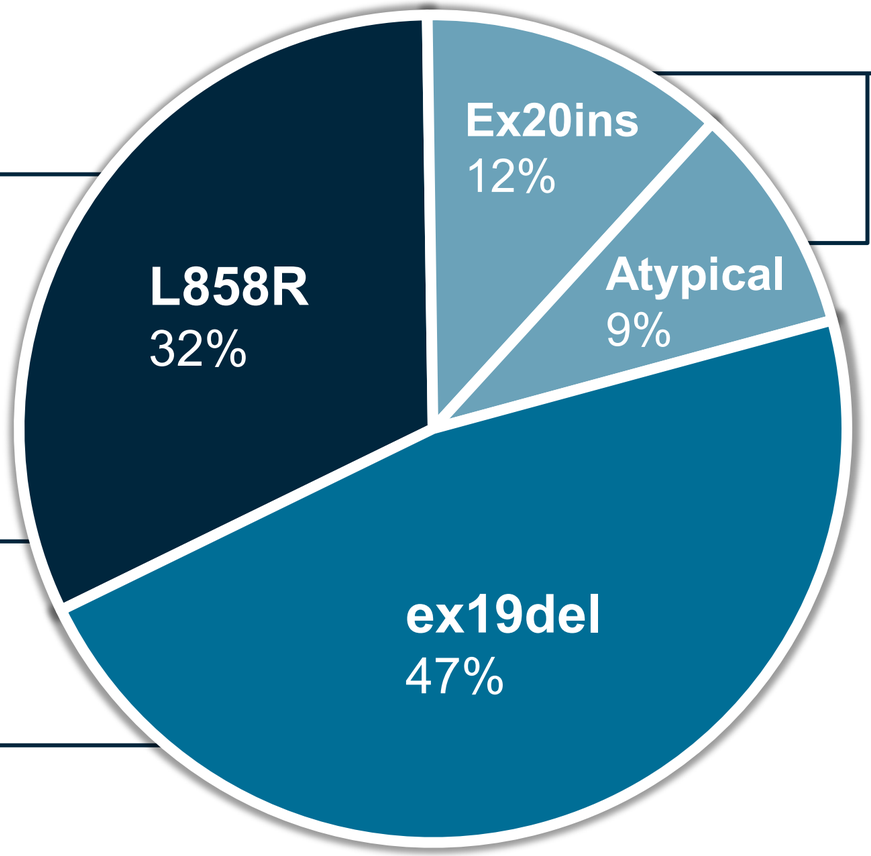
FULL SPECTRUM COVERAGE[1] OF EGFR DRIVERS[2]

BLU-945

- More potent on L858R than ex19del
- Covers T790M and C797X resistance
- Selectivity profile: best-in-class potential

BLU-525

- Potent coverage of L858R and ex19del
- Covers C797X resistance
- CNS penetration: best-in-class potential



BLU-451

- Potent coverage of all common ex20ins, plus atypical mutations (e.g., G719X, L861Q, etc.)
- CNS penetration: best-in-class potential

1 Target coverage based on preclinical data. 2 Riess, et al. J Thorac Oncol, 2018. CNS, central nervous system. Ex19del, exon 19 deletion. Ex20ins, exon 20 insertions.

Randomized SYMPHONY trial expansion designed to de-risk combination development in 1L EGFR L858R mutant NSCLC

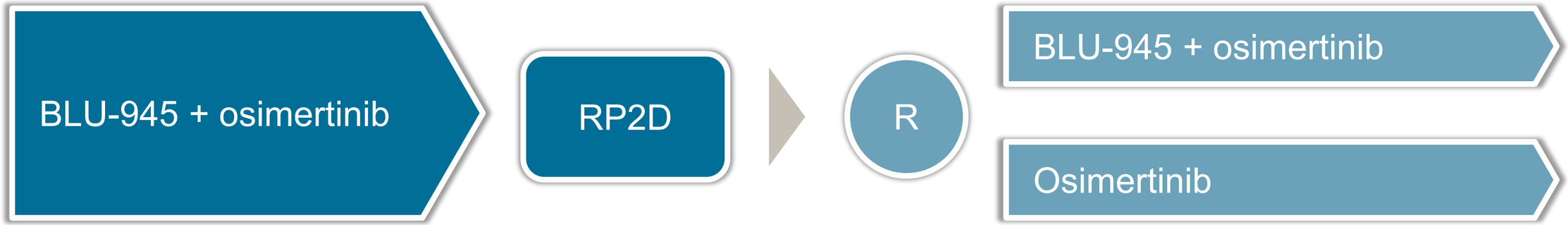
Symphony

ONGOING DOSE ESCALATION

- Late-line EGFR mutant NSCLC

PLANNED EXPANSION

- 1L EGFR L858R mutant NSCLC



1L, first-line. ctDNA, circulating tumor DNA. NSCLC, non-small cell lung cancer. R, randomized. RP2D, recommended Phase 2 dose.

Our goal is to establish BLU-222 as the essential component of treatment paradigms for cancers vulnerable to CDK2 inhibition

TARGET PRIMARY DRIVERS

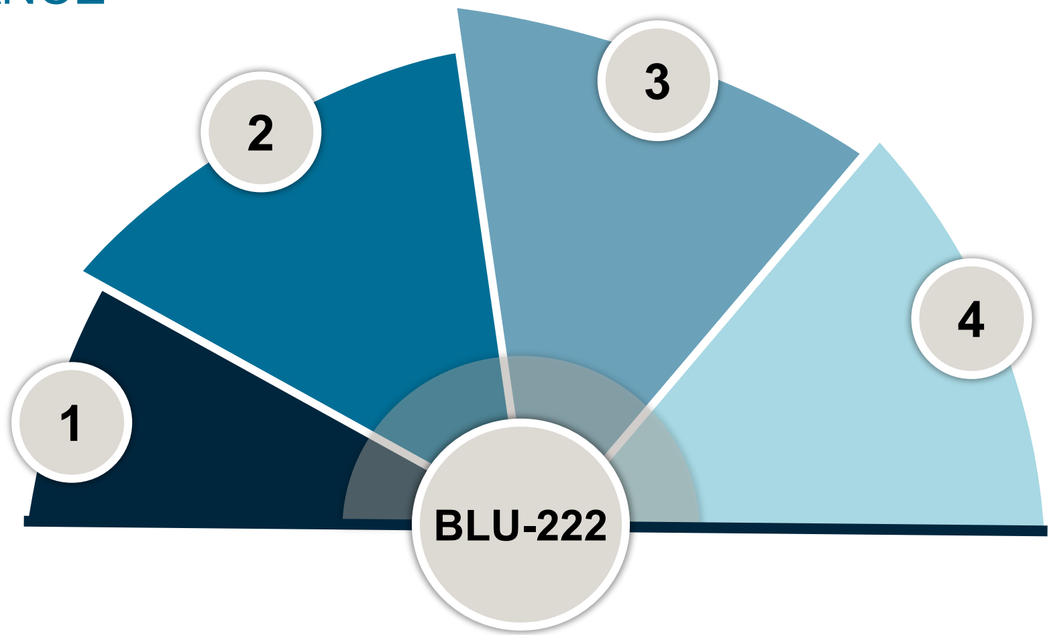
2L+ CCNE1-driven tumors

TARGET RESISTANCE MECHANISMS

2L+ CDK4/6i resistant
HR+ / HER2- mBC

TRANSFORM TREATMENT PARADIGMS

1L combinations in lead indications



EXPAND INTO OTHER POPULATIONS

CDK2 inhibition across broader tumor types

VELA trial dose escalation data, including RP2D, translational and initial combination safety, anticipated in 1H 2023

2L, second-line. CCNE1, cyclin E. CDK4/6i, CDK4/6 inhibitor. HER2-, HER2-negative. HR+, hormone-receptor-positive. mBC, metastatic breast cancer.

Blueprint is uniquely positioned with a diversity of significant growth drivers

SYSTEMIC MASTOCYTOSIS

>$1.5B

estimated global peak revenue opportunity[1]

LUNG CANCER

~$5B

osimertinib global sales in 2021[2]

BREAST CANCER

~$8B

CDK4/6 inhibitor global sales in 2021[2]

1 Blueprint Medicines estimate. 2 Based on company reports.

Key anticipated portfolio milestones in 2023

Area	Program	Milestone	Timing
Mast cell disorders	AYVAKIT	Present registrational PIONEER trial data in indolent SM at AAAAI Annual Meeting	Feb 2023
	AYVAKYT	Achieve EMA validation of a type II variation MAA for indolent SM	1H 2023
	AYVAKIT	Achieve FDA approval and initiate U.S. launch in indolent SM	Mid 2023
	Research	Nominate a development candidate targeting wild-type KIT for chronic urticaria	Mid 2023
	Elenestinib	Present Part 1 HARBOR trial data in indolent SM	2H 2023
EGFRm NSCLC	BLU-525	Submit IND to FDA	1H 2023
	BLU-451	Present initial CONCERTO trial dose escalation data in EGFR exon 20 NSCLC	1H 2023
	BLU-945	Provide initial update on SYMPHONY trial expansion in 1L L858R	2H 2023
CDK2 vulnerable cancers	BLU-222	Present initial VELA trial dose escalation data	1H 2023

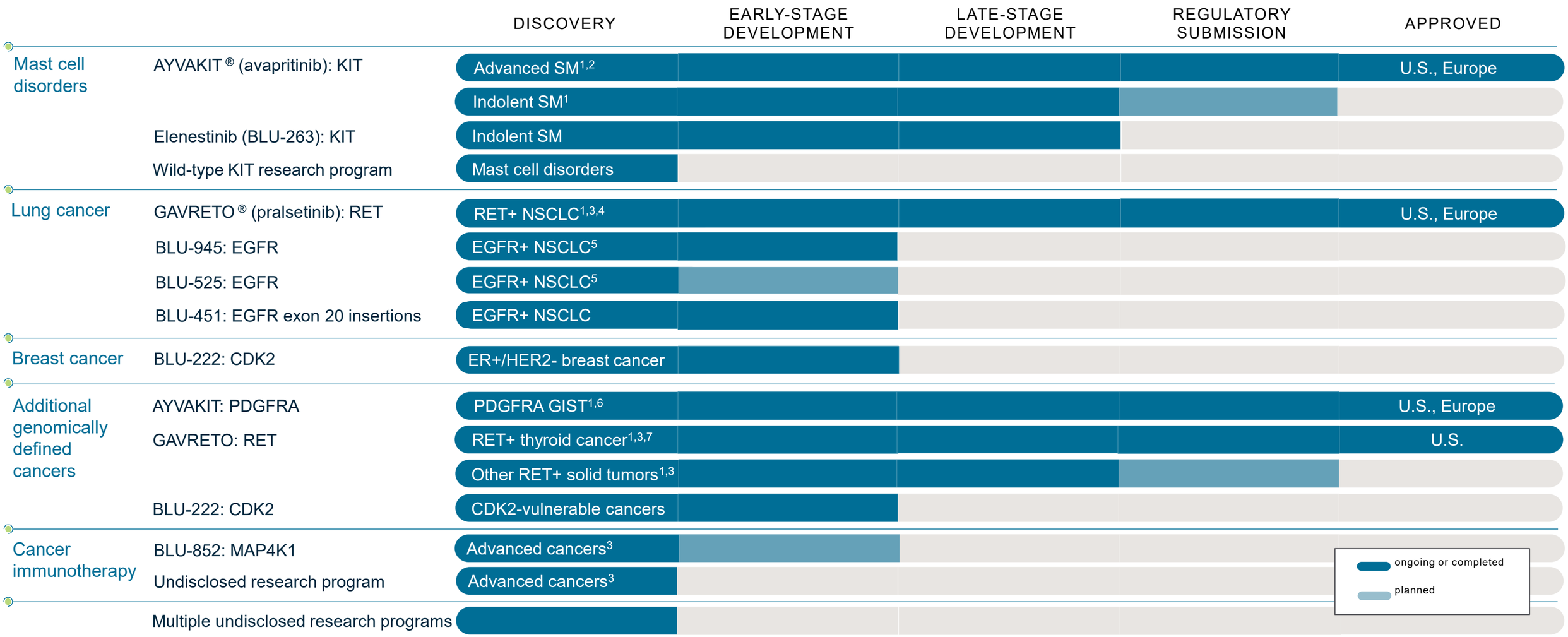
AAAAI, American Academy of Allergy, Asthma & Immunology. EGFRm, EGFR mutant. MAA, marketing authorization application.

Blueprint 2027: Doubling our impact, in half the time

blueprint™ 2027

	2011-2022	Planned 2022-2027
Approved medicines	2	4+
Disease leadership areas	1	3+
Late-stage clinical programs	2	4+
Research platforms	1	2
Cumulative development candidates	14	25+

precision at scale™



1. CStone Pharmaceuticals has exclusive rights to develop and commercialize avapritinib and pralsetinib in Greater China. 2. Approved in the U.S. for adults with advanced SM, including aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL). Approved in Europe (AYVAKYT®) for adults with ASM, SM-AHN or MCL, after at least one systemic therapy. 3. In collaboration with Roche. 4. Received U.S. accelerated approval for adults with metastatic RET fusion-positive NSCLC. Received conditional marketing authorization in Europe for adults with advanced RET fusion-positive NSCLC not previously treated with a RET inhibitor. 5. Zai Lab has exclusive rights to develop and commercialize BLU-945 and BLU-525 in Greater China. 6. Approved in the U.S. for adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. Approved in Europe (AYVAKYT®) for adults with unresectable or metastatic GIST harboring the PDGFRA D842V mutation. 7. Received U.S. accelerated approval for advanced or metastatic RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer.

Updated as of January 9, 2023.