UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): **April 8, 2022**

Blueprint Medicines Corporation
(Exact name of registrant as specified in its charter)

Delaware	**001-37359**	**26-3632015**
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

45 Sidney Street **Cambridge, Massachusetts** (Address of principal executive offices)	**02139** (Zip Code)

Registrant's telephone number, including area code: **(617) 374-7580**

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	BPMC	Nasdaq Global Select Market

Item 7.01 Regulation FD.

On April 8, 2022, Blueprint Medicines Corporation (the "Company") is hosting an investor conference call and webcast to review data presented at the American Association for Cancer Research ("AACR") Annual Meeting 2022 for multiple research- and clinical-stage programs across its precision oncology and hematology portfolio. A copy of the presentation from the investor conference call and webcast is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On April 8, 2022, the Company issued a press release announcing data for multiple research- and clinical-stage programs across its precision oncology and hematology portfolio from various poster presentations at the AACR Annual Meeting 2022. A copy of the press release is filed herewith as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate slide presentation of Blueprint Medicines Corporation dated April 8, 2022
99.2	Press release issued by Blueprint Medicines Corporation on April 8, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 101)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

BLUEPRINT MEDICINES CORPORATION

Date: April 8, 2022

By: /s/ Kathryn Haviland
Kathryn Haviland
Chief Executive Officer


blueprint™
MEDICINES
Precision
that Moves
blueprint™
MEDICINES
Diane L.
Patient

Blueprint Medicines call participants

PREPARED REMARKS

Introduction and portfolio overview	**Kate Haviland** Chief Executive Officer
Initial data from the SYMPHONY trial of BLU-945 presented at the AACR Annual Meeting 2022	**David Spigel, M.D.** Chief Scientific Officer Sarah Cannon Research Institute
Portfolio strategy and next steps	**Fouad Namouni, M.D.** President, Research and Develop
Q&A	**All**

AACR, American Association of Cancer Research

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," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-loo not all forward-looking statements contain these identifying words. In this presentation, forward-looking statements include, without limitation, express or implied st strategies, timelines and expectations for the current or future approved drugs and drug candidates of Blueprint Medicines Corporation (the "Company"), including timelines trials and trial cohorts, the results of ongoing and planned clinical trials, data publications, marketing applications and approvals; the anticipated benefits of the preclinical drug candidates; the Company's plans, strategies and timelines for the development of the Company's drug candidates as monotherapies and combination with other age for the Company's drug candidates; plans and timelines for additional marketing applications for avapritinib and pralsetinib and, if approved, commercialization of av 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 platform expansion plans and plans to announce new research programs; and the Company's financial performance, strategy, goals and anticipated milestones, business pl

The Company has based these forward-looking statements on management's current expectations, assumptions, estimates and projections. If such expectations, as 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 be assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks, uncertainties and oth 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- risks and uncertainties include, without limitation, risks and uncertainties related to the impact of the COVID-19 pandemic to the Company's business, operations, strat milestones, including the Company's ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current 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 infrastructure, and successfully launching, marketing and selling current or future approved products; the Company's ability to successfully expand the approved /AYVAKYT® (avapritinib) and GAVRETO® (pralsetinib) or obtain marketing approval for AYVAKIT/AYVAKYT in additional geographies in the future; the delay of any curre 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 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 studie candidates, which may not support further development of such drug candidates either as monotherapies or in combination with other agents or may impact the ant regulatory submissions; actions or decisions of regulatory agencies or authorities, which may affect the initiation, timing and progress of clinical trials or marketing applicati to obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT, GAVRETO or any drug candidates it is developing; the Compa 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 it 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 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 a ("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 the future. The Company cannot guarantee future results, outcomes, levels of activity, performance, developments, or achievements, and there can be no assurance that it 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, 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 other 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 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, pro 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 uncer

Blueprint Medicines is poised for growth in 2022 and beyond

KEY GOALS

Transform the lives of patients with systemic masto
improving treatment options across the spectrum di

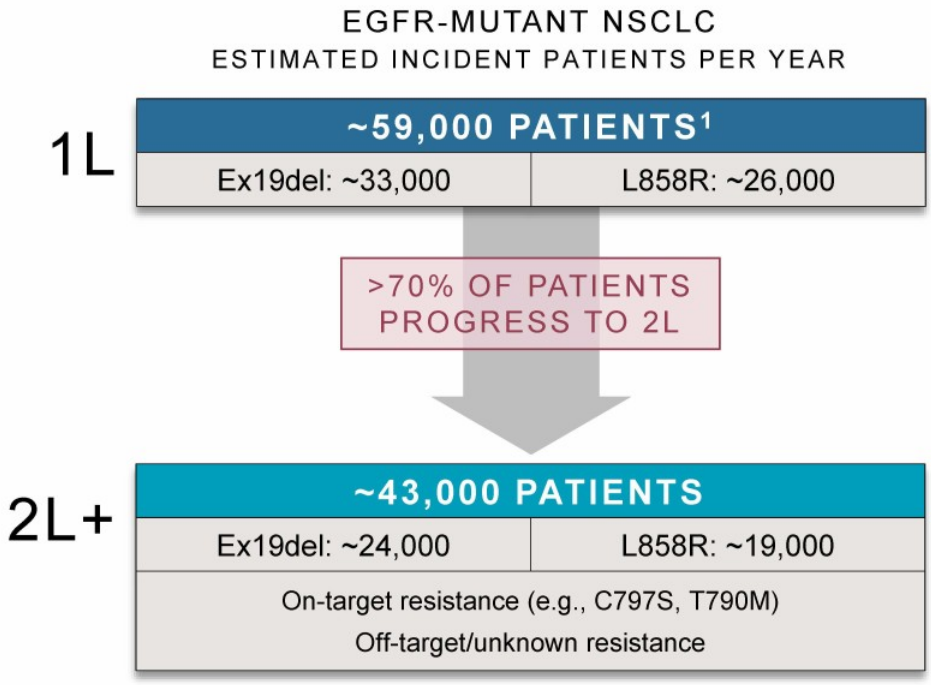
Advance our clinical-stage pipeline targeting difficul
and prevalent cancer drivers

Harness our research engine to bring forward new
oncology and hematology programs

STRONG FINANCIAL POSITION WITH ~$1B CASH AT YEAR-END 202

* Cash, cash equivalents and investments as of December 31, 2021.

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

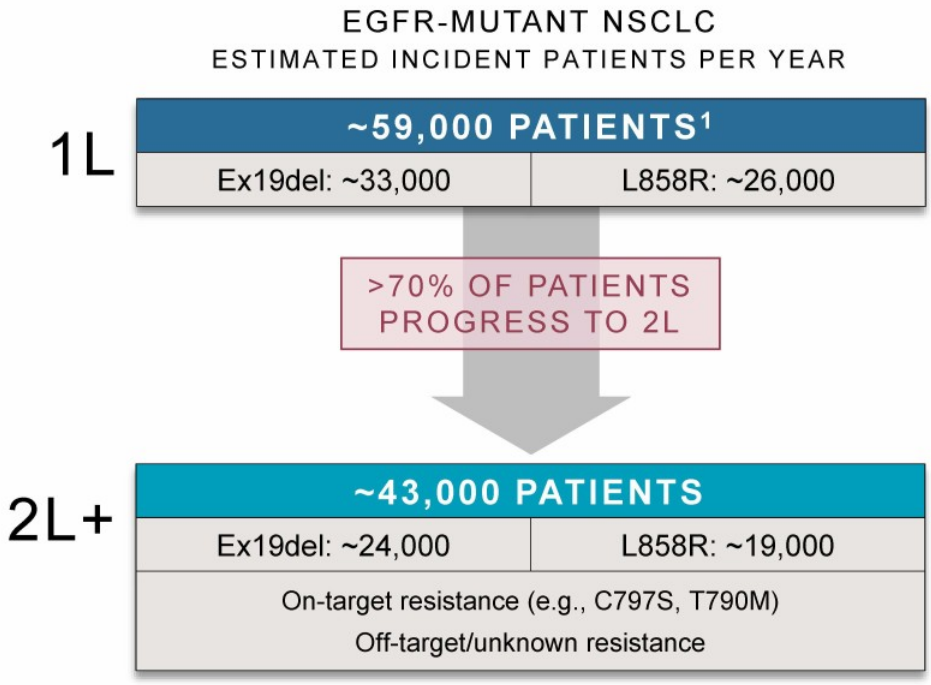


CHALLE

- Lower OS and PFS in with L858R activating
- On- and off-target re increasingly
- CNS is a commo disease pro

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

Opportunities for our next-generation EGFR precision therapie



OPPORTU

Enhance activity o activating

Prevent or treat c re

Treat off-target resista well-tolerated

Prevent or treat brain m enhanced CNS per

Approximate patient numbers covering major markets – US, EU4, UK, and Japan. 1. Excludes rare mutations including exon 20 insertio 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 medica

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
  - Potential for broader coverage at higher
- 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

blueprint MEDICINES

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

Emerging evidence of activity of BLU-945 in patients with advanced EGFR-mutant NSCLC utilizing circulating tumor DNA in the Phase 1/2 SYMPHONY study

Elaine Shum, Yasir Elamin, Karen L Reckamp, Zofia Piotrowska, Julie Rotow, Daniel SW Tan, Koichi Goto, Jagan Parepally, Faris Albayya, Melinda Louie-Gao, Renata Sawtell, Alena Zalutskaya, **David Spigel**

American Association for Cancer Research
Annual Meeting 2022
April 8, 2022

Disclosures

Dr. David Spigel, MD, Chief Scientific Officer, Sarah Cannon Research Institute

- Research funding: Aeglea Biotherapeutics, Agios, Apollomics, Arcus, Arrys Therapeutics, Astellas Bayer, BeiGene, BIND Therapeutics, BioNTech RNA Pharmaceuticals, Blueprint Medicines, Boeh Ingelheim, Bristol-Myers Squibb, Calithera, Celgene, Celldex, Clovis, Cyteir Therapeutics, Daiichi Denovo Biopharma, Eisai, Elevation Oncology, EMD Serono, Evelo Biosciences, GI Therapeutics Roche/Genentech, GlaxoSmithKline, GRAIL, Hutchison MediPharma, ImClone Systems, Incyte, Ipsen, Janssen, Kronos Bio, Eli Lilly, Loxo Oncology, MacroGenics, MedImmune, Merck, Molecul Molecular Template, Nektar, Neon Therapeutics, Novartis, Novocure, Oncologie, Pfizer, PTC The PureTech Health, Razor Genomics, Repare Therapeutics, Rgenix, Takeda, Tesaro, Tizona Thera Transgene, UT Southwestern, Verstem

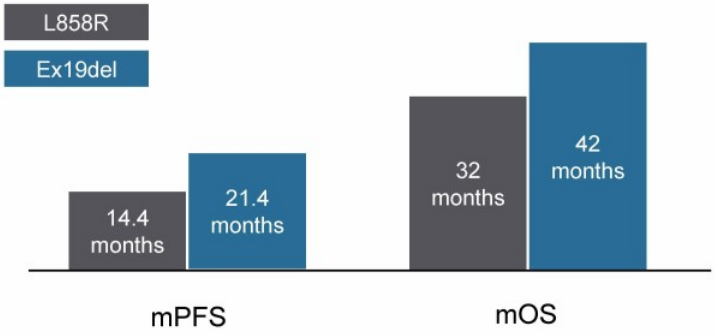
- Consulting/advisory: Amgen, AstraZeneca, Bristol-Myers Squibb, Curio Science, EMD Serono, Ev GlaxoSmithKline, Intellisphere, Ipsen, Janssen, Jazz, Lilly, Mirati Therapeutics, Molecular Templa Novocure, Pfizer, Puma Biotechnology, Regeneron Pharmaceuticals, Roche/Genentech, Sanofi-A

*All payments made to Sarah Cannon Research Institute

Combinations are needed to prevent and treat mutational heterogene and prolong patient benefit in EGFR mutant NSCLC

Osimertinib prolongs PFS and OS…

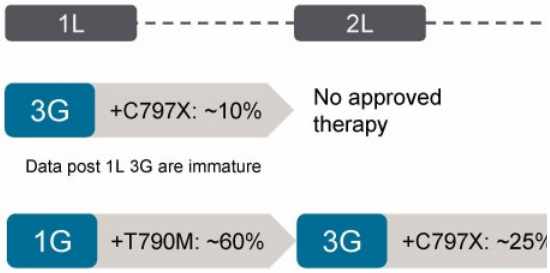
FLAURA study in 1L EGFRm NSCLC
osimertinib median PFS and OS[1]



…but patients with L858R have worse outcomes versus exon 19 deletion

In addition, resistance inevitably em

Estimated frequency of EGFR resist



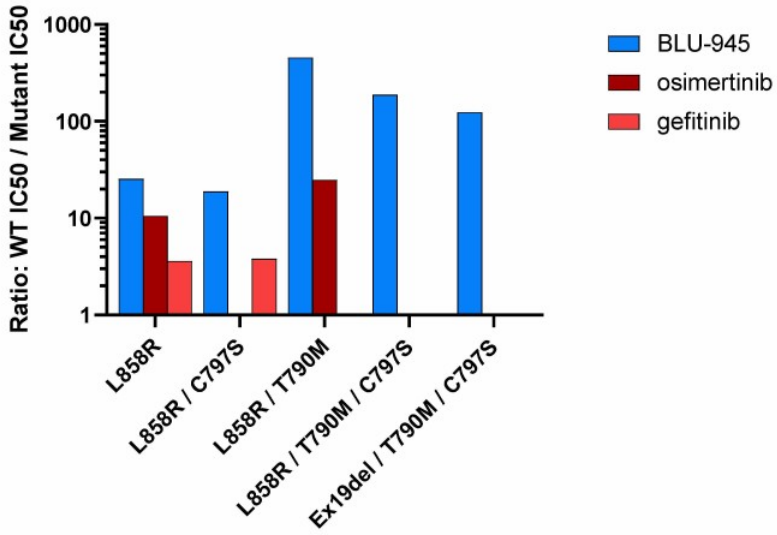
Off-target resistance may occur indepe
or co-occur with EGFR resistanc

…with C797X and T790M the most EGFR resistance mutations[2]

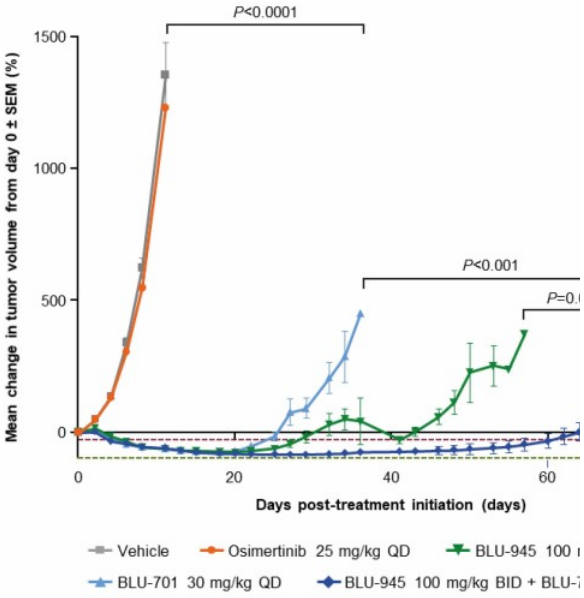
1. Supplemental data in Soria et al NEJM 2018. Ramalingam et al NEJM 2020. 2. Leonetti, et al. British Journal of Cancer, 2019. 1L, first-line; 2L, second-line; 3L, third-line; 1G, first-gener second-generation; 3G, third-generation; mPFS, median progression free survival; mOS, median overall survival.

BLU-945 potency and selectivity enable wide therapeutic index ar broad EGFR coverage, including activating L858R mutation

BLU-945's therapeutic index enables potent inhibition of EGFR mutants compared to SOC therapies[1]

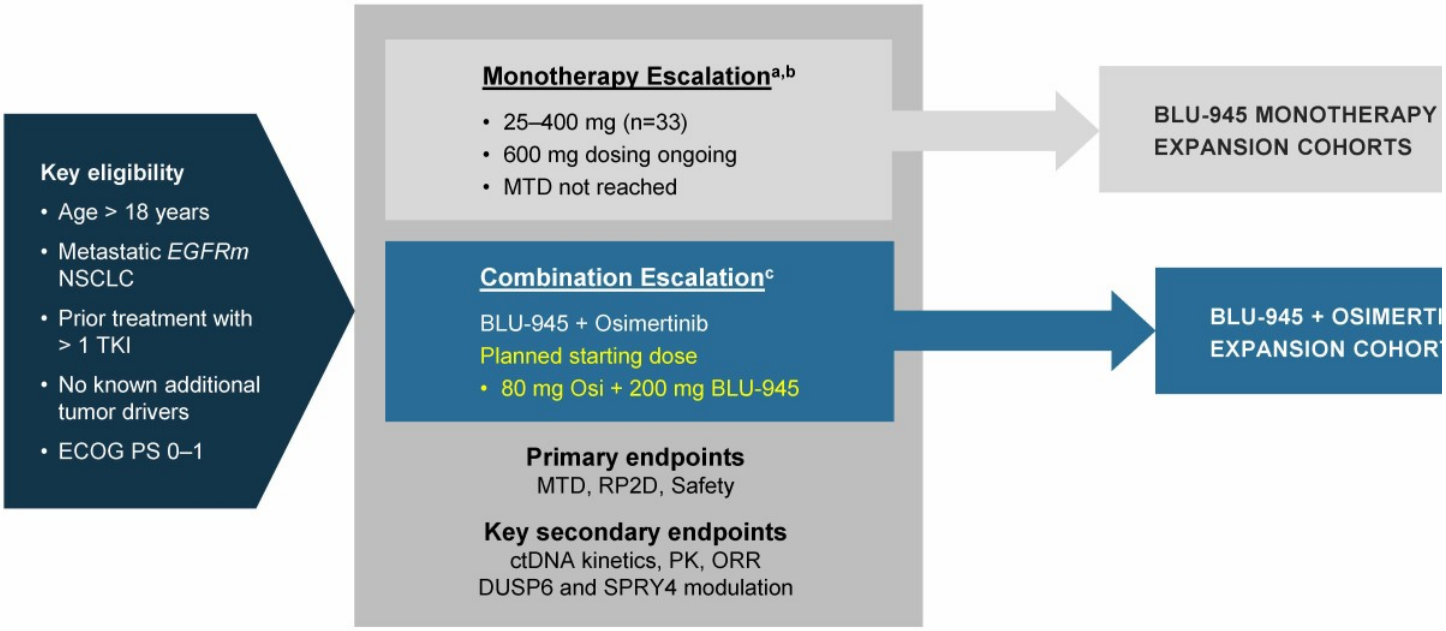


BLU-945 is active alone in combination in an osimertinib-resistant L858R/C797



1. Company data on file. IC_{50} measured by pEGFR in cells. 2. Data presented at AACR annual meeting 2022. Abstract #3328.

SYMPHONY first-in-human clinical trial of BLU-945



[a]Based on Bayesian Optimal Interval escalation design (BOIN); [b]BID dosing will also be evaluated; [c]Part 1B and Phase 2 have not been initiated and are dependent on Part 1A results. ctD tumor DNA; DUSP6, dual specificity phosphatase 6; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFRm, mutant epidermal growth factor receptor gene; PK, pha MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; ORR, overall response rate; Osi; osimertinib; RP2D, recommended phase 2 dose; SPRY4, sprouty RTK signaling anta tyrosine kinase inhibitor.

Demography and baseline characteristics

Characteristic		All patients (N=33)
Median age (range), years		61 (39–78)
Female, n (%)		23 (70)
Race, n (%)	White	14 (42)
	Asian	18 (55)
	Other/unknown	1 (3)
Smoking history, n (%)	Current/former	10 (30)
	Never	22 (67)
	Unknown	1 (3)
ECOG PS, n (%)[a]	0	8 (24)
	1	23 (70)
	2	2 (6)
History of CNS disease, n (%)		21 (64)
Prior therapy, median (range)		4 (1–9)
	Prior osimertinib	32 (97)
	1-2	7 (21)
	≥3	26 (79)

Characteristic	
EGFR mutation status at C1D1 by central ctDNA NGS assessment[b], n (%)	
	EGFRm/T790M/C797S
	EGFRm/T790M
	EGFRm/C797S
	EGFRm primary only
	T790M only
	No EGFR mutations detecte
	Not available[c]

- As of the data cut-off, ~33 patients treated with BLU-945 25–400 mg once daily (QD) and dose escalation is ongo
- Most patients were non-smokers and the majority (n=26 ≥3 lines of prior systemic therapy

[a]Original study protocol permitted ECOG PS of 0–2, but was later amended to ECOG PS of 0–1; [b]Patients with EGFR-mutant NSCLC are enrolled based on local mutation assessment of t ctDNA with central ctDNA assessment at C1D1; [c]Results for all patients were not available at the time of the data cut. C, cycle; ctDNA NGS, circulating tumor DNA next generation sequen PS, Eastern Cooperative Oncology Group performance status; EGFRm, primary EGFR activating mutation, exon 19 deletion or L858R. As of the data cut-off (March 9, 2022), 33 patients h 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 tria

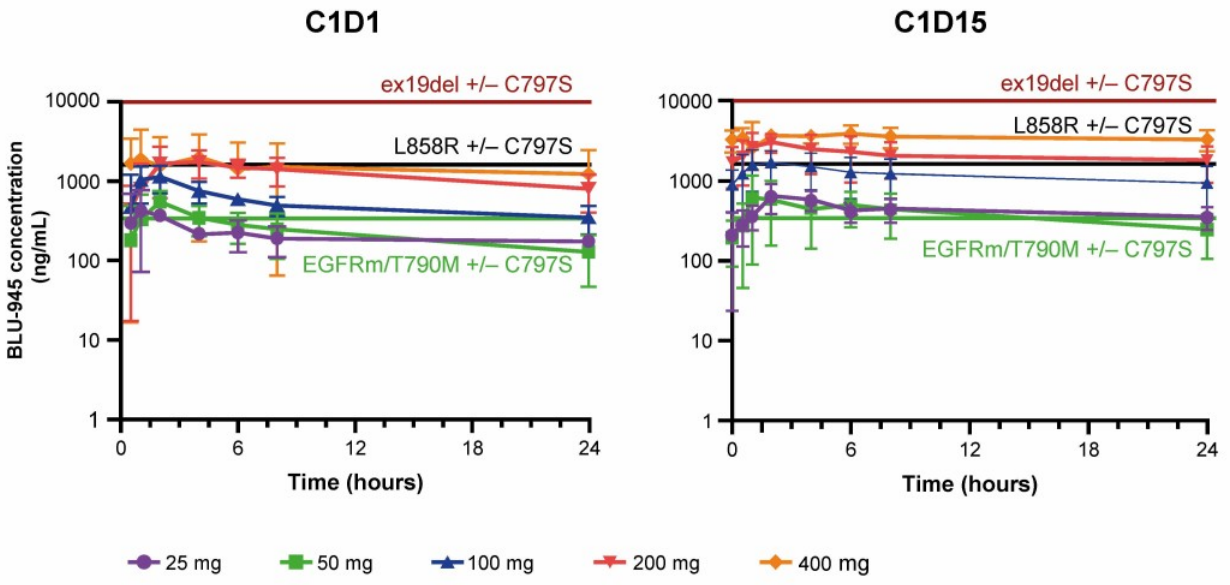
Most common AEs by preferred term in ≥10% of patients

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 r
  - Improved with dose interruption; pati
- AEs associated with EGFR wild-type inh
- No interstitial lung disease or QTc prolo
- 8 (24%) serious AEs, with 2 (6%) deeme
  - Grade 3 vomiting
  - Grade 3 transaminitis
- No treatment discontinuations due to AE
- Dose escalation continues and the MTD determined

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 m (QD) in the first 5 cohorts.

BLU-945 exposure showed increasing IC_{90} coverage of activating an resistance mutations at higher doses

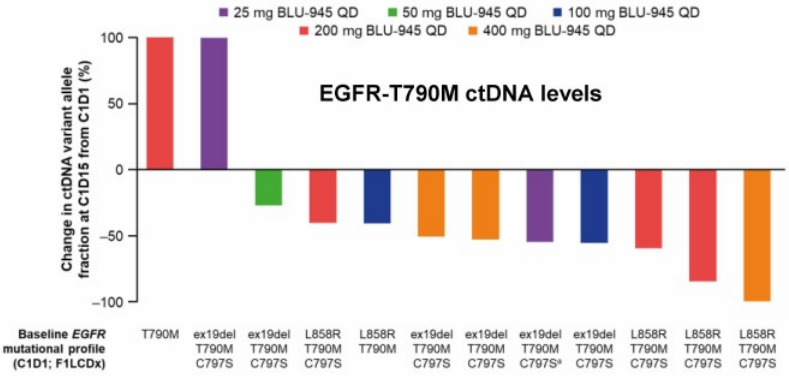


- The averag
  was 24.1 h
  the extent c
- Exposure at
  - EGFRm/T
    in all patie
  - L858R +/–
    in most pa

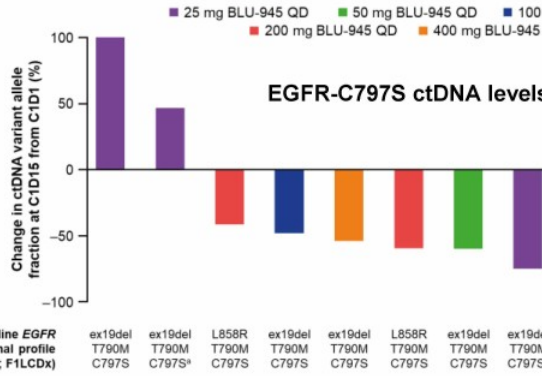
Dashed lines represent IC_{90} for indicated EGFR mutants. C, Cycle; D, day; QD, once daily. As of the data cut-off (March 9, 2022), 33 patients have been treated with BLU-945 a once daily (QD) in the first 5 cohorts.

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

83% OF EGFR-T790M VARIANT ALLELES REDUCED WITH TREATMENT



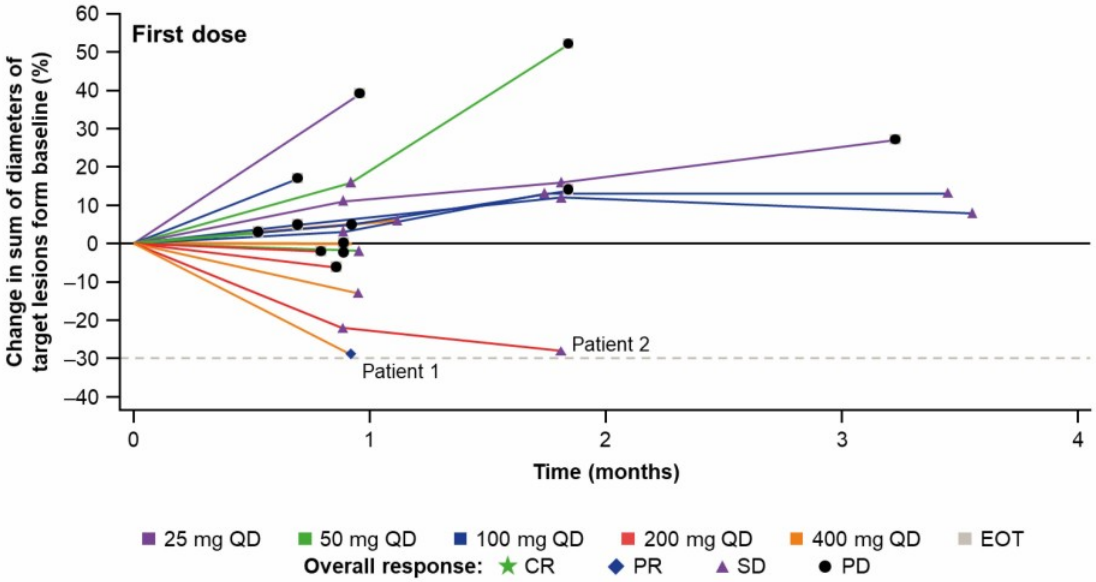
81% OF EGFR-C797S VARIANT A REDUCED WITH TREATME



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

[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 p 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; F1 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 e 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.

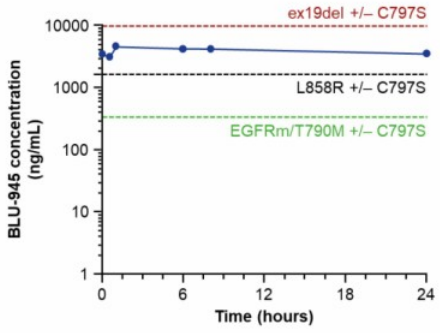
BLU-945 showed dose-dependent anti-tumor activity, with tumor shrinka reported at doses ≥200 mg QD

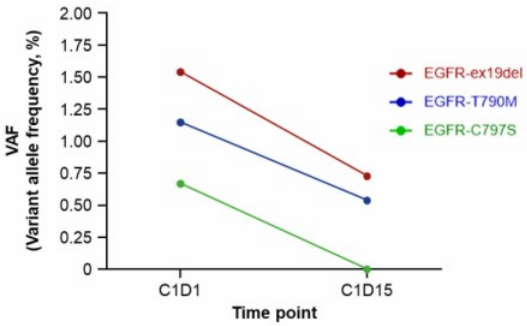


- Unconfirmed PR r patient with ex19del/T790M/C treated at 400 mg
- Dose escalation fr 200 mg QD led to of tumor growth ir

[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, pr 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. (March 9, 2022), 33 patients have been treated with BLU-945 at 25–400 mg once daily (QD) in the first 5 cohorts.

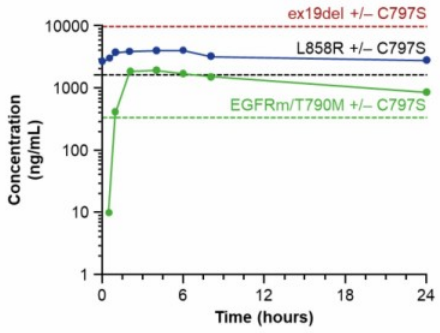
Patient cases: BLU-945 demonstrated encouraging signs of clinical a in patients treated at higher doses

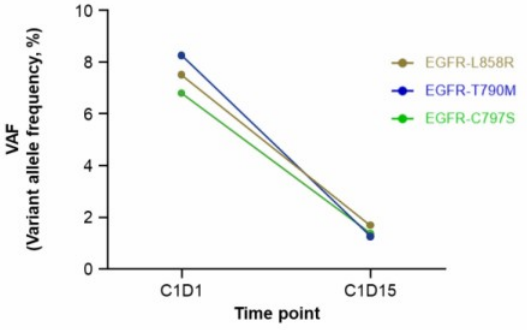




Patient 1

- 69-year-old Caucasian female, no
- Diagnosed stage IV NSCLC
- Three prior therapies with best res
- Multiple target and non-target lesi target in brain
- 400 mg QD
- All detectable mutations decrease C797S clearance
- **Unconfirmed PR; 30% tumor re**



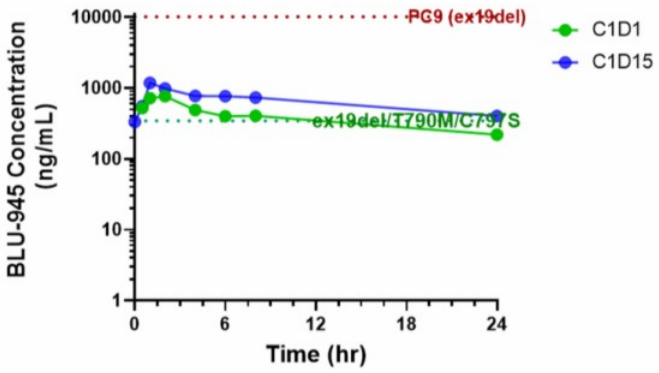


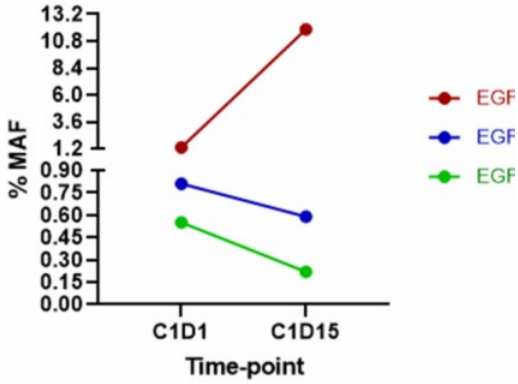
Patient 2

- 70-year-old Asian female, no smo
- Diagnosed stage IVB
- Three prior therapies, achieved PF
- Multiple target and non-target lesi
- 200 mg QD
- All detectable mutations decrease
- **21% and 28% tumor reduction a respectively**

QD, once daily. SD, stable disease. PR, partial response. PD, progressive disease. An unconfirmed PR is a PR in which tumor reduction ≥30% has occurred but has not ye 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.

Patient case: ctDNA and exposure analyses in patient treated at 50 m highlight polyclonal disease and potential of combination treatment





- 57-year-old Asian female
- Several prior therapies (multiple TKIs, chemo, I/O)
- No brain metastases at screening
- Treated with BLU-945 at 50 mg QD
- EOT at C2D1 due worsening pleural effusion

- Divergence in mutation allele fractions su disease with some tumors harboring ex19
- Combination therapy and/or increasing Bl at higher doses may hold promise for trea polyclonal disease

QD, once daily. EOT, end of treatment. I/O, immunotherapy. As of the data cut-off (March 9, 2022), 33 patients have been treated with BLU-945 at 25–400 mg once daily (cohorts.

Conclusions

- In the ongoing Phase 1 trial, BLU-945, a highly potent and selective oral EGFR inhibitor, was tolerated at clinically active doses in heavily pre-treated patients with EGFRm NSCLC
  - Few AEs characteristic of wild-type EGFR toxicity observed at doses up to 400 mg QD
- Despite presence of EGFR mutations conferring resistance to osimertinib, treatment with BL in rapid dose-dependent reductions in ctDNA, consistent with preclinical data
- Increasing BLU-945 doses were associated with increasing antitumor activity, with tumor shr at doses of 200 mg QD and above, including an unconfirmed partial response at 400 mg QD
- The clonal evolution and resulting mutational complexity of EGFR-driven NSCLC tumor cells the need for precision medicine combinations to improve clinical outcomes
- Initial safety and clinical activity results support expanded clinical development of BLU-945 ir with osimertinib and other complementary agents

AE, adverse event. QD, once daily. ctDNA, circulating tumor DNA. An unconfirmed PR is a PR in which tumor reduction ≥30% has occurred but has not yet been c 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.

Acknowledgements

- Participating patients and families
- SYMPHONY trial investigators and research coordinators
- Clinical trial sites:

Cedars-Sinai Medical Center, Los Angeles, CA
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Kanagawa Cancer Center, Yokohama-shi, Kanagawa, Japan
Massachusetts General Hospital, Boston, MA
National Cancer Centre Singapore, Singapore
National Cancer Center Hospital, Chuo Ku, Tokyo, Japan
National Cancer Center Hospital East, Kashiwa, Chiba, Japan
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NYU Langone Health, Laura and Isaac Perlmutter Cancer Center, New York, NY
Samsung Medical Center, Seoul, Korea
Sarah Cannon Research Institute, Nashville, TN
Seoul National University, Department of Internal Medicin
The Royal Marsden NHS Foundation Trust, Sutton, Surre
The University of Texas MD Anderson Cancer Center, Ho
UC Irvine Health, Chao Family Comprehensive Cancer C
University of Colorado Hospital - Anschutz Cancer Pavilio
Vall d'Hebron University Hospital, Oncology Department,
Yonsei Cancer Center, Severance Hospital, Yonsei Unive

- Colleagues at Blueprint Medicines Corporation

Portfolio strategy and next steps

Fouad Namouni, MD, President, R&D

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 resistance mutations at highe on pharmacokinetic data

Dose-dependent antitumor activity, with reductions in target lesions observed at 200 mg QD and higher

Generally well-tolerated, with significant adverse events as wild-type EGFR inhibition

DATA SUPPORT INITIATION OF BROAD COMBINATION DEVELOPMENT ST

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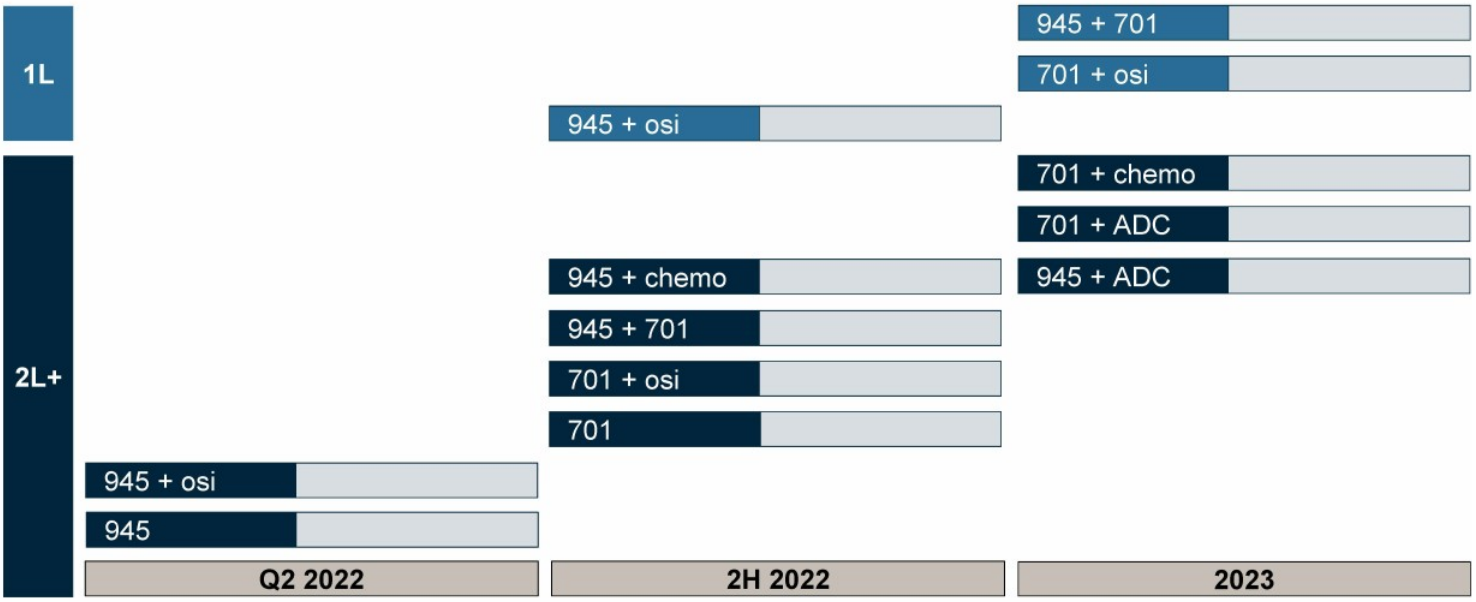
Phase 1/2 trials to rapidly generate data in broad populations, inform development and registration strategies



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

blueprint MEDICINES

Not for promotional use.

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

Vela

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

PHASE 1 DOSE ESCALATION (NOW ENROLLING)

Multiple dose cohorts*

**Includes monotherapy and combination regimens*

- Safety
- Preliminary clinical activity
- Patient selection strategy

RP2D

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 D

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

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

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 n research program vision for scientific p expansion at R&D

2H 2022

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Thank You

Exhibit 99.2

Blueprint Medicines Announces BLU-945 Proof-of-Concept Data Supporting Initiation of Comprehensive Combination Development Strategy in EGFR-mutant Non-Small Cell Lung Cancer

-- Early dose escalation data show dose-dependent reductions in ctDNA and tumor burden --

-- Generally well-tolerated with most AEs Grade 1 or 2, supporting continued dose escalation --

-- Initiating SYMPHONY trial cohort to evaluate BLU-945 in combination with osimertinib --

-- Clinical trial supply agreement signed with AstraZeneca to provide osimertinib for combination development in ongoing BLU-945 and BLU-701 trials --

-- Blueprint Medicines to host investor conference call and webcast on Friday, April 8 at 2:00 pm ET --

CAMBRIDGE, Mass., April 8, 2022 -- Blueprint Medicines Corporation (NASDAQ: BPMC) today announced proof-of-concept data from the Phase 1/2 SYMPHONY clinical trial of BLU-945, an investigational precision therapy for advanced EGFR-mutant non-small cell lung cancer (NSCLC). The trial results showed early evidence of safety and clinical activity consistent with preclinical data, supporting plans to expand development of BLU-945 in combination with multiple agents including osimertinib, with the goal of preventing or treating tumor resistance to prolong patient benefit. The data were reported today at the American Association for Cancer Research (AACR) Annual Meeting 2022 in New Orleans.

Early data from the ongoing Phase 1 dose escalation part of the SYMPHONY trial showed dose-dependent decreases in circulating tumor DNA (EGFR variant allele fractions) and radiographic tumor reductions, including a partial response (PR) in a patient treated with 400 mg once daily (QD), the highest dose tested as of the data cutoff date. Pharmacokinetic results showed BLU-945 exposures at higher doses were associated with broad EGFR mutation coverage, including the activating L858R mutation with or without the osimertinib-resistant C797S mutation. BLU-945 was generally well-tolerated, with no significant adverse events (AEs) associated with wild-type EGFR inhibition. The maximum tolerated dose and recommended Phase 2 dose have not yet been identified, and dose escalation is continuing.

“Today, targeted therapies are the mainstay treatment for EGFR-mutant lung cancer, but tumor resistance emerges in the majority of patients, driving mutational heterogeneity and disease progression. Innovative treatment strategies, including targeted therapy combinations, are urgently needed to prevent or treat this mutational heterogeneity and prolong patient benefit,” said Elaine Shum, M.D., assistant professor in the Department of Medicine and a medical oncologist at NYU Langone Health’s Perlmutter Cancer Center, and an investigator on the SYMPHONY trial. “The initial BLU-945 data reported today, which highlight its potential to address resistance to current standard of care therapies including osimertinib and enable well-tolerated, broad-acting combinations, are an important step forward toward improving outcomes for patients with EGFR-mutant lung cancer.”

“We believe BLU-945 is distinguished from other EGFR-directed therapies, based on its ability to inhibit the most difficult-to-target EGFR mutations while maintaining a wide therapeutic index over wild-type EGFR, a known driver of toxicity. As a result, BLU-945 has significant potential as a combination partner with other targeted therapies and broad-acting agents,” said Fouad Namouni, M.D., President, Research & Development at Blueprint Medicines. “We are excited to see the preclinical profile of BLU-945 translated in the clinic, with early dose escalation data showing evidence of clinical activity, broad EGFR mutation coverage and tolerability. Based on these promising data, we plan to rapidly expand development of BLU-945 in combination with osimertinib and other agents to address important medical needs across all lines of therapy.”

Blueprint Medicines is initiating a SYMPHONY trial cohort assessing BLU-945 in combination with osimertinib in patients with second-line or later EGFR-mutant NSCLC, following disease progression on osimertinib. After the selection of a recommended Phase 2 combination dose regimen, the company plans to initiate an expansion cohort with registration potential in biomarker-selected second-line patients, as well as an expansion cohort in front-line patients, by the end of 2022. Additional combinations with BLU-701, chemotherapy and antibody-drug conjugate therapy are planned across multiple mutation profiles and lines of therapy.

In addition, Blueprint Medicines announced today a clinical trial supply agreement with AstraZeneca (LSE/STO/Nasdaq: AZN). Under the terms of the agreement, Blueprint Medicines will evaluate BLU-945 and BLU-701 in combination with osimertinib in the ongoing SYMPHONY and HARMONY trials, respectively.

BLU-945: Data from the Phase 1/2 SYMPHONY Trial

As of a data cutoff date of March 9, 2022, 33 patients with EGFR-mutant NSCLC have been treated with BLU-945 across five dose escalation cohorts (range: 25-400 mg QD). The majority of patients (79 percent) previously received at least three lines of systemic therapy, including osimertinib (97 percent). Patient eligibility criteria require the presence of an EGFR mutation based on local assessment of tumor biopsy or circulating tumor DNA (ctDNA).

BLU-945 was generally well-tolerated at all doses tested. The most common AEs (regardless of relationship to BLU-945; ≥10 percent) were nausea, headache, fatigue, cough, dyspnea, vomiting, hyponatremia, dry mouth and anemia. Reported AEs associated with wild-type EGFR inhibition were infrequent and low grade, including rash (one patient; Grade 1) and diarrhea (three patients; all Grade 1). One dose-limiting toxicity (Grade 3 transaminitis) occurred in the 400 mg QD cohort, which improved with dose interruption. There were no treatment discontinuations due to AEs.

Pharmacokinetic data showed dose-proportional plasma concentrations, with exposures at increasing doses consistent with broad EGFR mutation coverage, based on preclinical activity thresholds. Mean plasma exposures at doses of 100 mg QD or higher exceeded the IC_{90} for mutants harboring the T790M and C797S resistance mutations, regardless of activating mutation. In addition, mean plasma exposure at 400 mg QD exceeded the IC_{90} for mutants harboring the activating L858R mutation with or without the C797S mutation.

The SYMPHONY trial is one of the first oncology studies to analyze plasma ctDNA via real-time next-generation sequencing to assess tumor biology and early drug activity. Results for patients with detectable T790M and C797S allele fractions at baseline and available post-baseline assessments showed dose-dependent reductions in both variant allele fractions. In patients treated with 400 mg QD, all detectable T790M and C797S allele fractions declined, including three that fell below the limit of detection (clearance).

Patients with measurable target lesions at baseline and at least one post-baseline scan were evaluable per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. In a heavily pre-treated population, higher BLU-945 doses led to increased antitumor activity. Tumor shrinkage was observed in patients treated with 200-400 mg QD, including an unconfirmed PR[1] in a patient treated with 400 mg QD. This patient had NSCLC harboring exon 19 deletion, T790M and C797S mutations, and previously received platinum-based chemotherapy, erlotinib and osimertinib with a best response of stable disease.

[1] An unconfirmed PR is a PR in which tumor reduction ≥30% has occurred, but has not yet been confirmed via a subsequent scan.

Copies of Blueprint Medicines data presentations from the AACR annual meeting, including the SYMPHONY trial presentation, are available in the "Science—Publications and Presentations" section of the company's website at www.blueprintmedicines.com.

Investor Conference Call Information

Blueprint Medicines will host a live webcast today, April 8, 2022 beginning at 2:00 p.m. ET, to discuss the data reported at AACR. To access the live call, please dial 844-200-6205 (domestic) or 929-526-1599 (international), and refer to conference ID 084402. A webcast of the conference call will be available in the Investors & Media section of Blueprint Medicines' website at http://ir.blueprintmedicines.com/. The archived webcast will be available on Blueprint Medicines' website approximately two hours after the conference call and will be available for 30 days following the call.

About Blueprint Medicines' Clinical Development Programs in EGFR-Mutant NSCLC

Blueprint Medicines is developing three investigational agents, BLU-701, BLU-945 and BLU-451, with the goal of addressing nearly all activating mutations (>90 percent) in EGFR-mutant NSCLC. The introduction of EGFR-targeted therapies, including osimertinib, has transformed the care of patients with EGFR-mutant NSCLC; however, there is a significant need for new treatment options designed to prevent or treat a broad range of resistance mechanisms before they emerge, with the goal of prolonging patient benefit. There are no approved targeted therapies for patients with disease progression following osimertinib, and limited treatment options for patients with EGFR exon 20 insertion-positive NSCLC.

BLU-701 and BLU-945 were designed to provide broad coverage of common activating and on-target resistance mutations, spare wild-type EGFR and other kinases to help limit off-target toxicities, and prevent or treat central nervous system (CNS) metastases. These preclinical profiles may enable BLU-701 and BLU-945 to become the backbones of a range of combination strategies across lines of therapy. The Phase 1/2 SYMPHONY trial (NCT04862780) of BLU-945 and the Phase 1/2 HARMONY trial (NCT05153408) of BLU-701 are currently ongoing for patients with EGFR-mutant NSCLC.

BLU-451 is a selective and potent inhibitor of EGFR exon 20 insertion-positive NSCLC. Based on preclinical data, BLU-451 potently inhibited all common EGFR exon 20 insertion variants with marked selectivity over wild-type EGFR and off-target kinases, and has shown CNS penetration. Blueprint Medicines has initiated a Phase 1/2 trial of BLU-451 (NCT05241873) in EGFR exon 20 insertion-positive NSCLC.

To learn about ongoing or planned clinical trials, contact Blueprint Medicines at medinfo@blueprintmedicines.com or 1-888-BLU-PRNT (1-888-258-7768). Additional information is available at blueprintclinicaltrials.com or clinicaltrials.gov.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding Blueprint Medicines' plans, strategies, timelines and expectations for clinical trials, trial cohorts and indications; the anticipated benefits of the preclinical profiles of BLU-945, BLU-701 and BLU-451; Blueprint Medicines' plans, strategies and timelines for the development of BLU-945 and BLU-701 as monotherapies and in combination with other agents; the potential benefits of Blueprint Medicines' current or future approved drugs or drug candidates in treating patients; and Blueprint Medicines' strategy, goals and anticipated milestones, business plans and focus. 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. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks and uncertainties related to the impact of the COVID-19 pandemic to Blueprint Medicines' business, operations, strategy, goals and anticipated milestones, including Blueprint Medicines' 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 products, and launching, marketing and selling current or future approved products; Blueprint Medicines' ability and plans in establishing a commercial infrastructure, and successfully launching, marketing and selling current or future approved products, including AYVAKIT® (avapritinib) and GAVRETO® (pralsetinib); Blueprint Medicines' ability to successfully expand the approved indications for AYVAKIT and GAVRETO or obtain marketing and reimbursement approvals for AYVAKIT and GAVRETO in additional geographies in the future; the delay of any current or planned clinical trials or the development of Blueprint Medicines' current or future drug candidates; Blueprint Medicines' advancement of multiple early-stage efforts; Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; the preclinical and clinical results for Blueprint Medicines' 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; the timing of the initiation of clinical trials and trial cohorts at clinical trial sites and patient enrollment rates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing applications; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for its current and future drug candidates; Blueprint Medicines' ability to successfully expand its operations, research platform and portfolio of therapeutic candidates, and the timing and costs thereof; Blueprint Medicines' ability to realize the anticipated benefits of its executive leadership transition plan; and the success of Blueprint Medicines' current and future acquisitions, collaborations, partnerships or licensing arrangements. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' filings with the Securities and Exchange Commission (SEC), including Blueprint Medicines' most recent Annual Report on Form 10-K, as supplemented by its most recent Quarterly Report on Form 10-Q and any other filings that Blueprint Medicines has made or may make with the SEC in the future. Any forward-looking statements contained in this press release represent Blueprint Medicines' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements.

About Blueprint Medicines

Blueprint Medicines is a global precision therapy company that invents life-changing therapies for people with cancer and blood disorders. Applying an approach that is both precise and agile, we create medicines that selectively target genetic drivers, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. Today, we are delivering approved medicines directly to patients in the United States and Europe, and we are globally advancing multiple programs for systemic mastocytosis, lung cancer and other genomically defined cancers, and cancer immunotherapy. For more information, visit www.BlueprintMedicines.com and follow us on Twitter (@BlueprintMeds) and LinkedIn.

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