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 25, 2024**

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 8.01 Other Events.

On April 25, 2024, Blueprint Medicines Corporation (the "Company") held a webinar focused on emerging opportunities for mast cell-targeted therapies and the Company's approach to modulating mast cells and building a pipeline in allergic and inflammatory diseases. Certain selected presentation materials used during the webinar are attached as Exhibit 99.1 to this Current Report on Form 8-K and are incorporated herein solely for purposes of this Item 8.01 disclosure.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Selected slides from presentation of Blueprint Medicines Corporation dated April 25, 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 101)

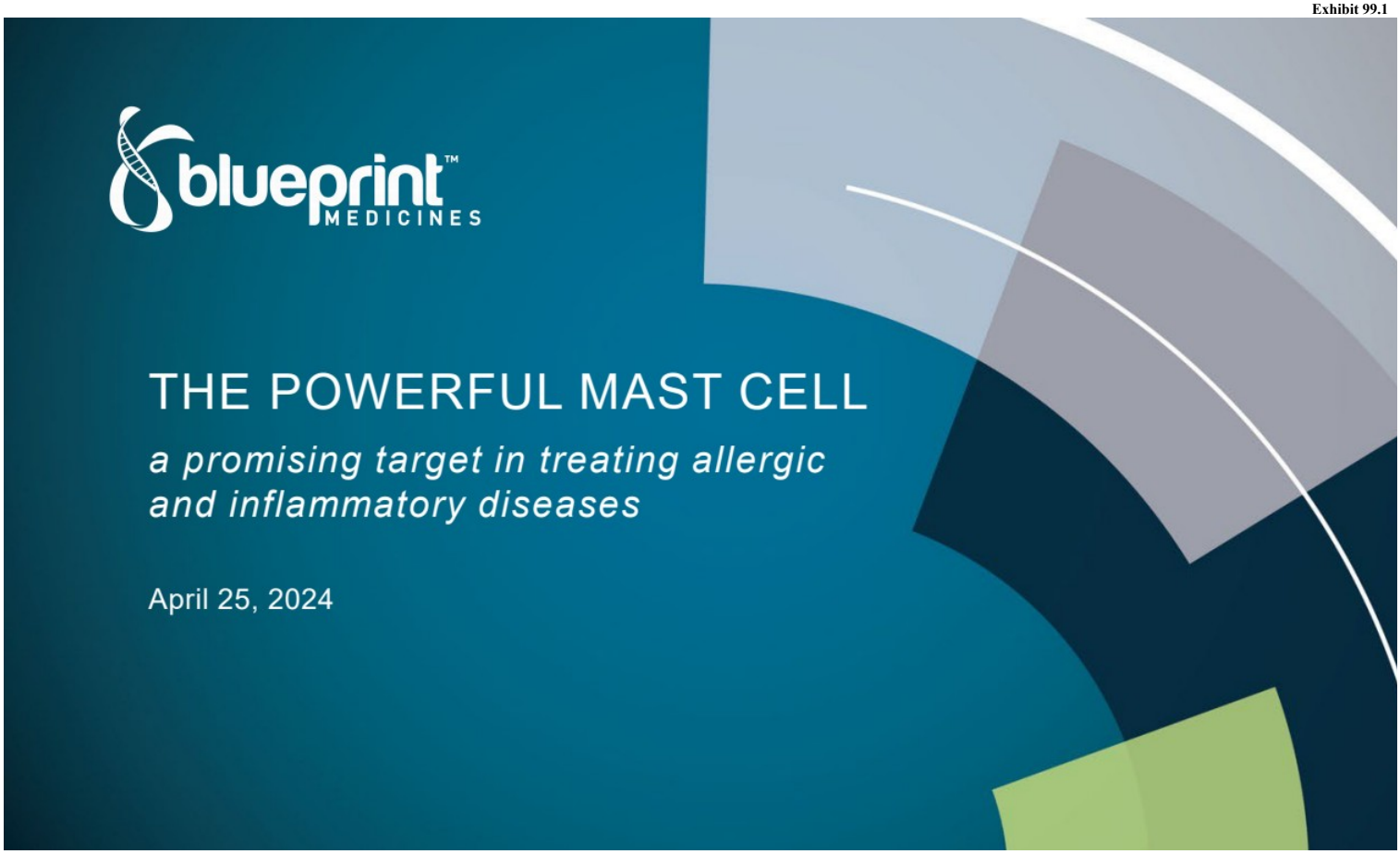
SIGNATURES

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 25, 2024

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


blueprint™
MEDICINES
THE POWERFUL MAST CELL
a promising target in treating allergic and inflammatory diseases
April 25, 2024

Today's agenda and speakers

WELCOME & INTRODUCTION

Fouad Namouni, MD
President, Research & Development

MAST CELLS: POWERFUL DRIVERS OF DISEASE

Becker Hewes, MD
Chief Medical Officer

Mariana Castells, MD, PhD
Brigham and Women's Hospital

A BLUEPRINT FOR TARGETING MAST CEL

Percy H. Carter, PhD, MB
Chief Scientific Officer

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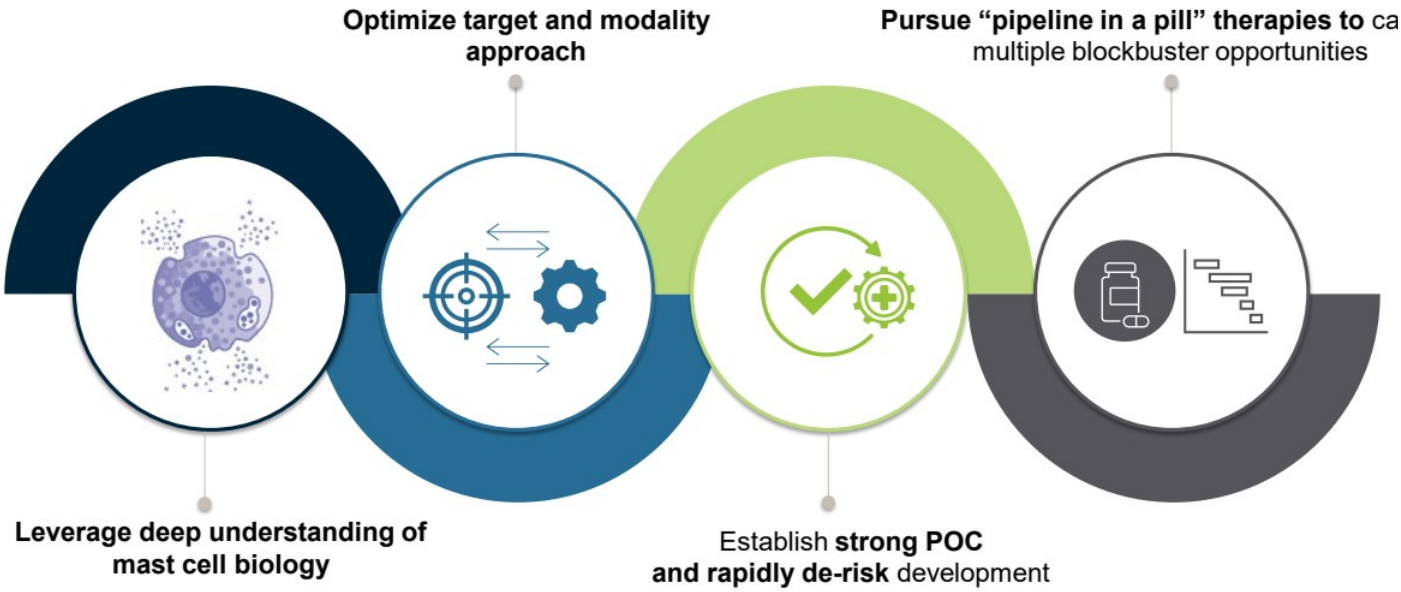
Forward-looking statements

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 the company's future business growth, including the company's vision for mast cell driven diseases and the possibility of capturing multiple blockbuster opportunities; statements regarding whether any of the company's product candidates will successfully address medical needs; statements regarding the company's potential to drive innovation in allergic and inflammatory disease and its potential to revolutionize the allergy/inflammation space with BLU-808; 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 strategy, goals, business plans and focus.

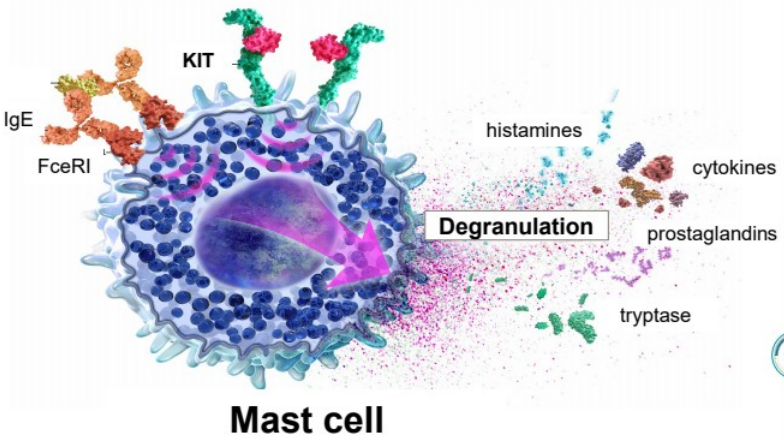
The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this presentation 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 presentation, including, without limitation, risks and uncertainties related 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 products, and launching, marketing and selling current or future approved products; the company's ability and plans to continue to expand a commercial infrastructure, and successfully launch, market and sell current or future approved products; the company's ability to successfully expand the approved indications for AYVAKIT/AYVAKYT 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 current or future drug candidates; the company's advancement of multiple early-stage efforts; the company's 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 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; 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; the company's ability to obtain, maintain and enforce patent and other intellectual property protection for AYVAKIT/AYVAKYT or any drug candidates it is developing; the company's ability to successfully expand its operations, research platform and portfolio of therapeutic candidates, and the timing and costs thereof; and the success of the company's current and future collaborations, financing arrangements, partnerships or licensing arrangements. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in the company's filings with the Securities and Exchange Commission (SEC), including the company's 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 the company has made or may make with the SEC in the future. 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's scientific vision for mast cell driven diseases

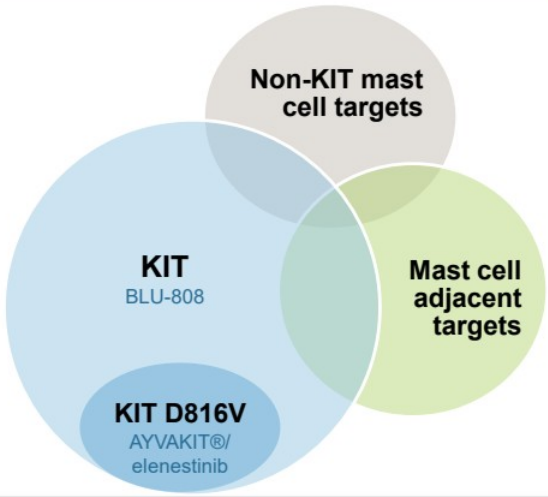


Mast cells are core drivers in a range of inflammatory diseases



Mast cell

- **Central effector cell** in many inflammatory diseases
- Activation leads to release of multiple classes of inflammatory molecules with a broad range of physiological effects
- KIT is a clinically validated **master control switch** for mast cells



- Monotherapy opportunities to inhibit wtKIT, a primary mast cell target
- Opportunities for novel regimens of combination approaches at intersections between therapeutic targets

Proprietary image; AVYAKIT® avapritinib

Blueprint is poised to drive a new wave of innovation in allergic and inflammatory disease

Mast cells are key drivers of inflammatory responses, yet therapeutic interventions have focused on the mediators not the source.

Directly inhibiting activation and degranulation of mast cells is an innovative approach to how we treat several allergic disorders.

Blueprint is well positioned to succeed in large patient populations with significant medical need by delivering blockbuster medicines.

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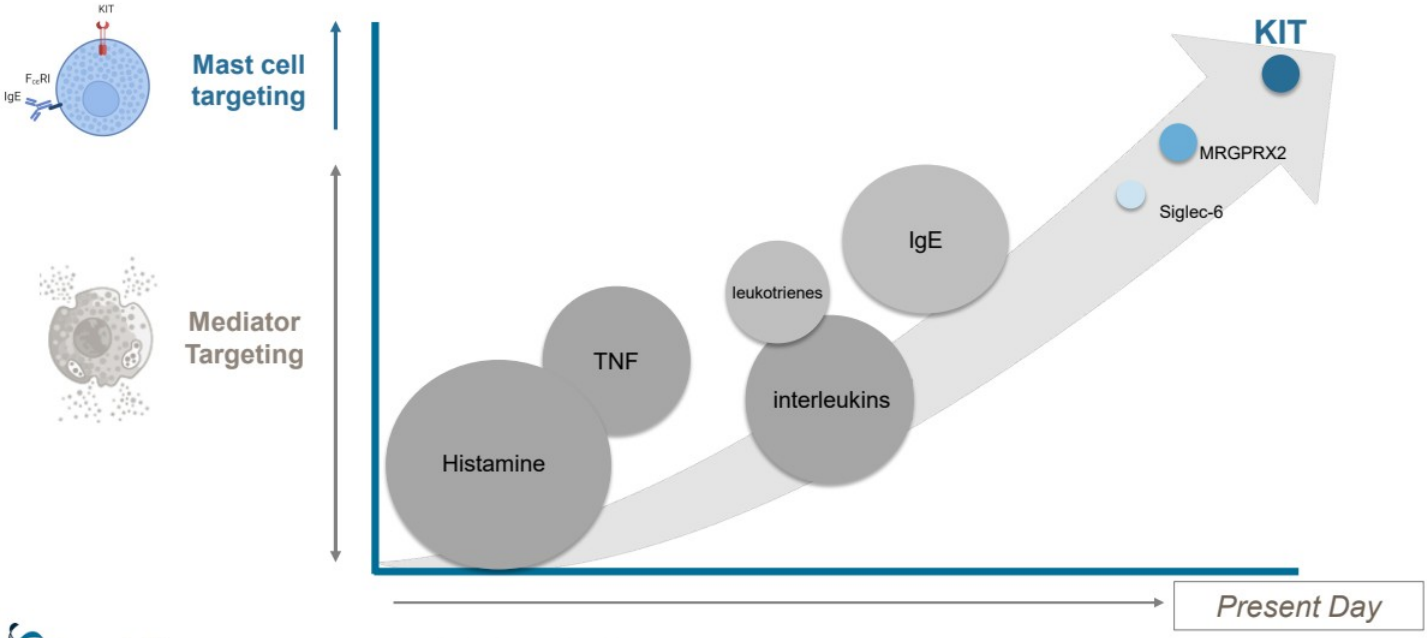
Directly targeting the mast cell stands out as an attractive opportunity in the allergy and inflammation space



Note: bubble size is illustrative of the competitive intensity directed at each target

Mast Cells: Powerful Drivers of Disease

A Conversation with Dr. Becker Hewes and Dr. Mariana Castells

A Blueprint for Targeting Mast Cells

Percy H. Carter

We are achieving R&D scale by leveraging our strengths

PROVEN TRACK RECORD OF SUCCESS

2 approved medicines

~80% success rate from IND to POC

17 development candidates nominated

SCIENTIFIC EXPERTISE IN A/I & ONCOLOGY

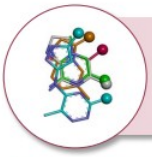
AYVAKIT® (avapritinib) and **elenestinib** for systemic mastocytosis

BLU-808 for mast cell diseases

BLU-222 and **BLU-956** for CDK2 vulnerable breast cancer

Multiple research programs

MODALITY AGNOSTIC DRUG DISCOVERY



Kinase inhibitor platform

Targeted protein degrader platform

Additional exploratory research

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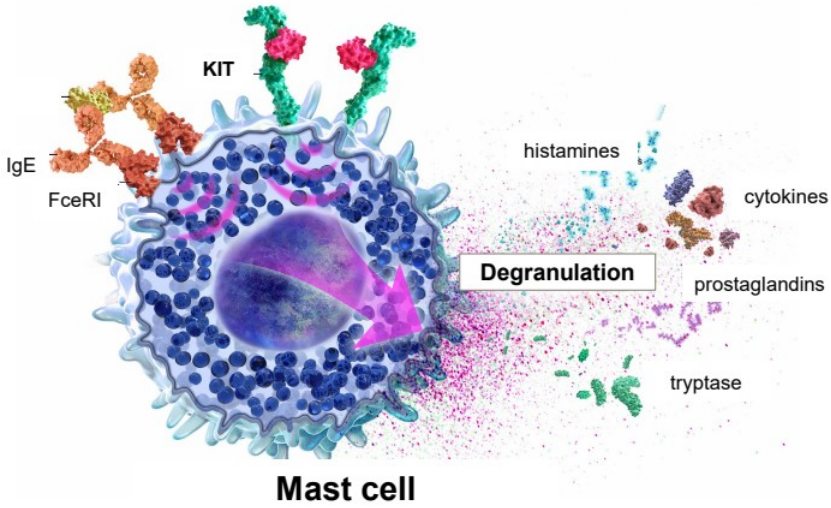
KIT is a key regulator of mast cell activation and proliferation



- Mast cells drive disease and exacerbate inflammation
- KIT regulates mast cell survival
- Blueprint track record of success in mast cell drug development
- Combination approaches may broaden opportunities within and beyond KIT

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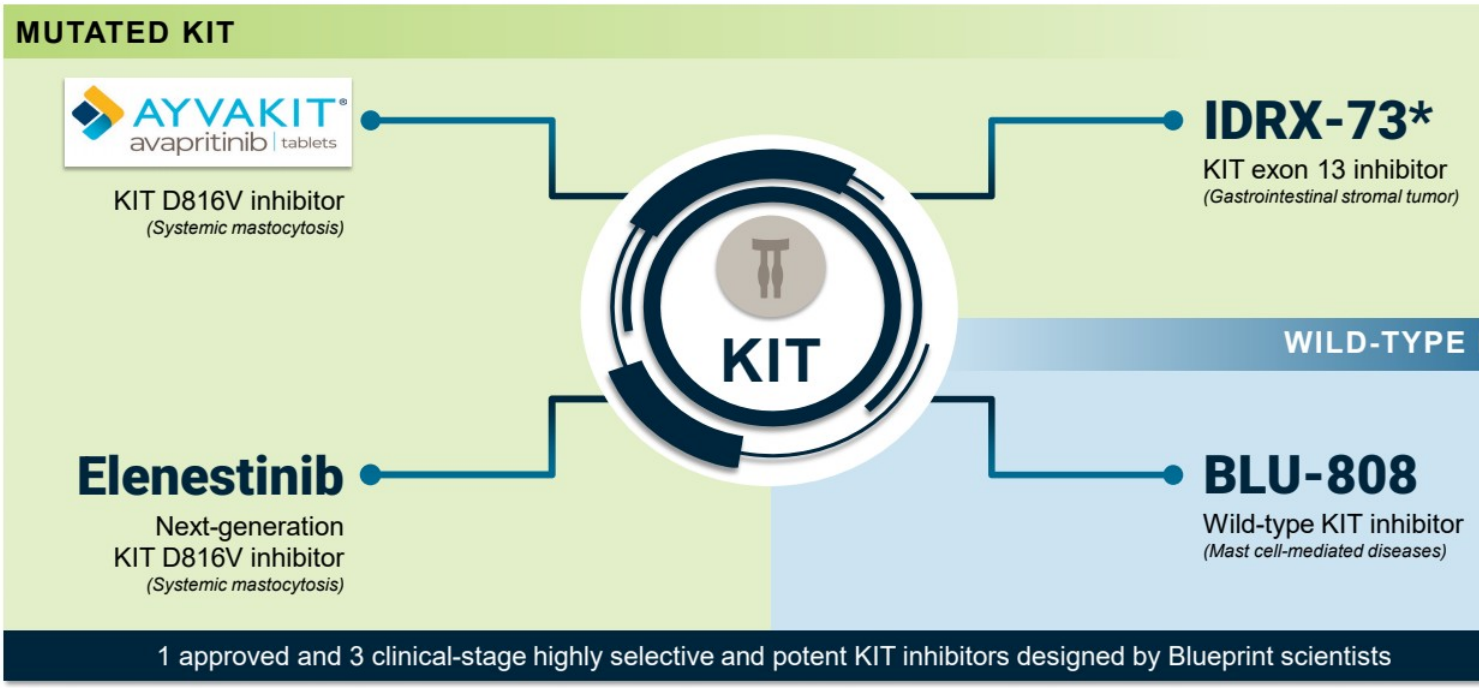
Proprietary image

Scientific leadership in KIT biology



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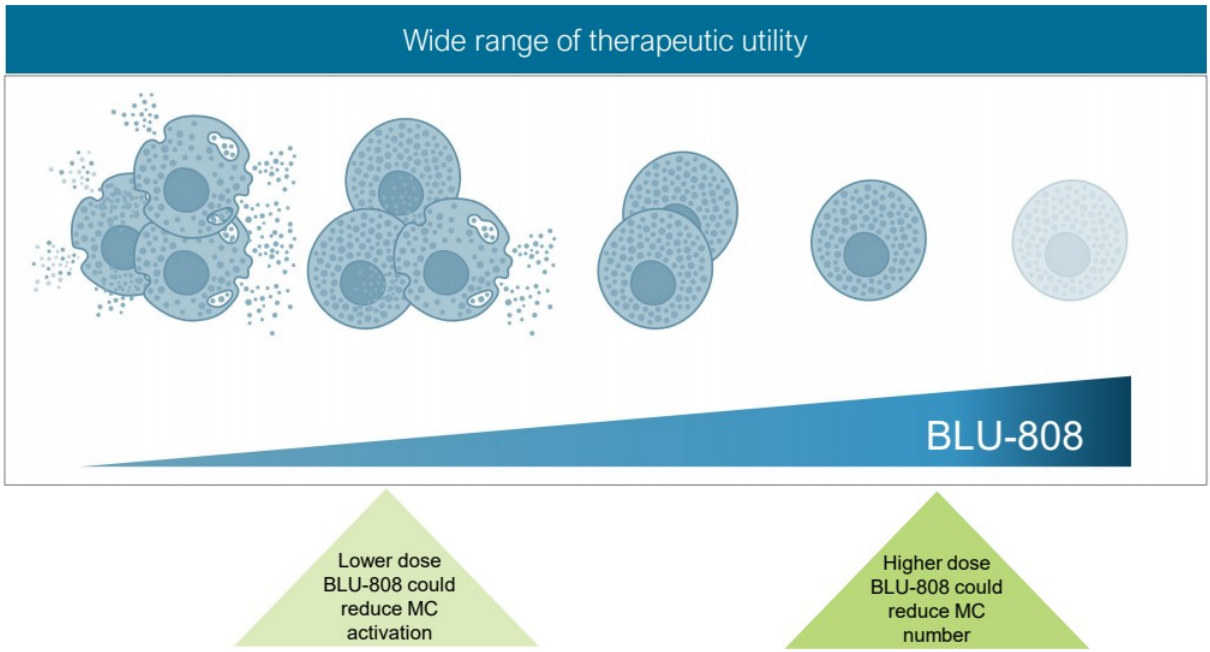
* IDRX-73, formerly known as BLU-654, was out-licensed to IDRx in 2022.

With BLU-808, tunable dosing could enable controlled reduction of mast cell number and activity



Lower dose BLU-808 could reduce MC activation

Higher dose BLU-808 could reduce MC number

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Created with BioRender.com

Wild-type KIT inhibitor BLU-808 has first- and best-in-class potential

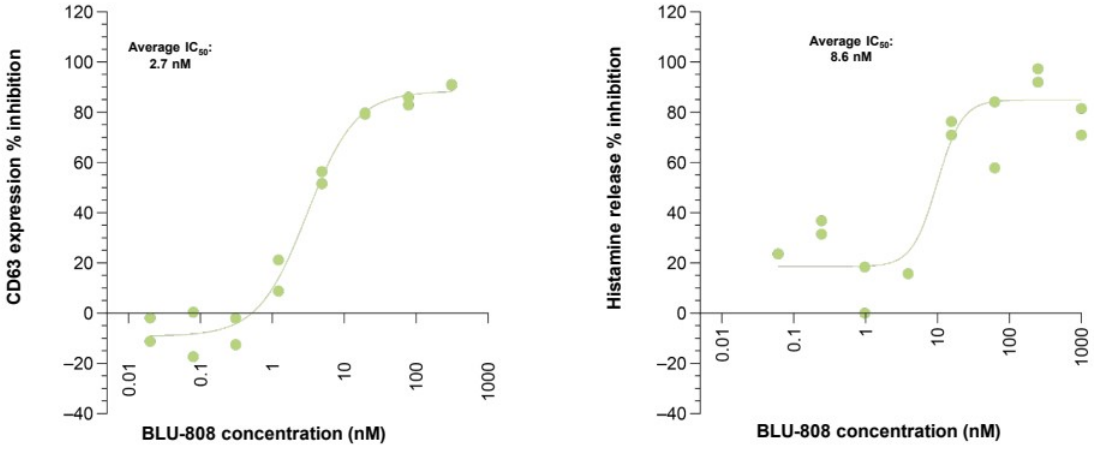
	BLU-808
Potency	
pKIT cellular IC_{50} (nM)	0.37
WT KIT-dependent proliferation IC_{50} (nM)	1.3
Human-derived $CD34^+$ mast cells: inhibition of CD63 extracellular expression IC_{50} (nM)	2.7
Human-derived $CD34^+$ mast cells: inhibition of histamine degranulation IC_{50} (nM)	8.6
Selectivity	
S(10) @ 3 µM	0.042
PDGFRA / PDGFRB / FLT3 cellular selectivity[a]	>300x/>400x/>9600x
CSF1R Kd selectivity	>800x
Brain penetrance ($Kp_{u,u}$)	0.021
Preclinical PK supports once daily oral dosing	

IND submission on-track for Q2 2024, then plan to initiate HV study

[a]Determined in a cellular assay. CSF1R, colony stimulating factor 1 receptor; FLT3, FMS-like tyrosine kinase 3; IC_{50}, half-maximal inhibitory concentration; PDGFRA/B, platelet-derived growth factor receptor alpha/beta; pKIT, phosphorylated KIT; S(10) @ 3 µM, selectivity score at a concentration of 3 µM; $Kp_{u,u}$, unbound brain to plasma partition

BLU-808 inhibits activation of human-derived CD34+ mast cells

Decreased CD63 expression and histamine release in treated human-derived CD34+ mast cells stimulated with IgE and anti-IgE

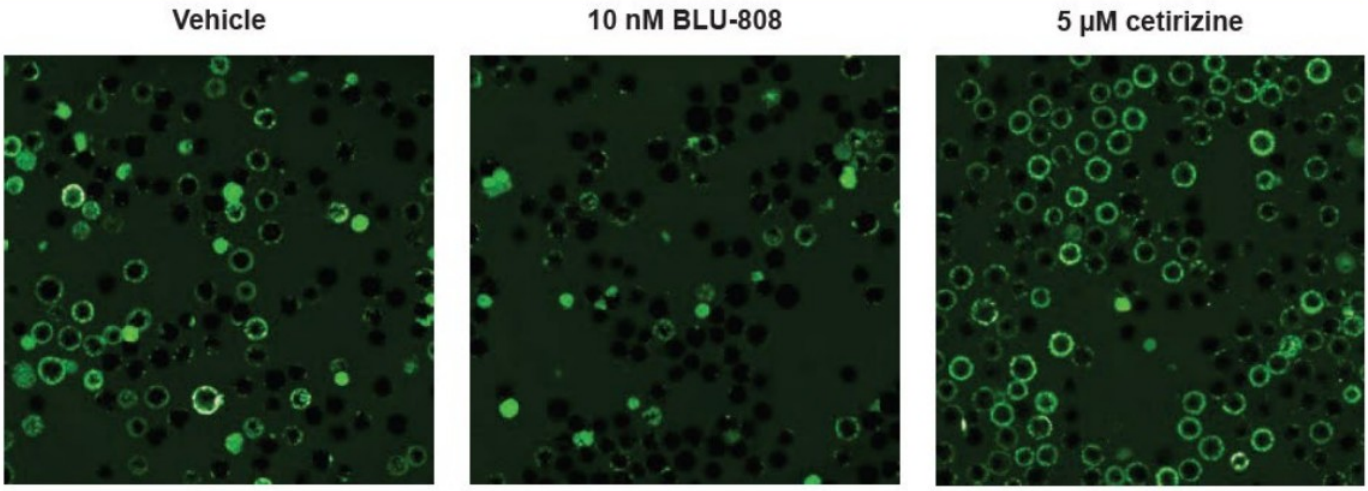


BLU-808 is potent in two human-derived CD34⁺ mast cell assays

- BLU-808 inhibits the expression of CD63 at the cell surface, which is a marker of mast cell degranulation
- Inhibition of histamine release shows that BLU-808 can reduce degranulation and subsequent release of inflammatory molecules

Grassian, A et al, AAAAI 2024

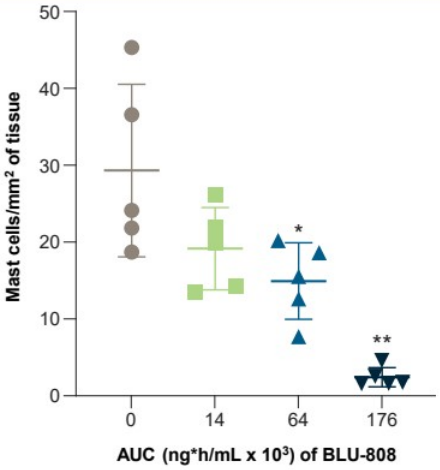
BLU-808 inhibits degranulation of human-derived CD34+ mast cells



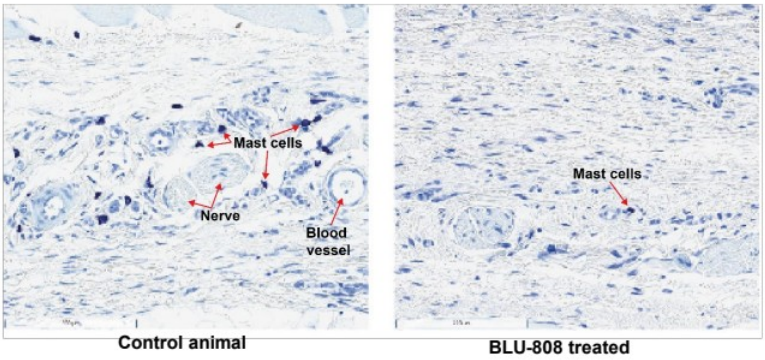
- **BLU-808 targets the source of histamine and other mediators by preventing mast cell degranulation**
  - Mast cells were labeled in green to visualize degranulation. Following stimulation, the increase in green fluorescence indicated that degranulation occurred in mast cells treated with vehicle and 5 µM cetirizine, however BLU-808 inhibited degranulation, as shown by reduced fluorescence intensity.
  - Cetirizine, a control here, is an antihistamine that does not affect degranulation in mast cells at lower concentrations[1,2]

Grassian, A et al, AAAAI 2024; IgE, immunoglobulin E. 1. Church DS et al. *World Allergy Organ J*. 2011;4:S22–S27; 2. Fujimura R et al. *Drug Discov Ther*. 2022;16:245–250.

BLU-808 can decrease mast cells in an exposure-dependent manner



Total mast cell % reduction from control:	--	35%	49%	92%



Haired skin: Subcutis at high magnification, toluidine blue staining

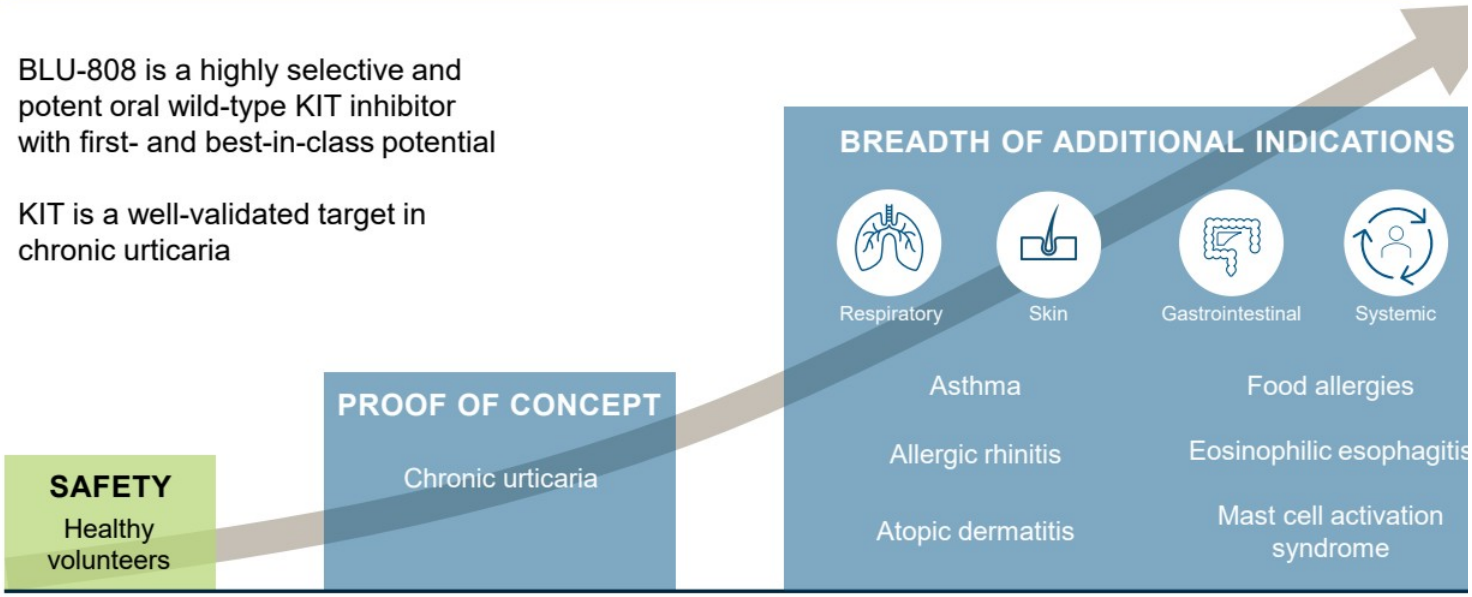
- BLU-808 was administered for 7 days at different specific doses in rats
- Mast cells were quantified by toluidine blue staining and showed a dose-dependent reduction
- *In vivo* data in mouse model of asthma also support dose-dependent response

Grassian, A et al, AAAAI 2024; AUC, area under curve. *, P<0.05; **, P<0.005; all per two-way analysis of variance with Tukey's correction for multiple comparisons. Horizontal lines represent mean and standard deviation.

Potential to revolutionize the allergy/inflammation space with BLU-808

BLU-808 is a highly selective and potent oral wild-type KIT inhibitor with first- and best-in-class potential

KIT is a well-validated target in chronic urticaria



Phase 1 healthy volunteer safety, pharmacokinetic and pharmacodynamic data represent key de-risking event

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Thank you!