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Presentation of Initial SGR-1505 Phase 1 Clinical Data

June 12, 2025

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These forward-looking statements reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. Actual results may differ materially from those described in the forward-looking statements and are subject to a variety of assumptions, uncertainties, risks and important factors that are beyond our control, including the demand for our software solutions, the reliance upon our third-party drug discovery collaborators, the uncertainties inherent in drug development and commercialization, such as the conduct of research activities and the timing of and our ability to initiate and complete preclinical studies and clinical trials, whether results from preclinical and early clinical studies will be predictive of the results of later preclinical studies and clinical trials, whether initial data from clinical trials will be predictive of the final results of the clinical trials, uncertainties associated with the regulatory review of clinical trials and applications for marketing approvals, factors adversely affecting the life sciences industry, and other risks detailed under the caption "Risk Factors" and elsewhere in our Securities and Exchange Commission (“SEC”) filings and reports, including our Quarterly Report on Form 10-Q for the quarter ended March 31, 2025, filed with the SEC on May 7, 2025, as well as future filings and reports by us. Any forward-looking statements contained in this presentation speak only as of the date hereof. Except as required by law, we undertake no duty or obligation to update any forward-looking statements contained in this presentation as a result of new information, future events, changes in expectations or otherwise.

This presentation includes statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this presentation involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. We have not independently verified such third-party data, and we undertake no obligation to update such data after the date of this presentation.

Today’s Agenda

Introduction — Ramy Farid

Rationale for MALT1 Inhibition & Discovery of SGR-1505 — Karen Akinsanya

Therapeutic Landscape — Margaret Dugan

SGR-1505 Phase 1 Data Review — Margaret Dugan

Opportunity and Next Steps — Karen Akinsanya

Q&A



Ramy Farid, Ph.D.
Chief Executive Officer, Board Member



Karen Akinsanya, Ph.D.
President, Head of Therapeutics R&D
and Chief Strategy Officer, Partnerships

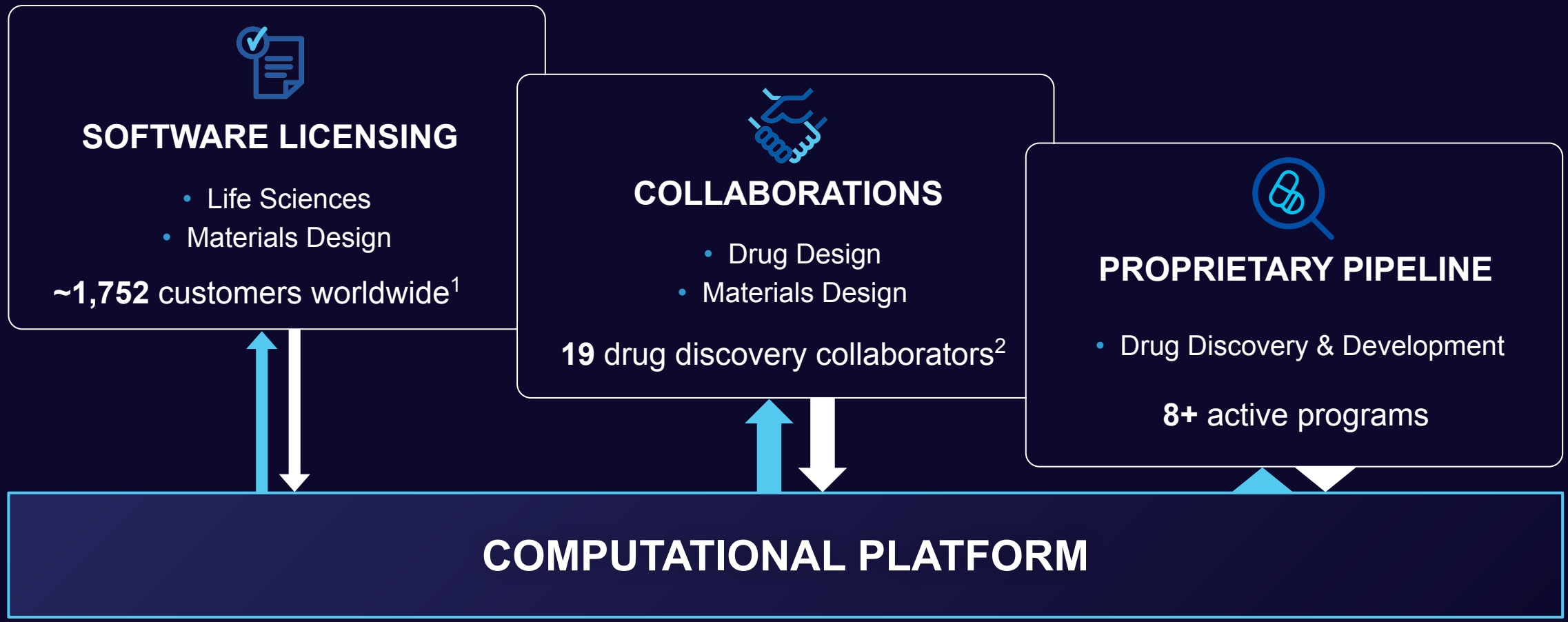


Margaret Dugan, M.D.
Chief Medical Officer



Richie Jain
Chief Financial Officer

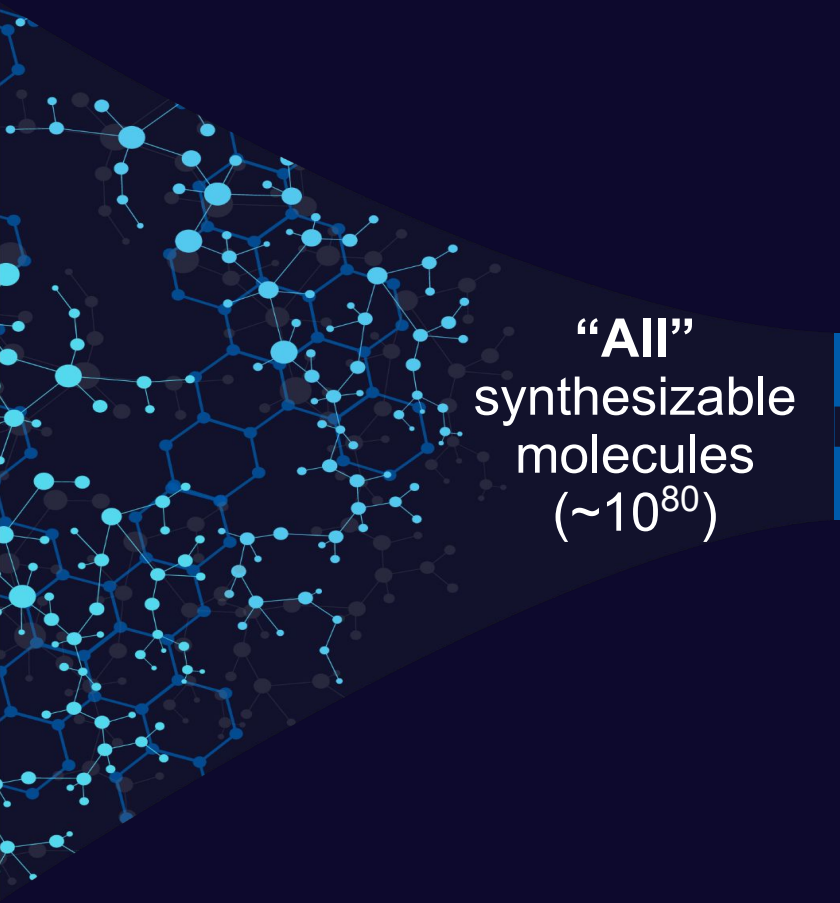
Multi-Pronged Business Enabled by Highly Differentiated Computational Platform



[1] Active customers (# of customers who had an ACV >$1,000) as of Dec. 31, 2024.
[2] Cumulative number of collaborators since 2018.

Schrödinger's Vision for the Future of Drug Discovery

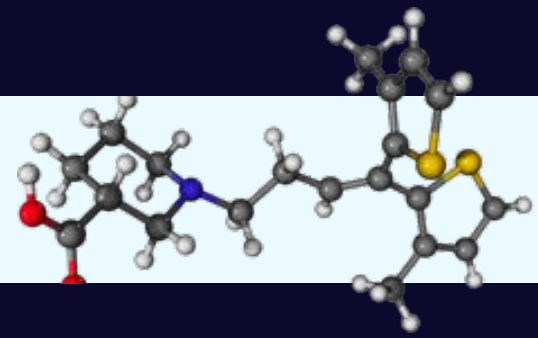
If all properties can be calculated with perfect accuracy, designing drugs would have a much **higher success rate**, be much **faster** and **cheaper**, and would produce much **higher-quality** molecules.



"All" synthesizable molecules ($\sim 10^{80}$)



Select **THE** best molecule



- ✓ Potency
- ✓ Selectivity
- ✓ Solubility
- ✓ Bioavailability
- ✓ Clearance / Half-life
- ✓ Permeability
- ✓ Drug-Drug Interactions
- ✓ Synthesizability

Platform Validated by Clinical Success[1][2]

Phase 1	
nimbus THERAPEUTICS	Immuno-oncology
Ajax THERAPEUTICS	Myelofibrosis
Schrödinger	Hematologic Malignancies
Schrödinger	AML/MDS
Schrödinger	Solid Tumors
Undisclosed	Undisclosed
Undisclosed	Undisclosed

Phase 2	
GILEAD	Metabolic Diseases[3]
Lilly	Inflammatory Bowel Disease[5]
STRUCTURE THERAPEUTICS	Obesity

Phase 3	
Takeda	Psoriasis[3]

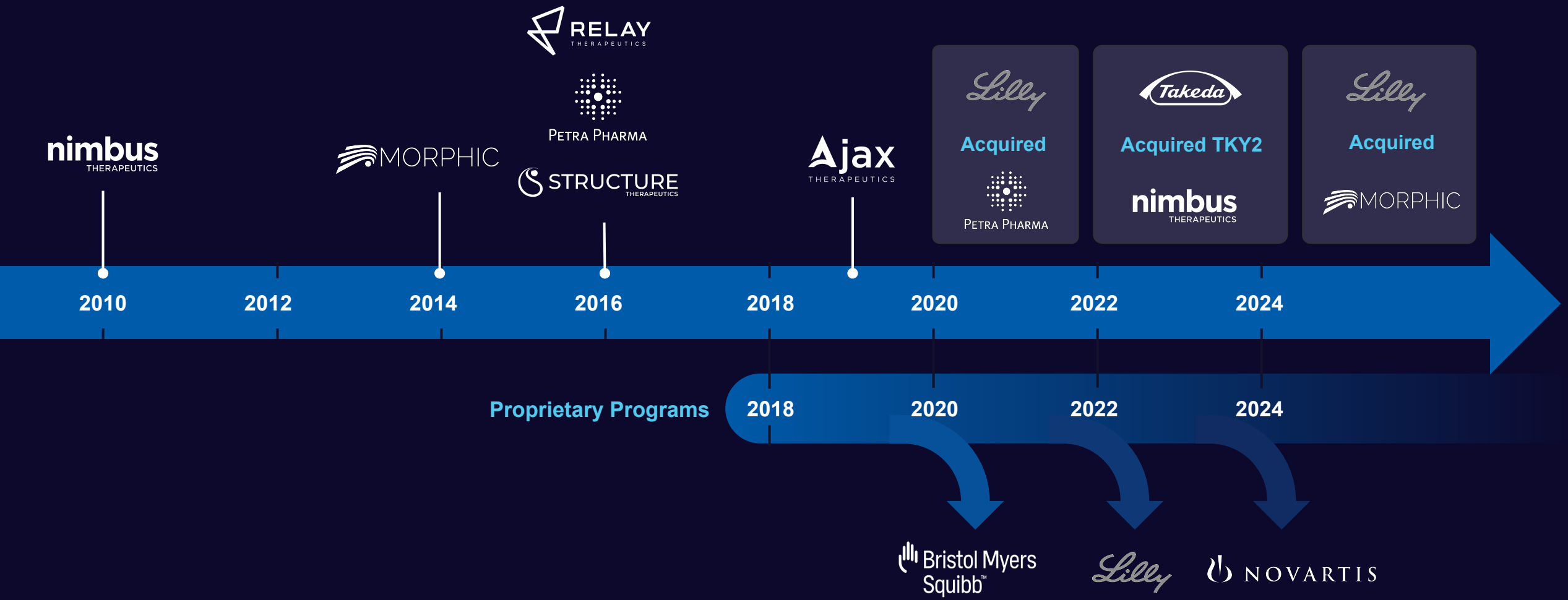
FDA-Approved	
agios	*TIBSOVO*[4] *IDHIFA*[4]

Additional programs in discovery and preclinical development with:

Bristol Myers Squibb™ · Lilly · Otsuka · STRUCTURE THERAPEUTICS · NOVARTIS

[1]Based on publicly available information or information disclosed to us.
[2]All of the programs being pursued under these collaborations are owned and controlled by each respective collaborator.
[3]Acquired from Nimbus.
[4]Acquired by Servier.
[5]Acquired from Morphic.

Capturing Value from Collaborative and Proprietary Programs



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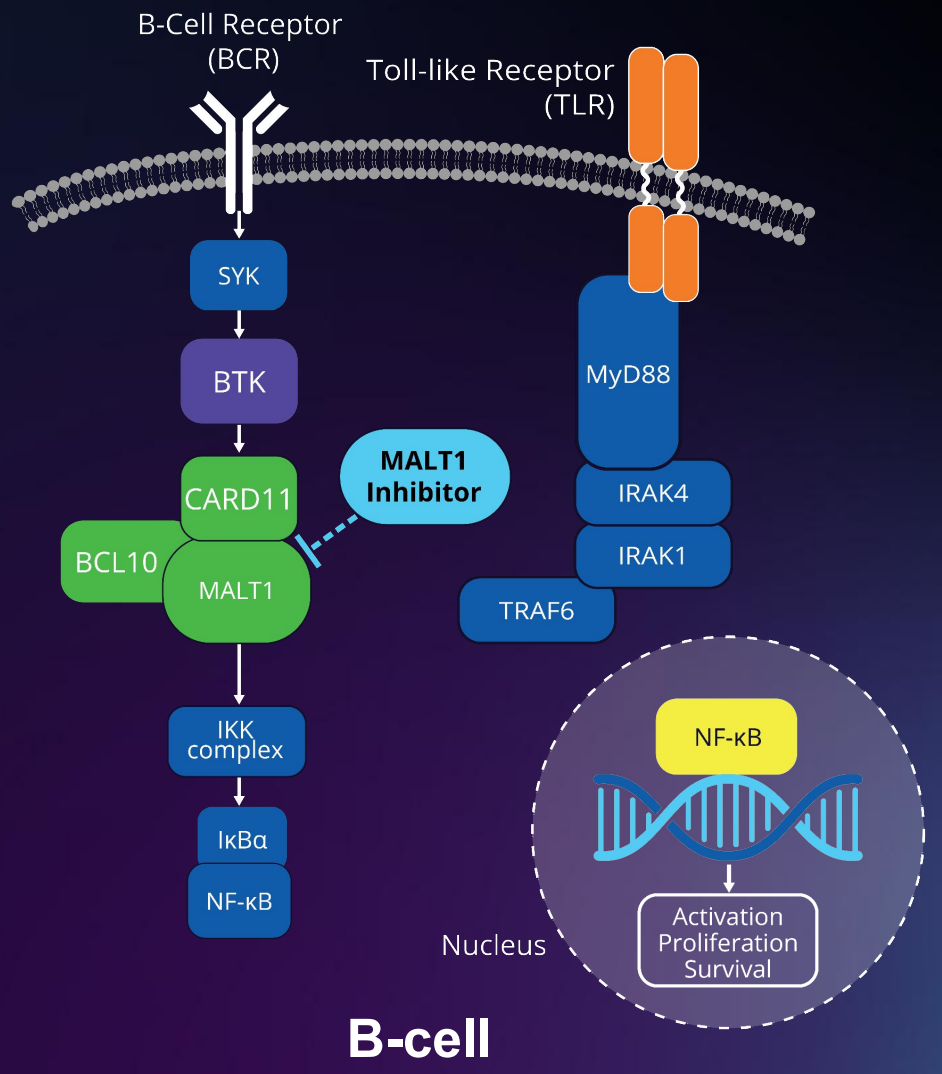


Richie Jain
Chief Financial Officer

MALT1: An Emerging Mechanism in a Validated Pathway

Lymphoma cell survival is associated with dysregulated NF-κB signaling

BTK inhibitors are standard-of-care in B-cell malignancies, but resistance develops

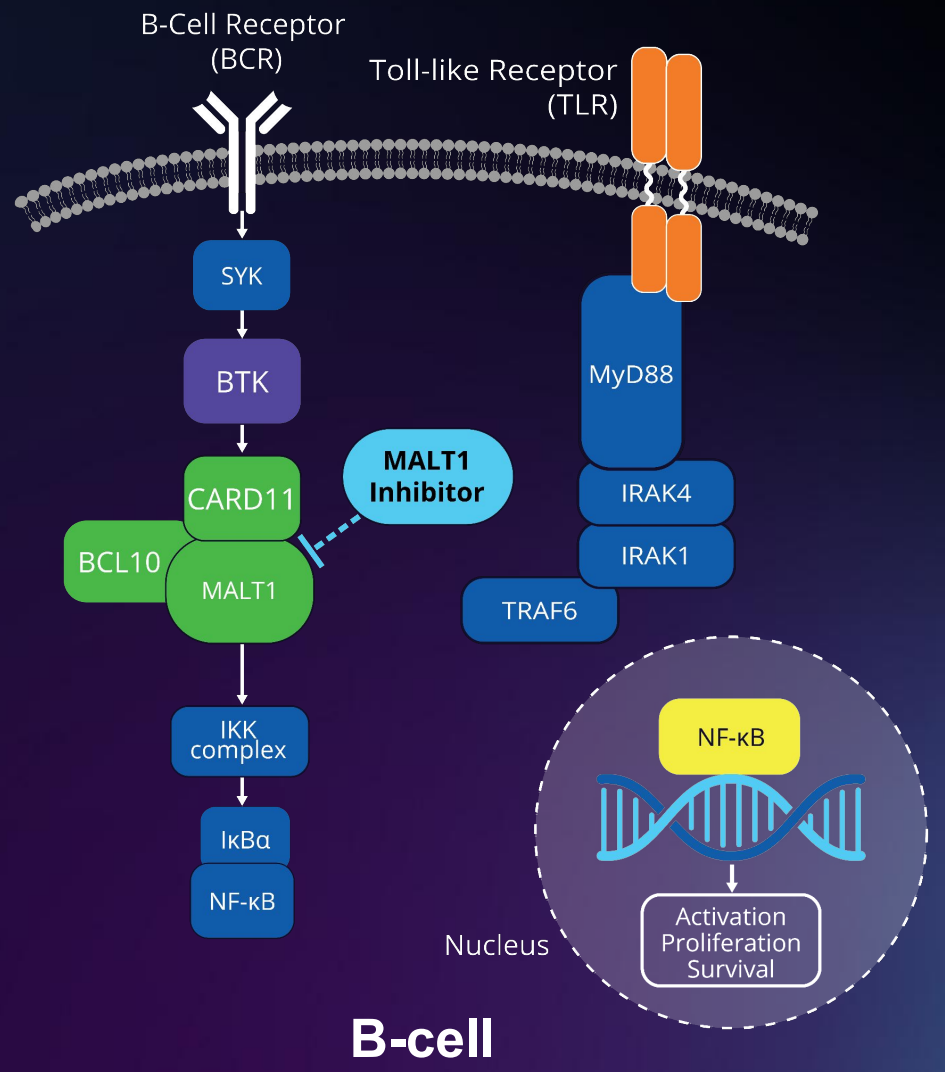


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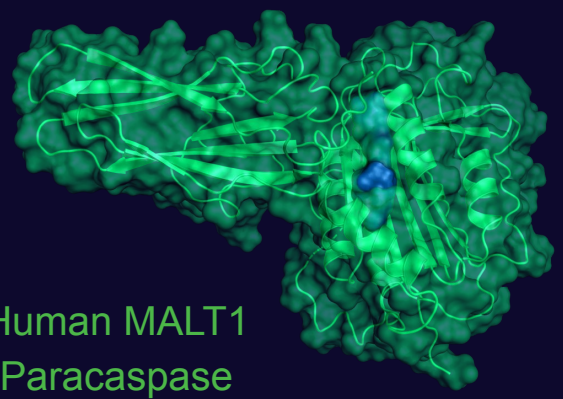
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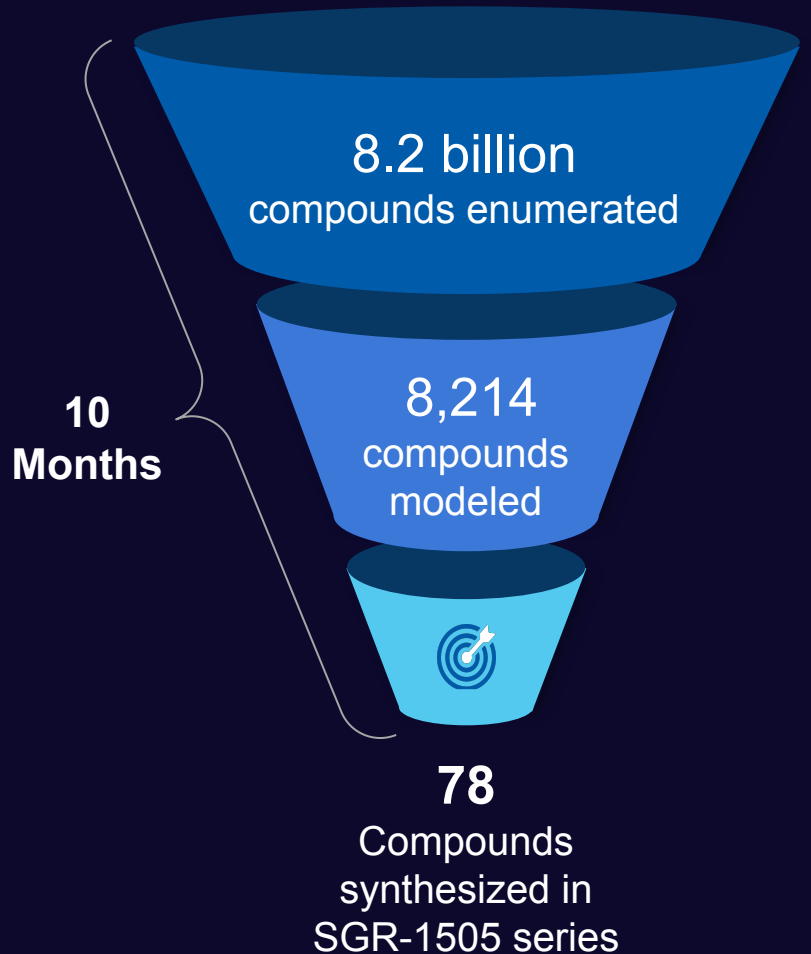
MALT1 is a key regulator of NF-κB signaling in B-cells and T-cells



Rapid Design of a Best-in-Class MALT1 Inhibitor



Human MALT1
Paracaspase

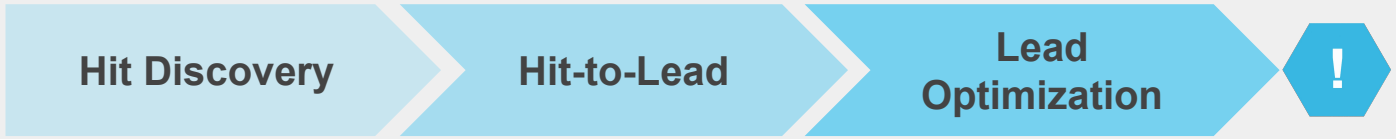


- ✓ Novel allosteric pocket inhibitor
- ✓ Optimized *in vitro* cellular potency
- ✓ Selective against common off targets
- ✓ Optimized *in vivo* anti-tumor monotherapy and combination activity
- ✓ Optimized IL-2 inhibition in human blood cells

Impact of Schrödinger Drug Discovery Approach

Traditional Drug Design

- **Manual** molecule design
- **~5,000** molecules synthesized and tested over **~4 – 6 years**



Drug candidates with potential **property issues**

SGR-1505



- **8.2 billion** compounds scored with **Physics+AI/ML**
- SGR-1505 identified in **10 months**

Phase 1 package

Optimized profile confirmed in global patient study

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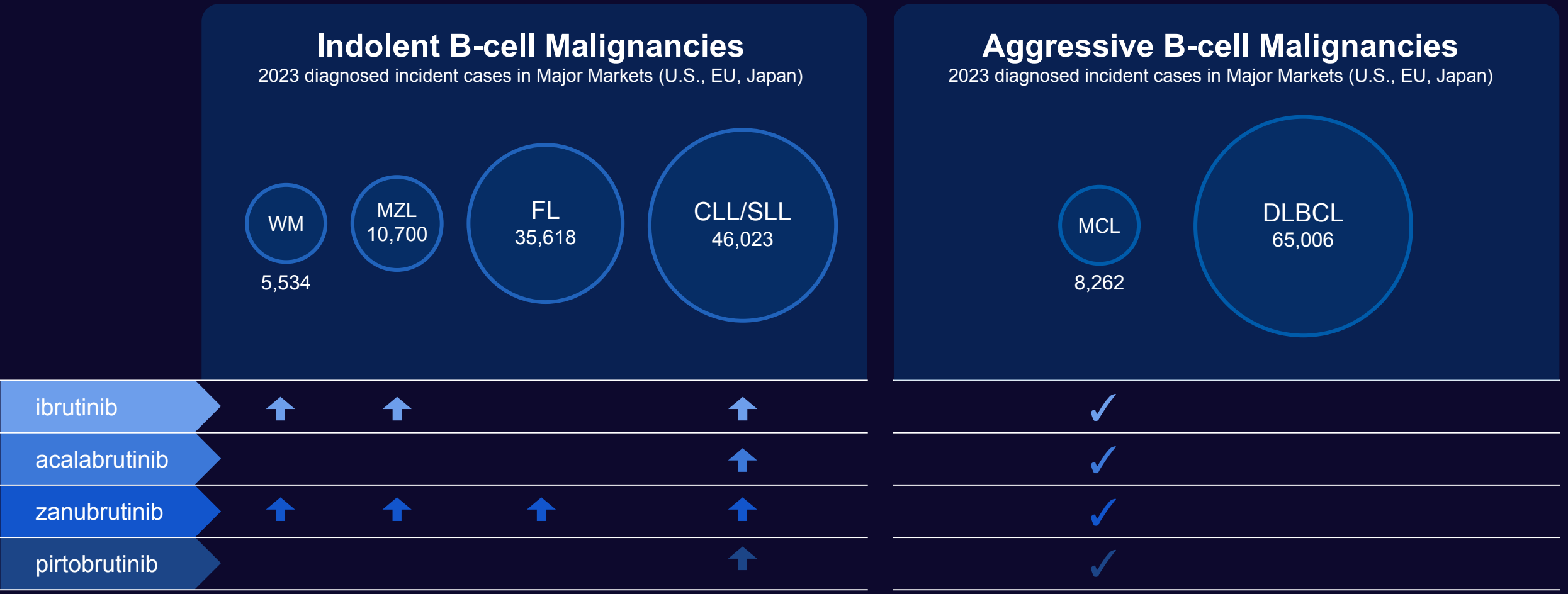


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Chief Medical Officer



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BTK Inhibitor Approvals in B-Cell Malignancies



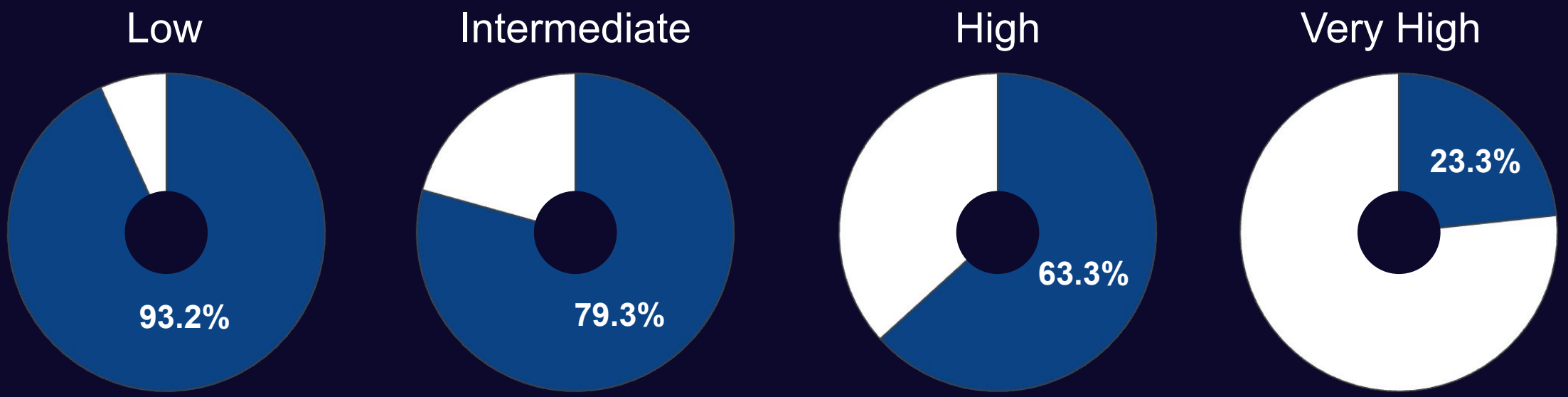
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Sources: Product prescribing information; Decision Resources Group Clarivate NHL Market Analysis.

Potential MALT1 Opportunity in Higher-Risk CLL Patients

Five-Year Survival Rate in CLL- IPI Risk Subgroups

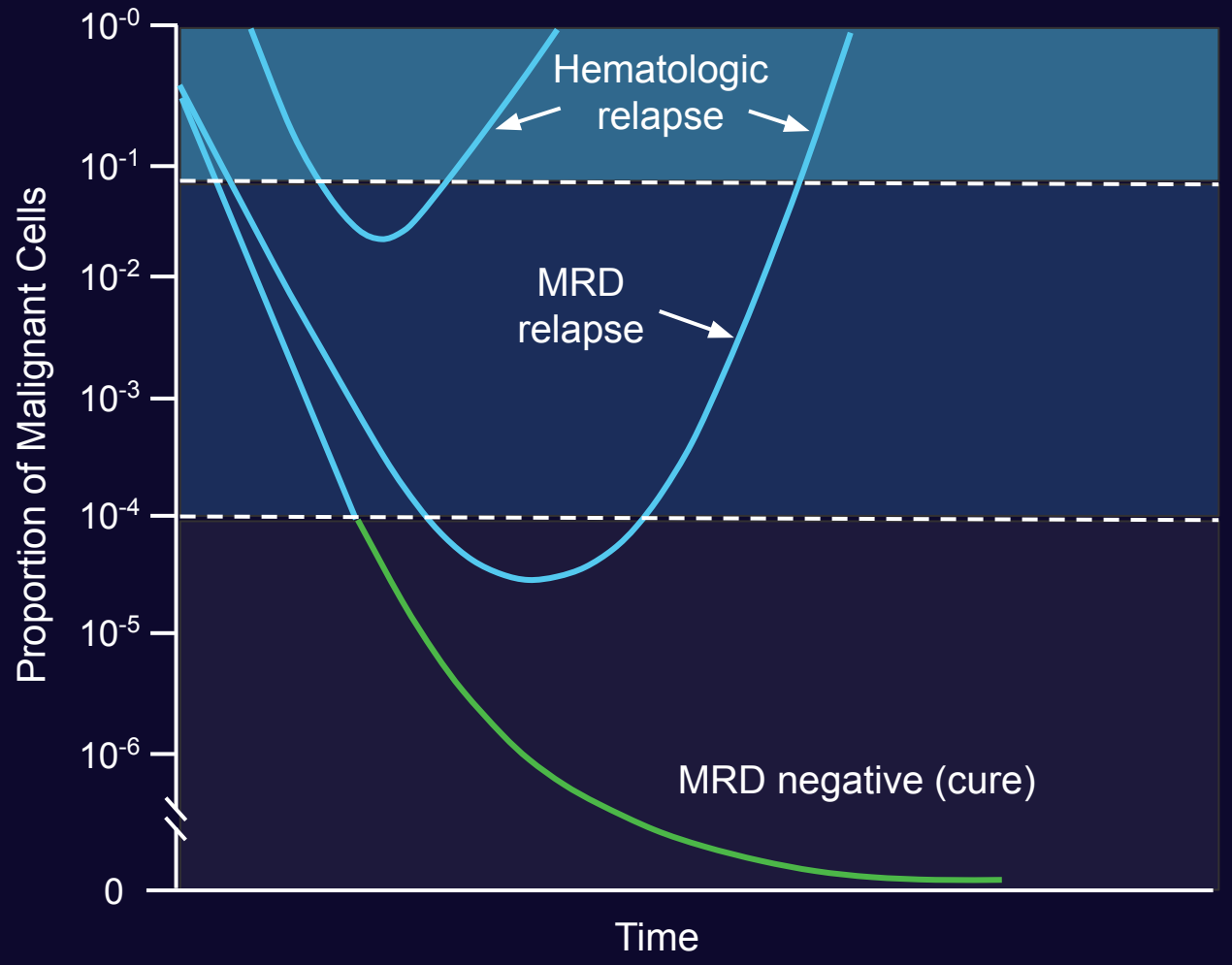
Risk subgroups are based on genetic, biochemical, and clinical parameters*[1,2]



*Includes age, TP53 and/or 17p deletion mutation status, IGHV mutational status.

[1]International CLL-IPI Working Group. *Lancet Oncol.* 2016;17(6):779-790. [2]Hallek M, Al-Sawaf O. *Am J Hematol.* 2021;96(12):1679-1705.

New Mechanisms and Combinations Needed to Achieve Minimal Residual Disease



- Minimal residual disease (MRD) being evaluated to monitor disease
- Patients with CR who remain MRD positive may benefit from further treatment
- Patients who revert from MRD negative to MRD positive may benefit from further treatment

Adapted from Woyach JA, Byrd JC. *NEJM* 2023: 388(19).

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Successful Phase 1 Study: Key Findings

- SGR-1505 was observed to have a favorable safety profile and was well-tolerated
- Confirmed strong target engagement
- Encouraging preliminary efficacy across range of B-cell malignancies
- Monotherapy signal in CLL and Waldenström macroglobulinemia (WM)

Spurgeon et al., EHA 2025. As of the data cut-off date (May 13, 2025).

Study Design & Objectives

Primary objectives:

- Safety and tolerability
- Identification of maximum tolerated dose (MTD) or maximum administered dose (MAD) and/or recommended dose(s) (RD)

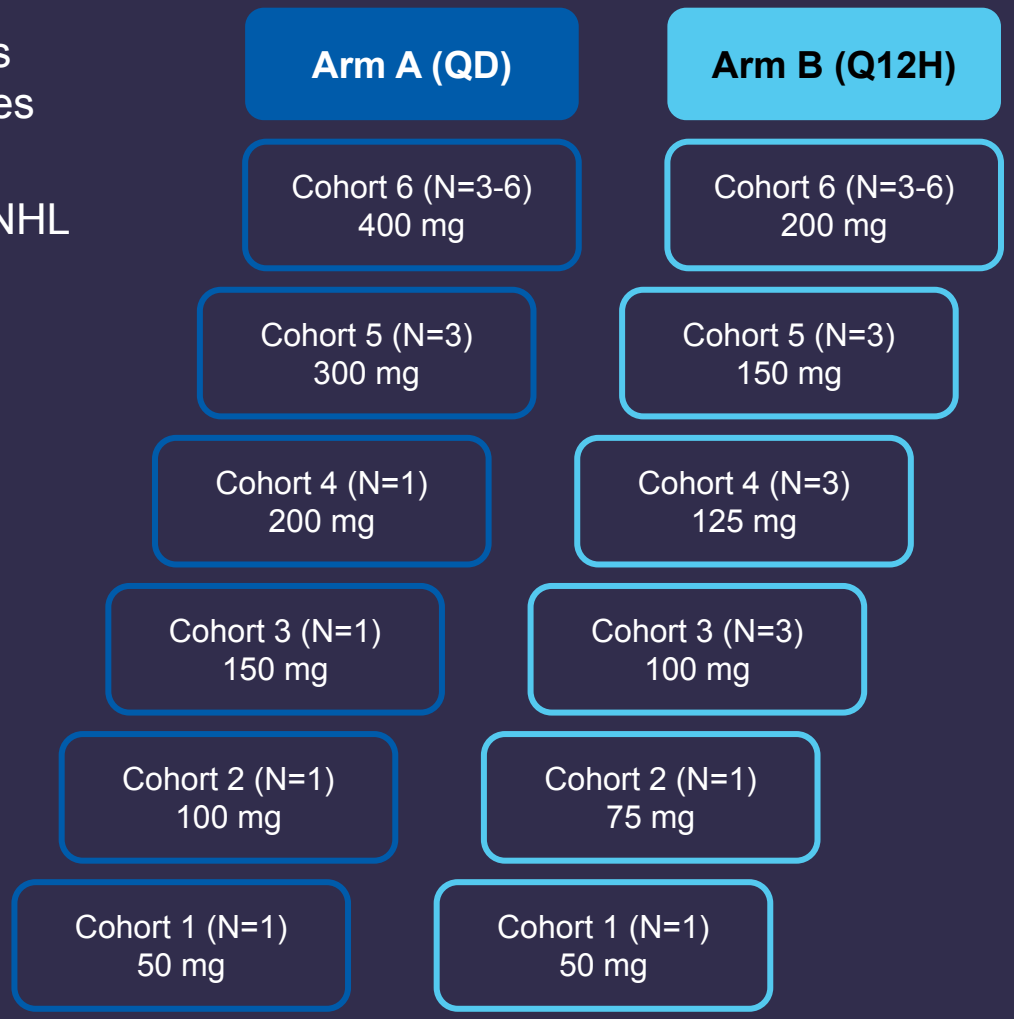
Secondary objectives:

- Pharmacokinetics (PK)
- Preliminary anti-tumor activity

Exploratory objective:

- Pharmacodynamics (PD)

- R/R B-cell neoplasms following ≥ 2 prior lines
- Indolent forms and aggressive forms of NHL
- Continuous dosing
- 21-day cycles



Spurgeon et al., EHA 2025; Clinicaltrials.gov ID: NCT05544019. QD: once daily dosing; Q12H: dosing every 12 hours

Study Conducted in Highly Refractory Patient Population

Demographics (N=49)

Median age, years (range)	64 (31 - 82)
Male, n (%), **female**, n (%)	32 (65.3), 17 (34.7)
ECOG PS, n (%)	
0, 1	25 (51.0), 24 (49.0)
Median prior lines of therapy (range)	4 (2 - 9)
Histologies, n (%)	
Chronic lymphocytic leukemia/small lymphocytic leukemia Diffuse large B-cell lymphoma Waldenstrom macroglobulinemia Marginal zone lymphoma Mantle cell lymphoma Other (4 FL, 1 PMBCL, 1 THRLBCL)	18 (36.7) 9 (18.4) 6 (12.2) 5 (10.2) 5 (10.2) 6 (12.2)
Select previous treatments, n (%)	
BTK inhibitor BCL-2 inhibitor BTK inhibitor + BCL-2 inhibitor Anti-CD20	27 (55.1) 9 (18.4) 9 (18.4) 46 (93.9)

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Spurgeon et al., EHA 2025. FL: follicular lymphoma; PMBCL: primary mediastinal large b-cell lymphoma; THRLBCL: t-cell/histiocyte rich large b-cell lymphoma

SGR-1505 Observed to Have a Favorable Safety Profile and Was Well-Tolerated

Common (≥10%) TEAE/TRAEs	TEAE		TRAE	
	Any grade (n, %)	Grade ≥3 (n, %)	Any grade (n, %)	Grade ≥3 (n, %)
Any TEAE	**42 (85.7)**	**23 (46.9)**	**21 (42.9)**	**12 (24.5)**
Neutrophil count decreased	10 (20.4)	10 (20.4)	3 (6.1)	3 (6.1)
Fatigue	8 (16.3)	0 (0.0)	6 (12.2)	0 (0.0)
Rash*	7 (14.3)	3 (6.1)	6 (12.2)	3 (6.1)
Blood bilirubin increased	5† (10.2)	4 (8.2)	4 (8.2)	4 (8.2)

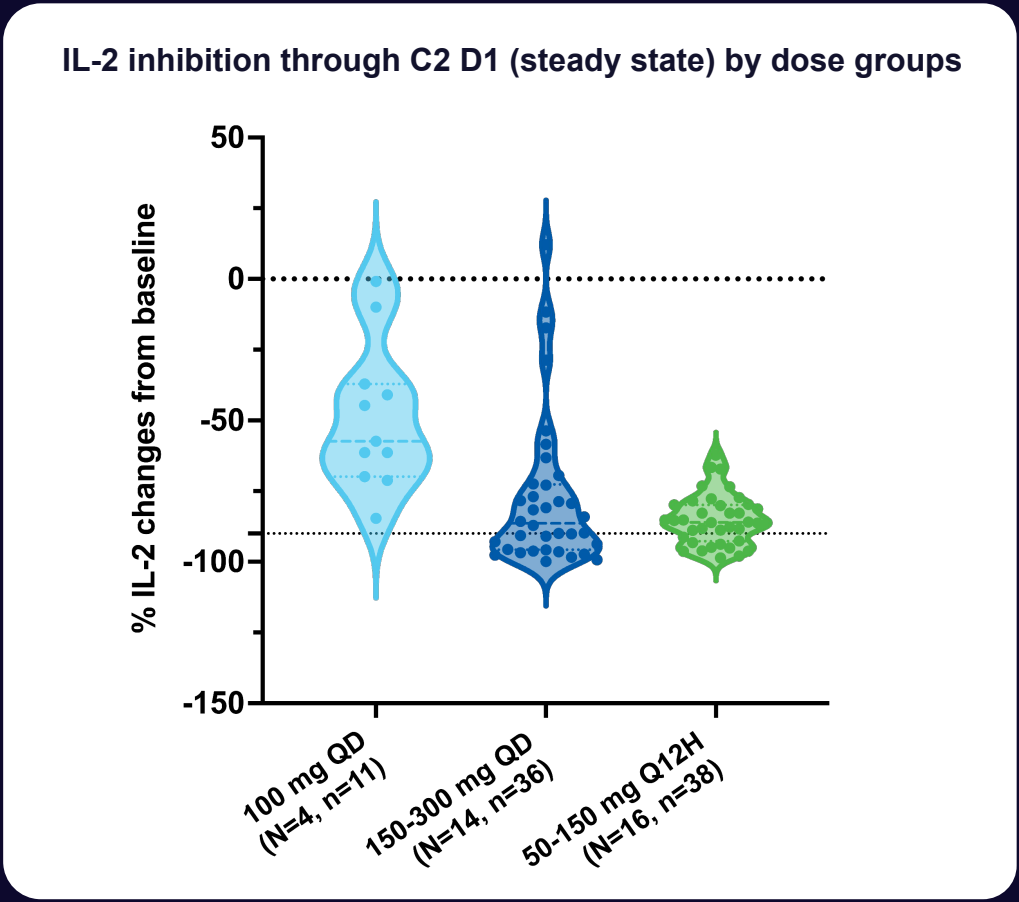
*Includes rash, papular rash, and maculo-papular rash.

† All were asymptomatic, from participants with UGT1A1 polymorphisms, and none were G4. One participant with G2 unrelated hyperbilirubinemia reported a G1 AST elevation 23 days later, when the participant was progressing radiographically.

- 43% of patients experienced ≥1 treatment-related adverse event (TRAE)
- Well-tolerated with no dose limiting toxicities or deaths due to treatment-emergent adverse events (TEAE)
- No cases of Hy's law
- All blood bilirubin increased TEAEs were asymptomatic, from participants with UGT1A1 polymorphisms, and none were G4

Spurgeon et al., EHA 2025.

IL-2 Response at Steady State Confirms Inhibition of NF-κB Signaling



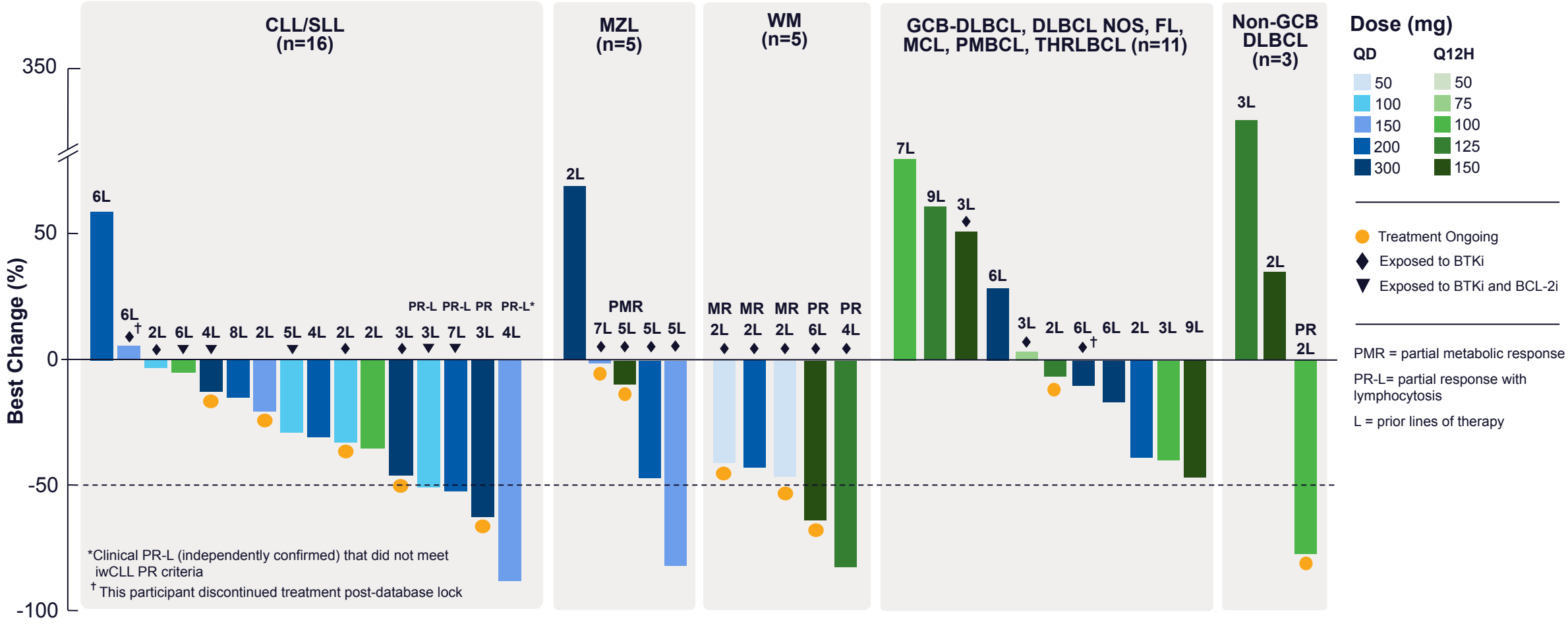
N = number of participants in the dose groups
n = number of data points in the dose groups

- SGR-1505 inhibits T-cell derived IL-2 upon *ex vivo* stimulation
  - ~90% inhibition in the majority of PD-evaluable patients treated at ≥150 mg QD and all Q12H doses at steady state
- Q12H dosing provided more sustained IL-2 inhibition compared to QD dosing
- Approximately 90% inhibition of IL-2 was observed as early as Day 8 and 15

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Spurgeon et al., EHA 2025.

Encouraging Preliminary Efficacy Across Range of B-Cell Malignancies

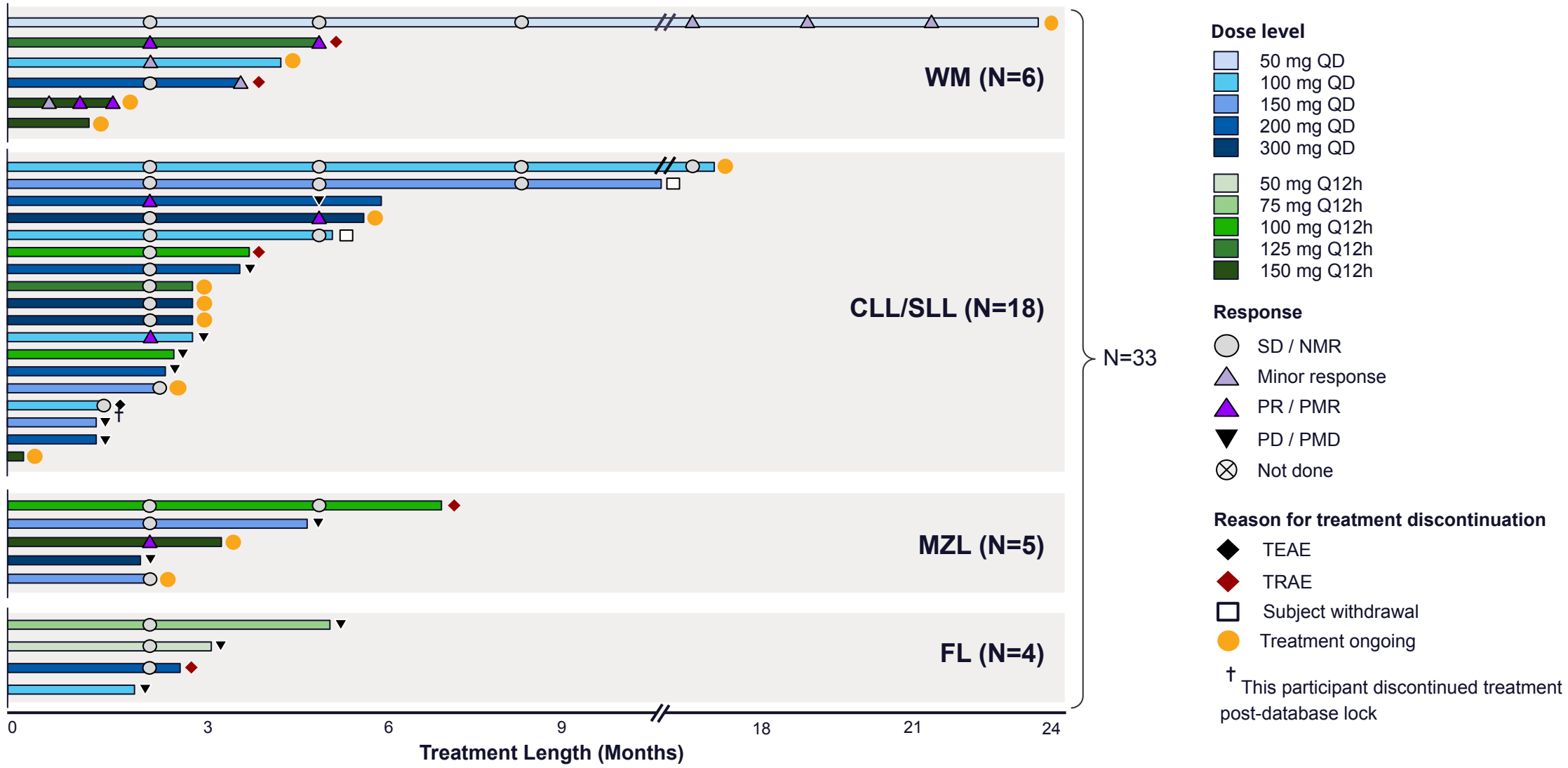


Includes 40 subjects with ≥1 follow-up disease assessment with measurable disease or IgM assessment.

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Spurgeon et al., EHA 2025.

Preliminary Duration of Treatment in Indolent Lymphomas

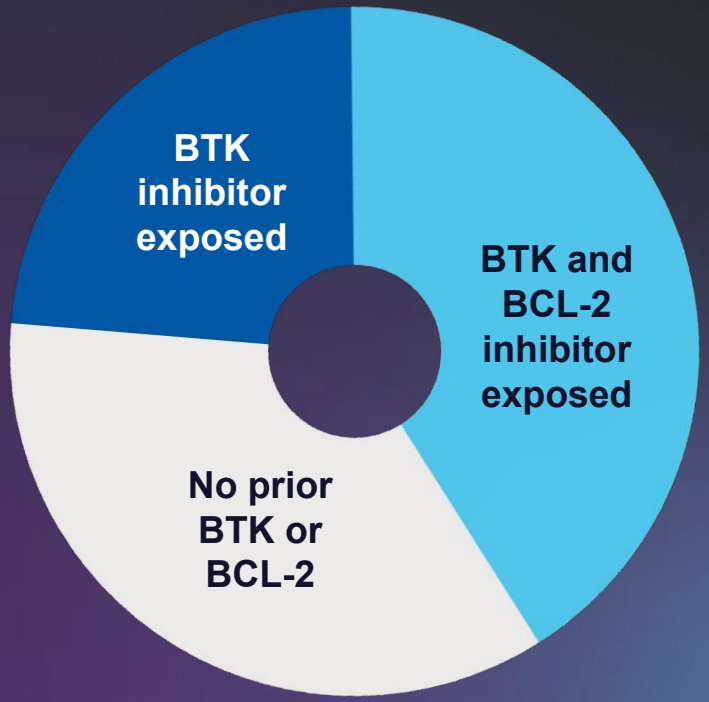


Spurgeon et al., EHA 2025.

Prior BTK Exposure in CLL/SLL Patients

- More than half of the evaluable CLL/SLL patients had been previously exposed to a BTK inhibitor
- 35% of evaluable CLL/SLL participants were double-exposed to both BTK and BCL-2 inhibitors
  - Encouraging preliminary efficacy signals in these evaluable CLL/SLL patients (2/6)

35% of evaluable CLL/SLL participants were double-exposed to BTK and BCL-2 inhibitors (n = 17)



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Spurgeon et al., EHA 2025.

Phase 1 Summary and Next Steps

Key Study Findings

- SGR-1505 observed to be well-tolerated with a favorable safety profile
- Strong target engagement
- Encouraging preliminary efficacy across range of B-cell histologies
  - Monotherapy signal in CLL and WM

Study Status and Next Steps

- Dose escalation is complete
- Recommended Phase 2 dose to be discussed with FDA later this year

Spurgeon et al., EHA 2025.

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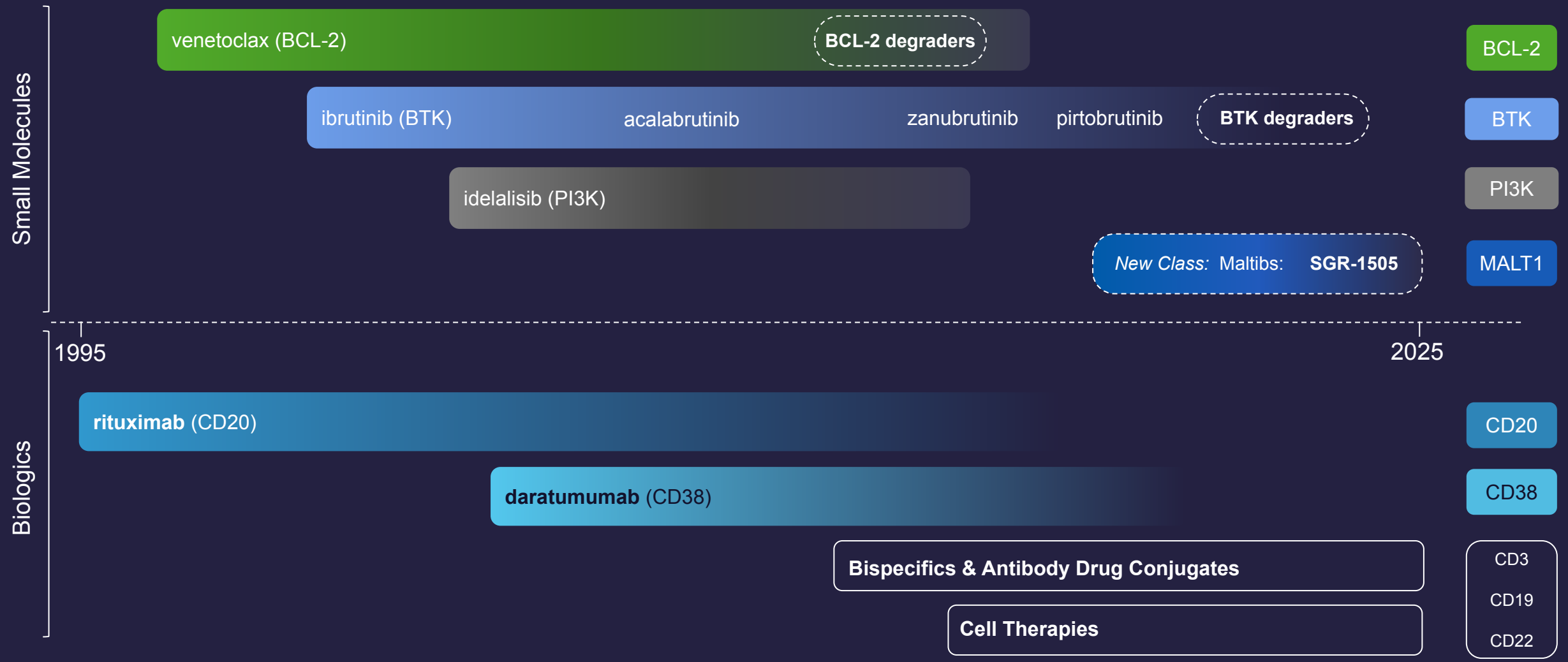


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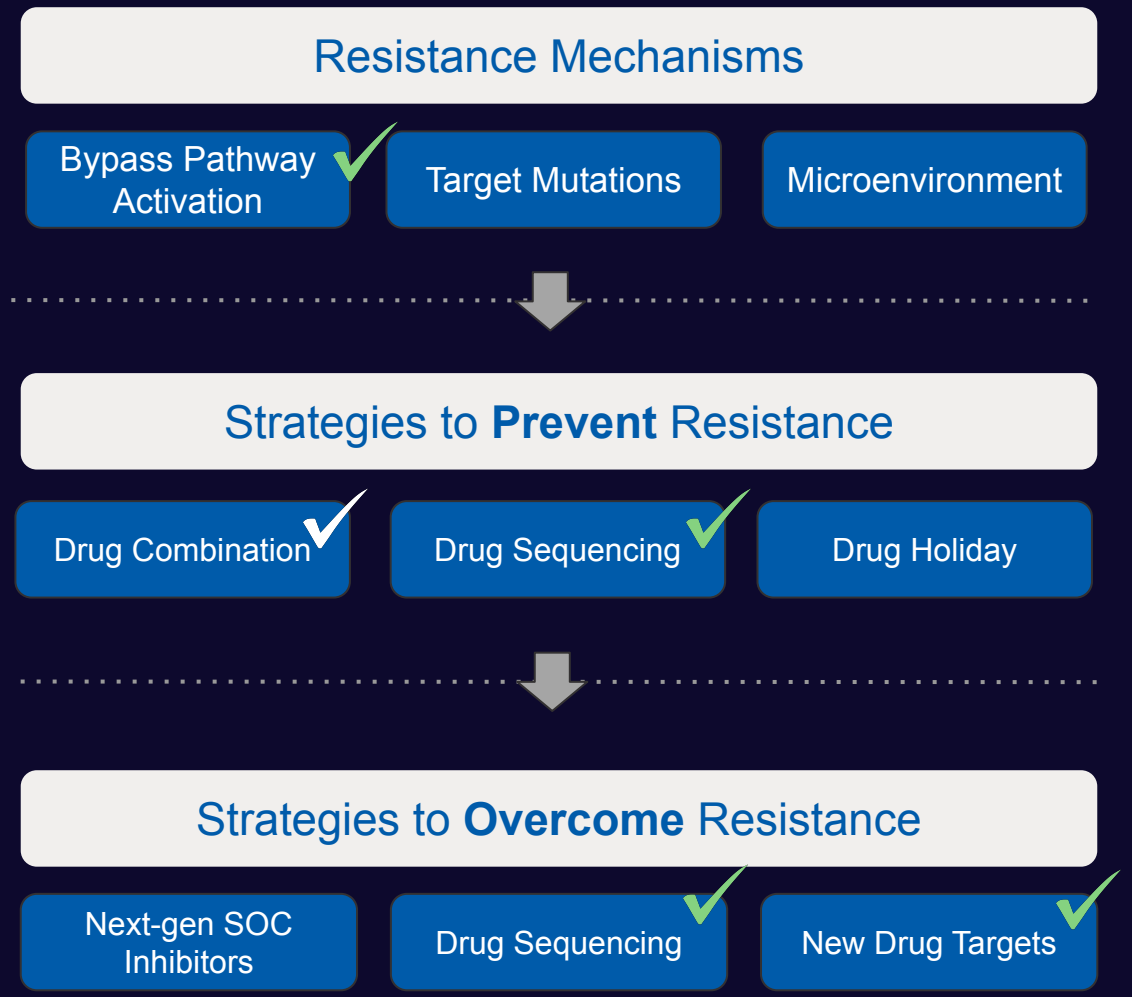


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Emerging Mechanism in the Lymphoma Therapeutics Landscape



MALT1 Opportunity in Relapsed Refractory Lymphoma

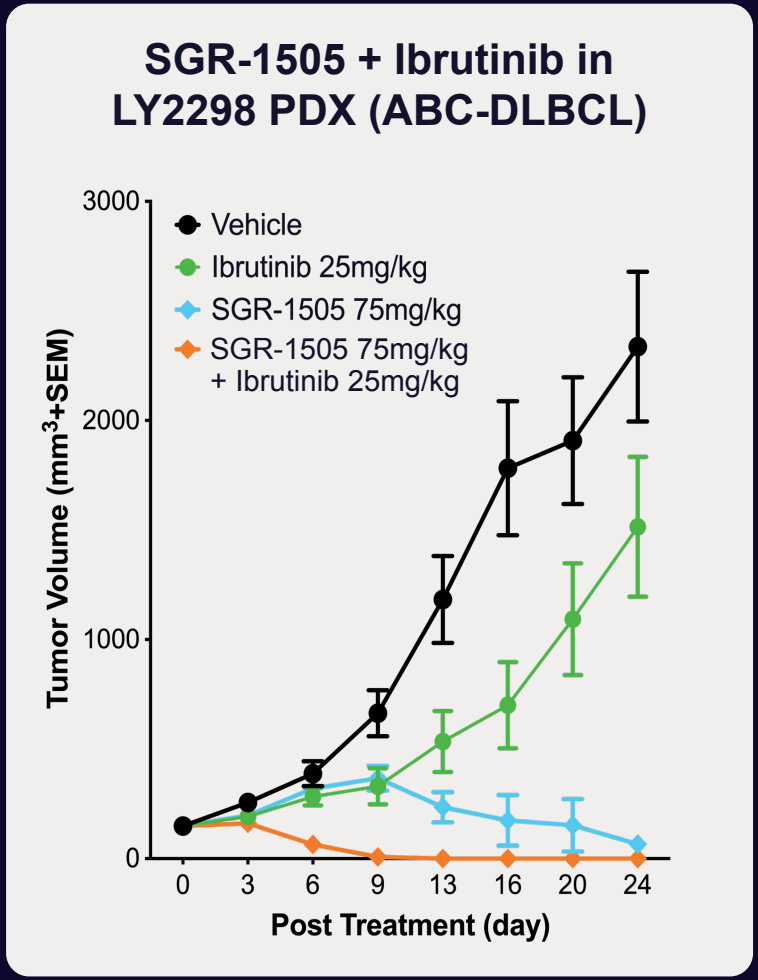


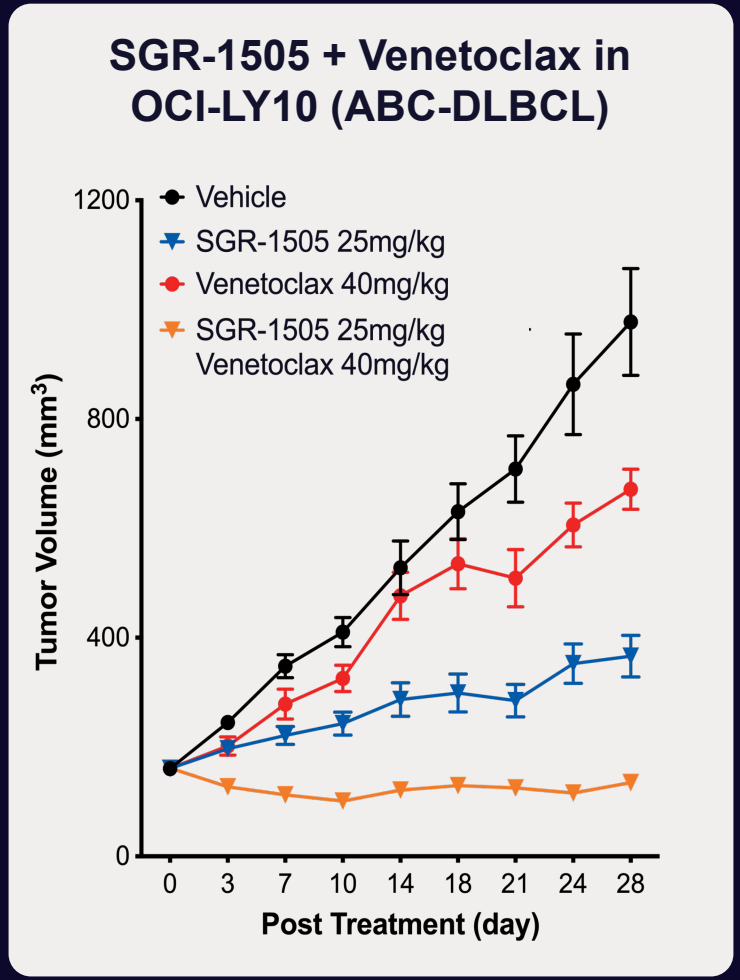
Strong Mechanistic & Therapeutic Rationale

- MALT1 is an escape mechanism in resistant patients with hyperactive NF-KB
  - SGR-1505-induced IL-2 decreases confirm pathway inhibition
- SGR-1505 is safe and clinically active in double-exposed patients
- Preclinical combination synergy for MALT1 plus BTK and/or BCL-2 activity confirmed in BTK resistant models

Skånland, Mato; Overcoming resistance to targeted therapies in chronic lymphocytic leukemia. *Blood Adv* 2021; 5 (1): 334–343.
Jiang, et al. *J Clin Invest.* 2023.

Preclinical Proof of Concept for Combination Activity



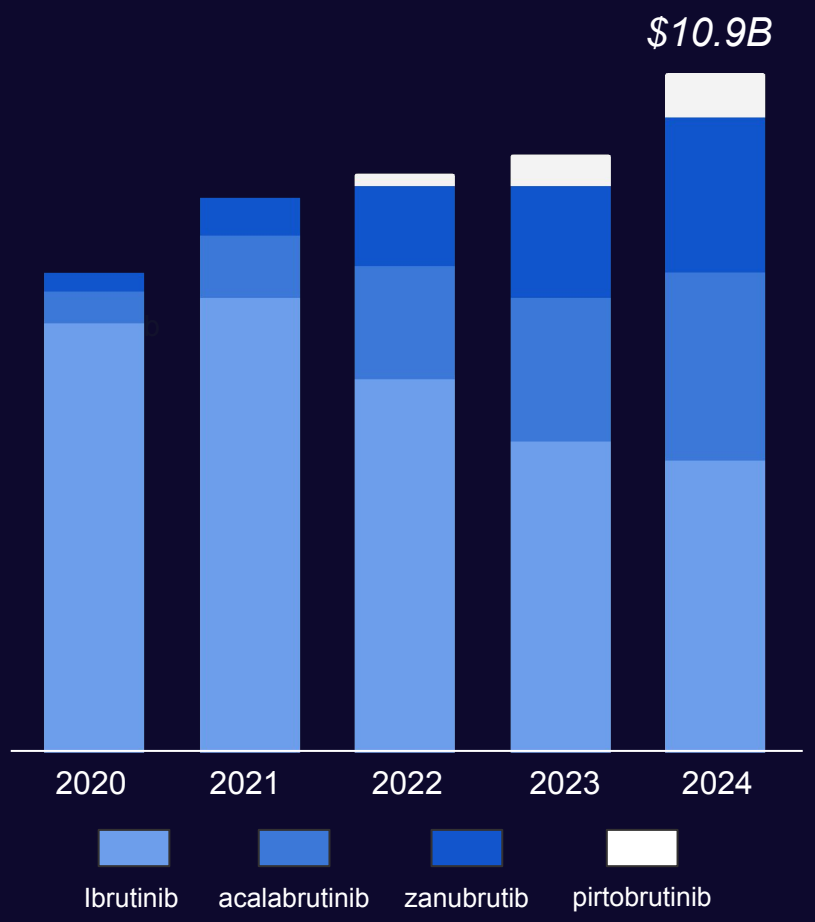


- Deeper anti-tumor activity observed in patient-derived tumors after combining SGR-1505 with BTK and BCL-2 inhibitors
- Expansion into clinical combinations supported by our current SGR-1505 clinical package

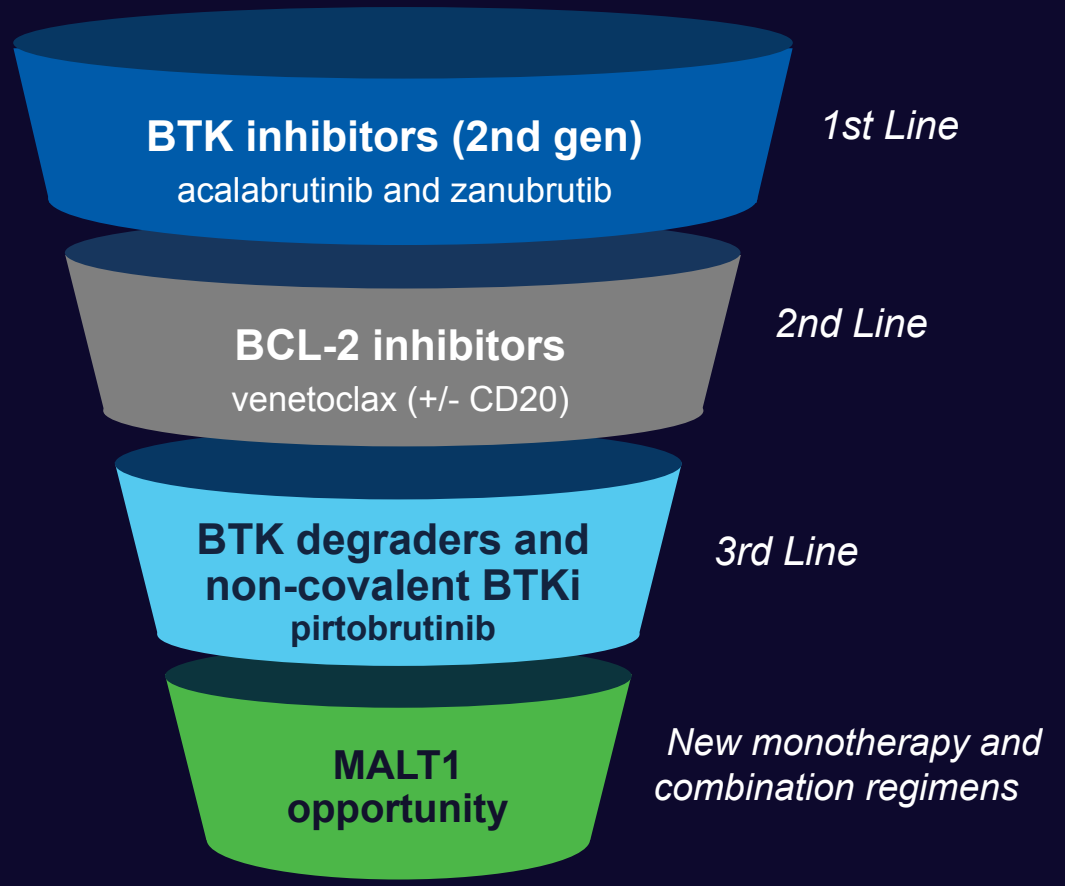
Yin et al., ASH 2021.

Limited Treatment Options for Patients with Resistance to BTK Agents Provides an Opportunity for MALT1 Inhibitors

BTK Inhibitor Sales ($ Million)

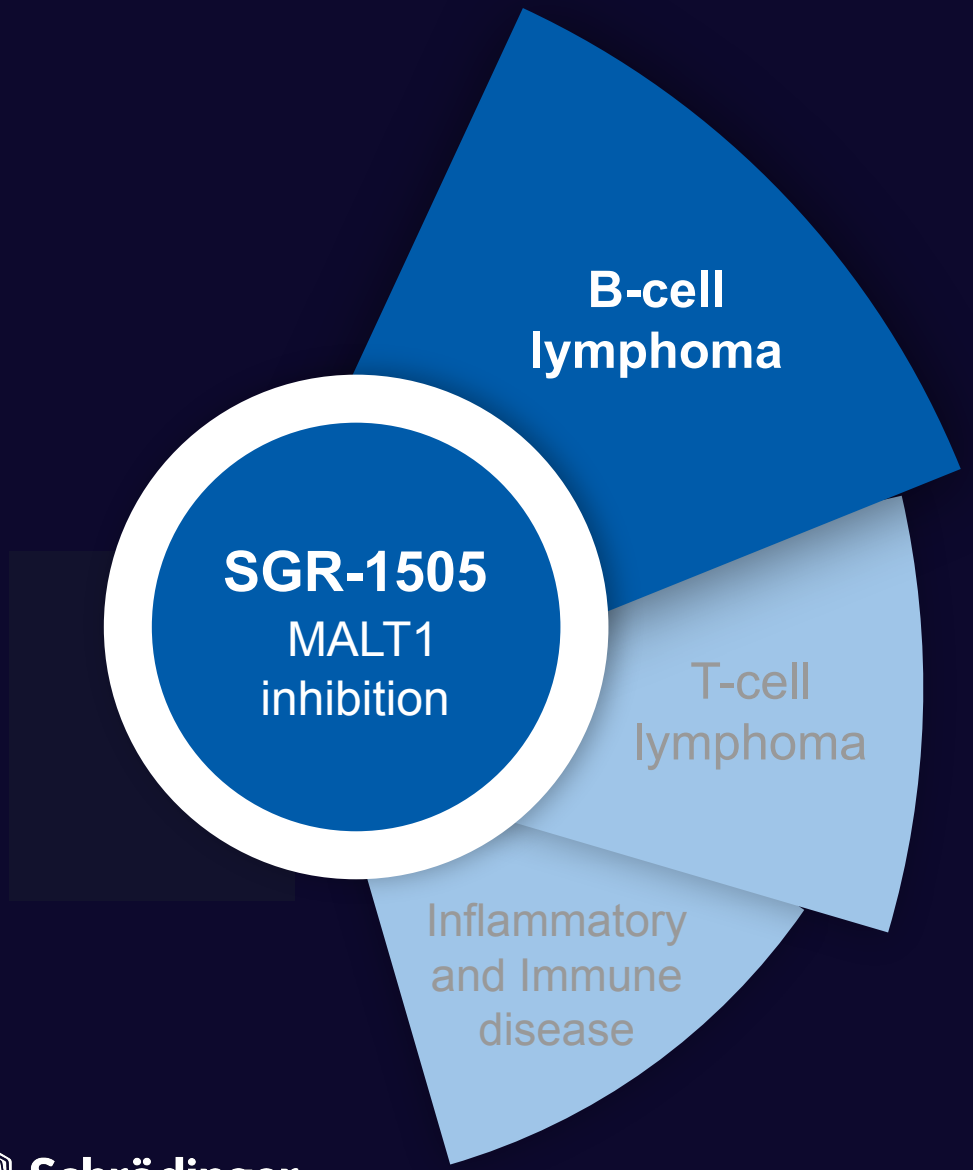


CLL Treatment Paradigm



1. Based on Evaluate Pharma and Wall Street Research reports. 2. Earnings reports from Johnson & Johnson, Abbvie, AstraZeneca, Beigene, and Eli Lilly.
3. Evaluate Pharma assumes ROW ~44% of total based on ROW:US ratio of ~80%.

SGR-1505 – Potential In Multiple Indications



Monotherapy B-Cell Malignancy Proof of Concept

- All evaluable ***Waldenstrom macroglobulinemia*** participants achieved objective responses
  - All had prior BTKi therapy as the last therapy
- Double-exposed ***CLL/SLL*** participants responded to monotherapy SGR-1505

Realizing Schrödinger's Vision

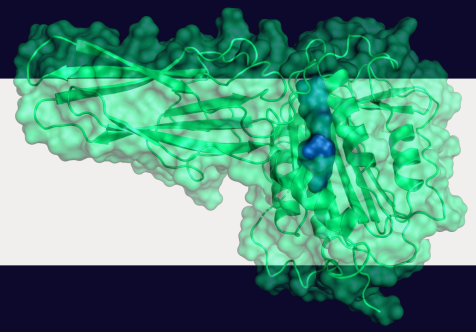
Most molecular properties were calculated with near-experimental accuracy, leading to a potential best-in-class molecule

10^{10} synthesizable molecules

Schrödinger Platform
(Physics + AI/ML)



SGR-1505



Phase 1 development

- ✓ Novel allosteric pocket inhibitor
- ✓ Optimized *in vitro* cellular potency
- ✓ Selective against common off targets
- ✓ Optimized *in vivo* anti-tumor monotherapy and combination activity
- ✓ Optimized IL-2 inhibition in human blood cells

- ✓ Favorable safety profile, well tolerated
- ✓ Confirmed IL-2 inhibition
- ✓ Encouraging clinical monotherapy activity
- ✓ Dose escalation complete
- – RP2D to be discussed with FDA

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Presentation of Initial SGR-1505 Phase 1 Clinical Data

June 12, 2025