Meeting the Needs of Patients with CLL and WM – Bexobrutideg Clinical Update from ASH 2025

American Society of Hematology

December 8, 2025

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Nurix Is Advancing a Pipeline of Proprietary and Partnered Programs in Oncology and Inflammation & Immunology

Oncology

Program	Target	Modality	Therapeutic area	Discovery	IND-Enabling	Phase 1A	Phase 1B/2	Pivotal
Bexobrutideg (NX-5948)	BTK	Degrader	B-cell malignancies					
Zelebrudomide (NX-2127)	BTK-IKZF	Degrader	B-cell malignancies					
NX-1607	CBL-B	Inhibitor of degradation	Immuno-oncology					
BRAF degrader	Pan-mutant BRAF	Degrader	Solid tumors					
Multiple	Undisclosed	Degrader	Undisclosed					
Multiple	Undisclosed	Degrader	Undisclosed					GILEAD
Multiple	Undisclosed	DAC	Undisclosed					Pfizer

Inflammation & Immunology

Program	Target	Modality	Therapeutic area	Discovery	IND-Enabling	Phase 1A	Phase 1B	Phase 2/3
Bexobrutideg (NX-5948)	BTK	Degrader	Autoimmune cytopenia in CLL patients					
NX-0479 / GS-6791	IRAK4	Degrader	Rheumatoid arthritis and other inflammatory diseases					GILEAD
NX-3911	STAT6	Degrader	Type 2 inflammatory diseases					sanofi
Undisclosed	Undisclosed	Degrader	Inflammation / autoimmune					sanofi
Multiple	Undisclosed	DAC	Inflammation / autoimmune					

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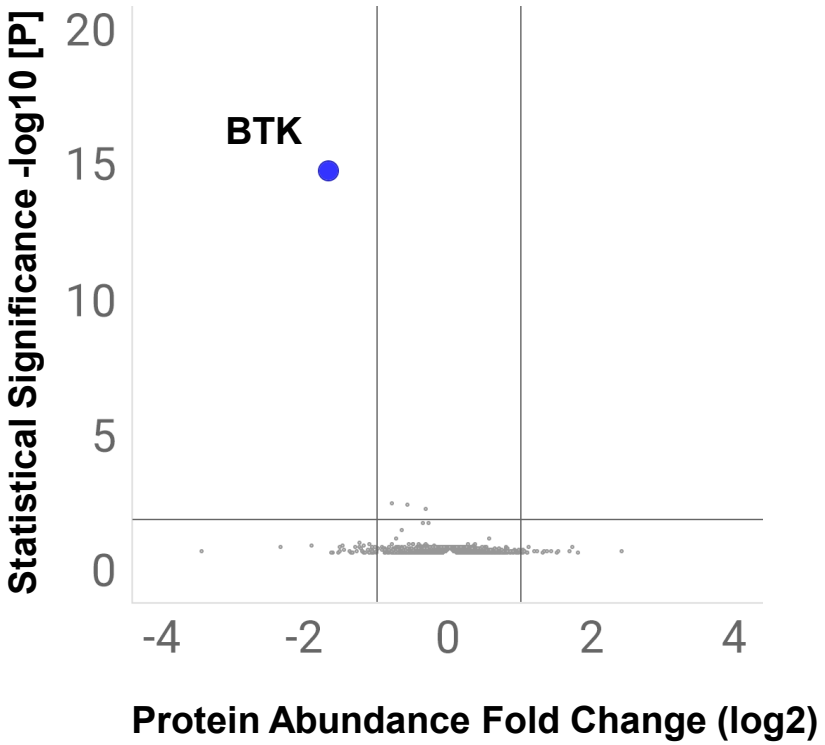
Bexobrutideg – The First “deg” with a Potential Best-in-Class Profile

Novel MOA Against a Clinically and Commercially Proven Target



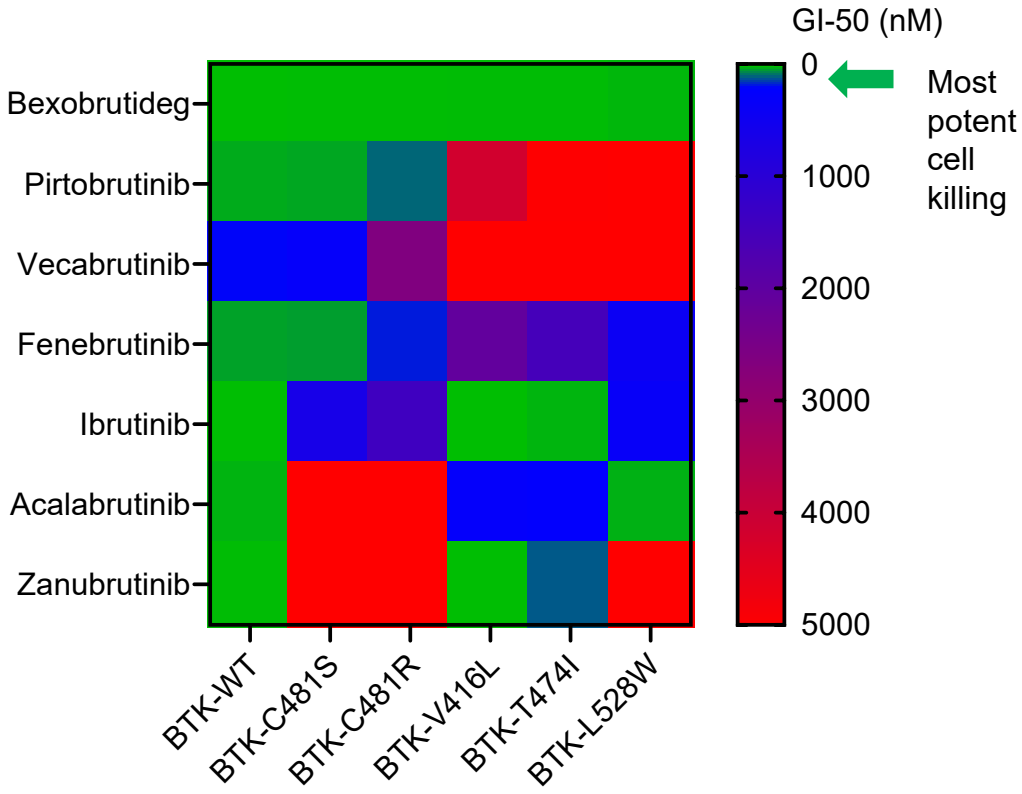
- ✓ Potent and exquisitely selective degrader of BTK
- ✓ Active against wildtype BTK and demonstrated ability to overcome treatment-emergent resistance mutations
- ✓ Addresses BTK scaffolding function unlike current BTK inhibitors
- ✓ Acts catalytically driving degradation at low free-plasma concentrations
- ✓ Crosses the blood brain barrier and demonstrated clinical activity in the CNS
- ✓ Demonstrates robust clinical activity in difficult to treat B-cell malignancies

***BTK**, Bruton's tyrosine kinase; **CNS**, central nervous system; **MOA**, mechanism of action.*

Bexobrutideg – The First "deg" with a Potential Best-in-Class Profile

Novel MOA Against a Clinically and Commercially Proven Target

Bexobrutideg shows superior mutational coverage and cell killing compared to BTK inhibitors



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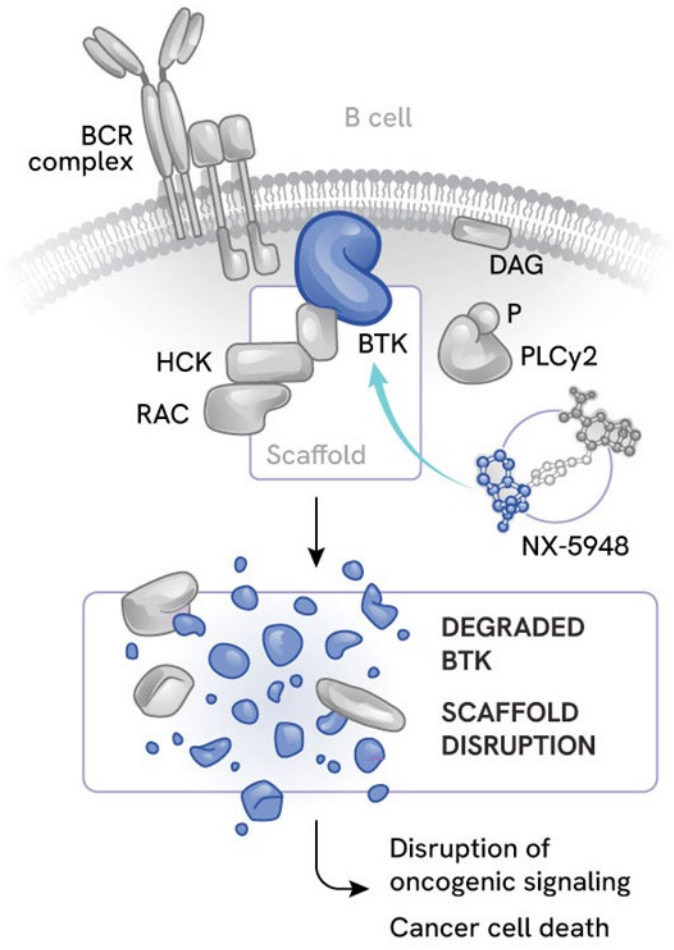

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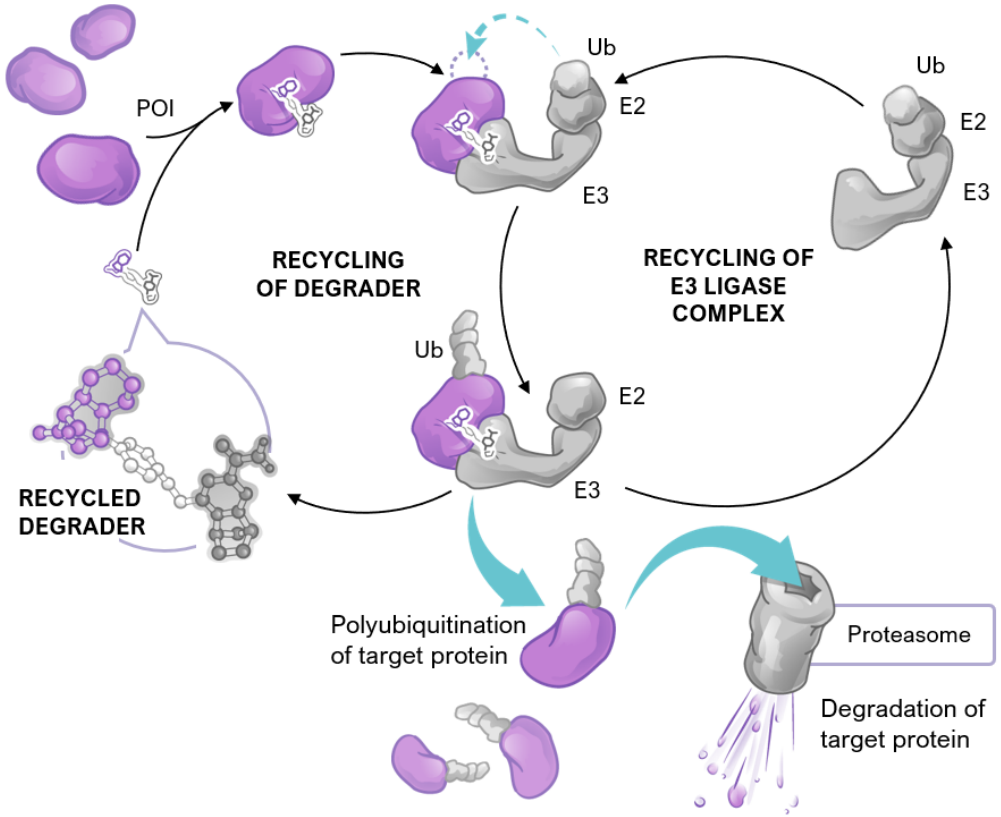
Novel MOA Against a Clinically and Commercially Proven Target

One molecule of bexobrutideg degrades thousands of BTK proteins per hour at clinically-relevant concentrations



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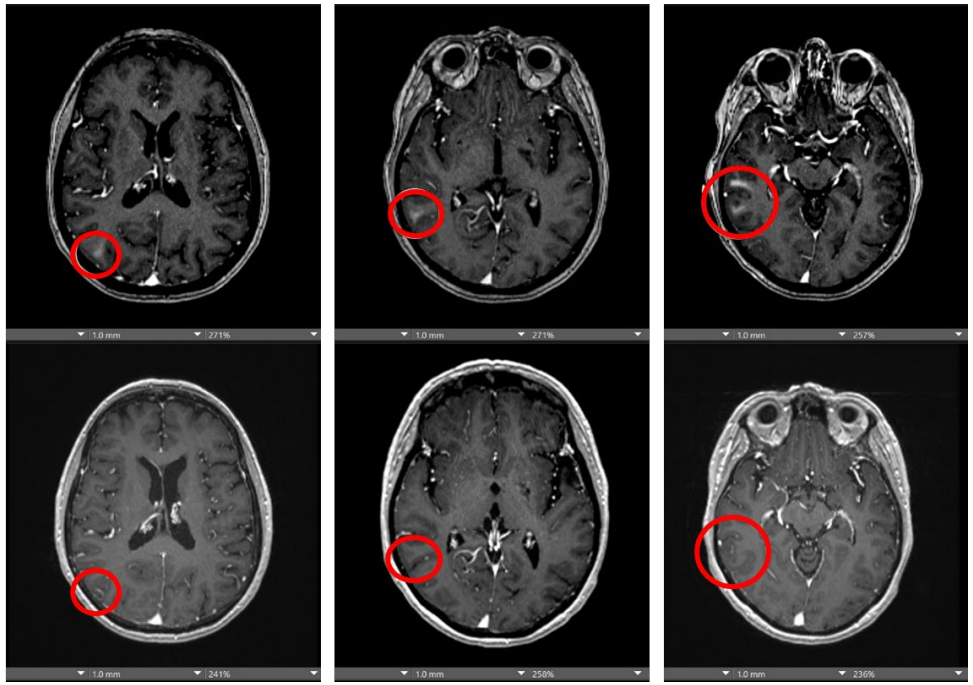
Bexobrutideg – The First “deg” with a Potential Best-in-Class Profile

Novel MOA Against a Clinically and Commercially Proven Target

Clinical activity against CLL and NHL in the central nervous system



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Bexobrutideg – The First "deg" with a Potential Best-in-Class Profile

Novel MOA Against a Clinically and Commercially Proven Target

High objective response rate and prolonged PFS in r/r CLL patients in Phase 1a

Response-evaluable patients	Phase 1a (n=47)
Objective response rate (ORR)	**83.0%**
Median progression-free survival (PFS)	22.1 months

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***BTK**, Bruton's tyrosine kinase; **CNS**, central nervous system; **MOA**, mechanism of action; **r/r CLL**, relapsed or refractory chronic lymphocytic leukemia.*

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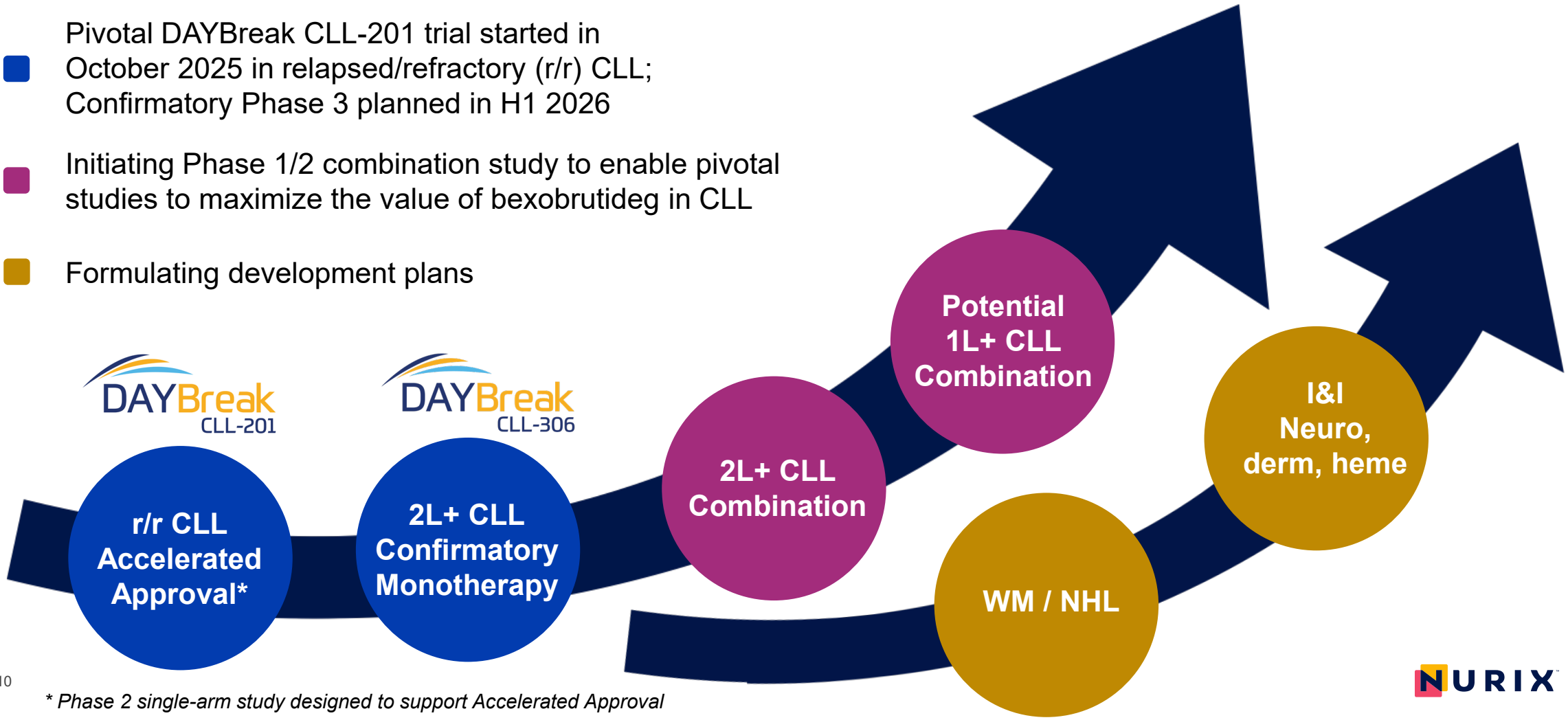
Unlocking a Wave of Clinical Benefit and Value Creation

Bexobrutideg has the potential to create significant value through its broad application across BTK mediated diseases

- Pivotal DAYBreak CLL-201 trial started in October 2025 in relapsed/refractory (r/r) CLL; Confirmatory Phase 3 planned in H1 2026
- Initiating Phase 1/2 combination study to enable pivotal studies to maximize the value of bexobrutideg in CLL
- Formulating development plans



** Phase 2 single-arm study designed to support Accelerated Approval*

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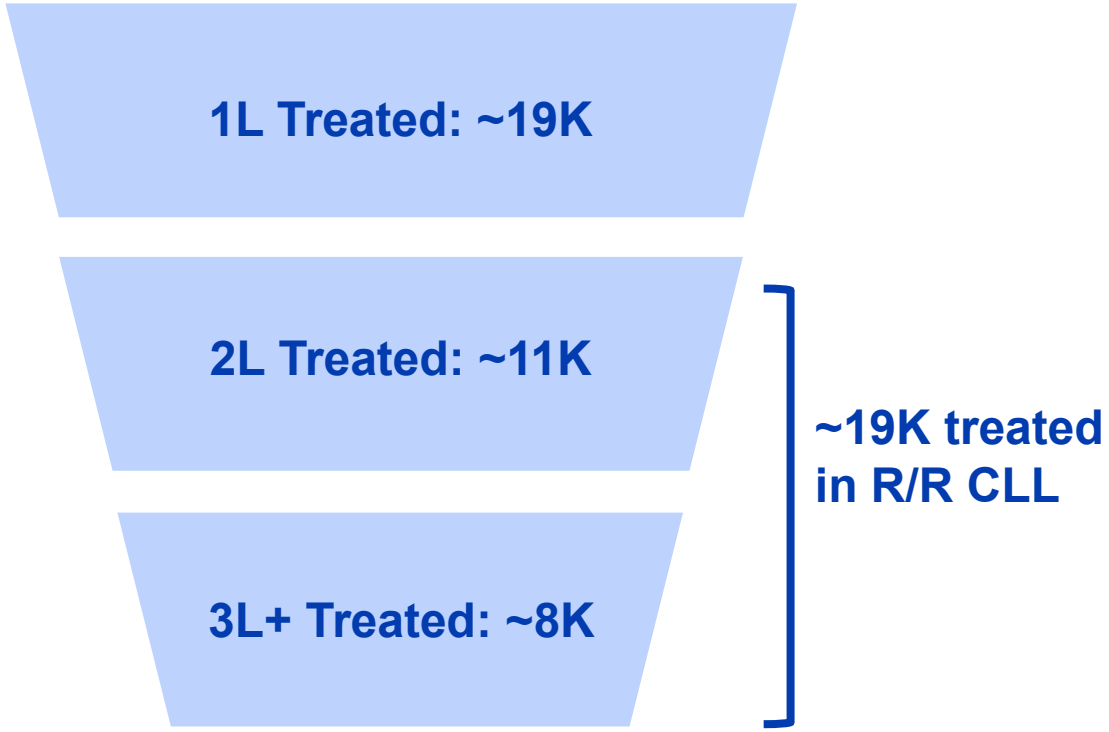
Nurix Has a Clinical Development Plan as Both a Mono- and Combo-Therapy to Address Large Segments of the CLL Market

Major Markets Drug-Treated Incidence

US, Canada, Europe, Japan, China

US Drug-Treated Incidence



Current BTK inhibitor sales annualizing at $12.5 billion with approximately $9.5 billion in CLL

Sources for US, EU4+UK, and Japan: [1] Clarivate / DRG Landscape and Forecast Research Report NHL and CLL, April 2023
For Canada, we assume similar drug treated incidence as US and adjust for the smaller Canadian population; For Europe, we adjust EU4+UK drug treated incidence for the total Europe population; For China, we assume lower drug treated incidence based on literature reference: https://ashpublications.org/ashclinicalnews/news/1473/Disease-Detectives-CLL-in-Asia

ASH 2025: Two Clinical Updates for Bexobrutideg

Saturday, December 6, 9:45 a.m. – 10:00 a.m. ET

Bexobrutideg (NX-5948), a Novel Bruton's Tyrosine Kinase (BTK) Degrader, Demonstrates Rapid and Durable Clinical Responses in Relapsed / Refractory Chronic Lymphocytic Leukemia (CLL): New and Updated Findings from an Ongoing Phase 1a/b Trial

Presenting author: Zulfa Omer, M.D.
Abstract # 86
ORAL SESSION I

Session title: Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Treatment of CLL in Relapse and in Richter Transformation

Monday, December 8, 2025, 6:00 p.m. – 8:00 p.m. ET

Bexobrutideg (NX-5948), a Novel Bruton's Tyrosine Kinase (BTK) Degrader, Shows High Clinical Activity and Tolerable Safety in Patients with Waldenström Macroglobulinemia: Updated Results from an Ongoing Phase 1a/b Study

Presenting author: Scott Huntington M.D., MPH
Abstract # 5359
POSTER SESSION III

Session title: 623. Mantle Cell, Follicular, Waldenstrom's, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological:

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Investor Call Agenda

01

Alvaro Alencar, M.D.
University of Miami Sylvester Cancer Center

Bexobrutideg (NX-5948), a Novel Bruton's Tyrosine Kinase (BTK) Degrader, Demonstrates Rapid and Durable Clinical Responses in Relapsed / Refractory Chronic Lymphocytic Leukemia (CLL): New and Updated Findings from an Ongoing Phase 1a/b Trial

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02

Paula G. O'Connor, M.D.
Chief Medical Officer, Nurix Therapeutics

Bexobrutideg Program Updates and Next Steps

03

Arthur T. Sands, M.D., Ph.D.
Chief Executive Officer, Nurix Therapeutics

2025 Highlights and 2026 Preview

Q&A

Q&A to follow

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Bexobrutideg (NX-5948), a novel Bruton's tyrosine kinase (BTK) degrader, demonstrates rapid and durable clinical responses in relapsed/refractory chronic lymphocytic leukemia (CLL): New and updated findings from an ongoing Phase 1a/b trial

[1]Zulfa Omer, [2]Alexey Danilov, [3]Francesco Forconi, [4]Talha Munir, [5,6]Mary Gleeson, [7]Nirav N. Shah, [8]Graham P. Collins, [9]Alvaro Alencar, [10]Jane Robertson, [11]Jonathon B. Cohen, [12]Karan Dixit, [13]Danielle Brander, [1]John C. Byrd, [14]Allison Winter, [15]Jeffery Smith, [16]Dima El-Sharkawi, [17]Michal Kwiatek, [18]Iwona Hus, [19]Prioty Islam, [20]Sebastian Grosicki, [21]Michael Tees, [22]Thorsten Zenz, [23]Joanna Romejko-Jarosinska, [24]Sarah Injac, [25]Wojciech Jurczak

[1]University of Cincinnati, Cincinnati, OH, USA; [2]City of Hope National Medical Center, Duarte, CA, USA; [3]University Hospital Southampton NHS Trust, Southampton, UK; [4]St James's Hospital, Leeds, UK; [5]Guy's and St Thomas' NHS Foundation Trust, London, UK; [6]Sarah Cannon Research Institute, London, UK; [7]Medical College of Wisconsin, Milwaukee, WI, USA; [8]Oxford Cancer and Haematology Centre, Churchill Hospital, Oxford, UK; [9]Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL, USA; [10]The Christie Hospital NHS Foundation Trust, Manchester, UK; [11]Emory University Winship Cancer Institute, Atlanta, GA, USA; [12]Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; [13]Duke Cancer Institute, Durham, NC, USA; [14]Cleveland Clinic Foundation, Cleveland, OH, USA; [15]The Clatterbridge Cancer Centre, Liverpool, UK; [16]Royal Marsden NHS Foundation Trust, Sutton, UK; [17]AidPort Hospital, Skórzewo (Poznań), Poland; [18]Medical University of Lublin, Lublin, Poland; [19]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [20]Medical University of Silesia, Katowice, Poland; [21]Colorado Blood Cancer Institute/Sarah Cannon Research Institute, Denver, CO, USA; [22]Department of Medical Oncology and Hematology, University of Zurich & University Hospital Zurich, Zurich, Switzerland; [23]Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [24]Nurix Therapeutics, Inc., San Francisco, CA, USA; [25]Maria Sklodowska-Curie National Research Institute of Oncology, Kraków, Poland

ASH 2025 Annual Meeting, Orlando, FL, USA, 6–9 December 2025

Bexobrutideg Phase 1a/b (NX-5948-301) Trial Design

Phase 1a/b clinical trial in adults with relapsed/refractory B-cell malignancies

Phase 1a dose escalation (fully enrolled)

CLL/SLL

- 600 mg QD
- 450 mg QD
- 300 mg QD
- 200 mg QD
- 100 mg QD
- 50 mg QD

CLL Phase 1b randomized cohort 1 (fully enrolled; 200 vs 600 mg)

- **CLL/SLL 200 mg QD Prior BTKi and BCL2i**
- **CLL/SLL 600 mg QD Prior BTKi and BCL2i**

CLL Phase 1b expansion, other cohorts (ongoing; all 600 mg)

- Non-C481S BTK mutations, prior BTKi and BCL2i
- Prior non-covalent BTKi, no BCL2i
- TP53 or 17p deletion, 2L, prior BTKi, no BCL2i
- 2L+, prior BTKi, no BCL2i
- BTKi-naïve
- With wAIHA, prior BTKi
- With CNS involvement, prior BTKi

WM/NHL

- 600 mg QD
- 450 mg QD
- 300 mg QD
- 200 mg QD
- 100 mg QD
- 50 mg QD

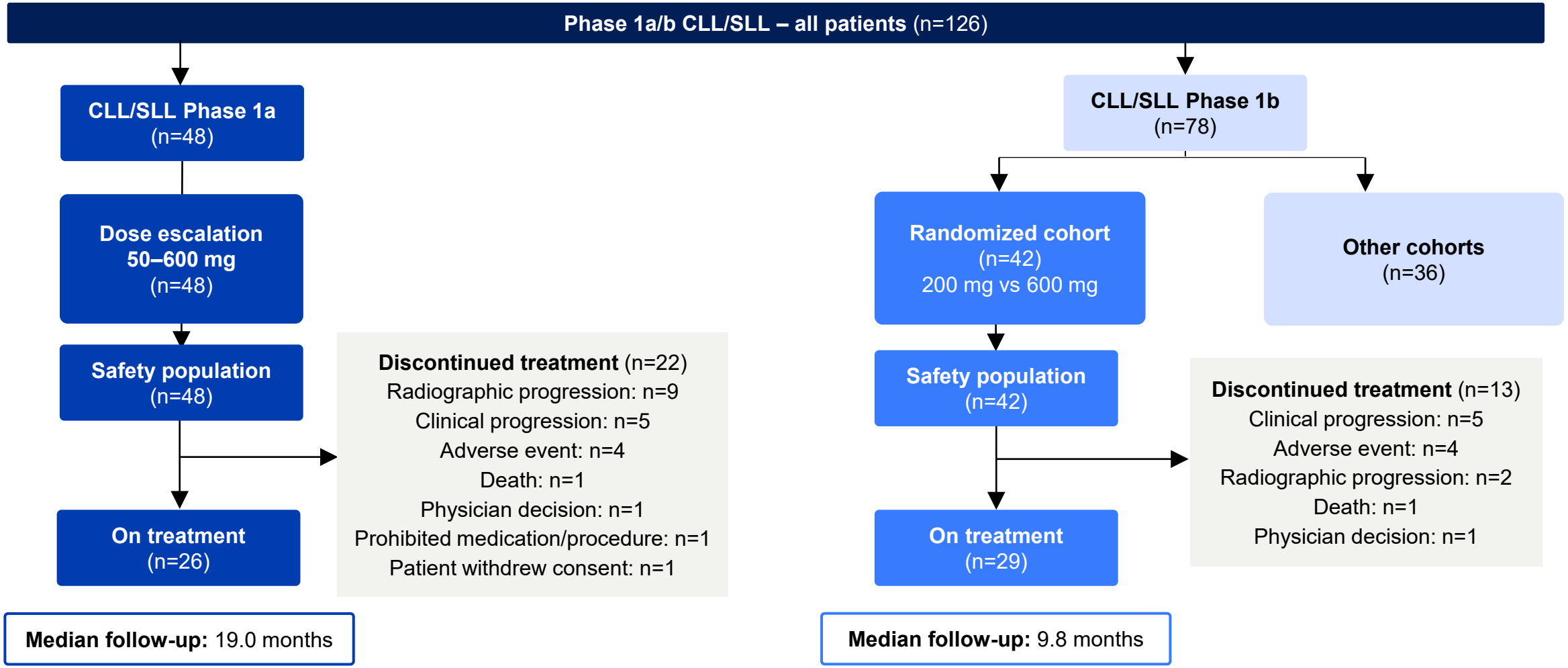
NHL/WM Phase 1b expansion cohorts (600 mg)

- **MZL** Marginal zone lymphoma
- **FL** Follicular lymphoma
- **WM** Waldenström macroglobulinemia
- **MCL** Mantle cell lymphoma
- **DLBCL** Diffuse large B-cell lymphoma
- **PCNSL** Primary CNS lymphoma

***2L+**, second line +; **BCL2i**, B-cell lymphoma 2 inhibitor; **BTKi**, Bruton's tyrosine kinase inhibitor; **CLL**, chronic lymphocytic leukemia; **CNS**, central nervous system; **NHL**, non-Hodgkin's lymphoma; **QD**, once daily; **SLL**, small lymphocytic lymphoma; **wAIHA**, warm autoimmune hemolytic anemia; **WM**, Waldenström macroglobulinemia*

NX-5948-301: CLL/SLL Patient Disposition

Multiple study cohorts with distinct doses and median follow-up



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Data cutoff: 19 Sep 2025

NX-5948-301: CLL/SLL Patient Disposition

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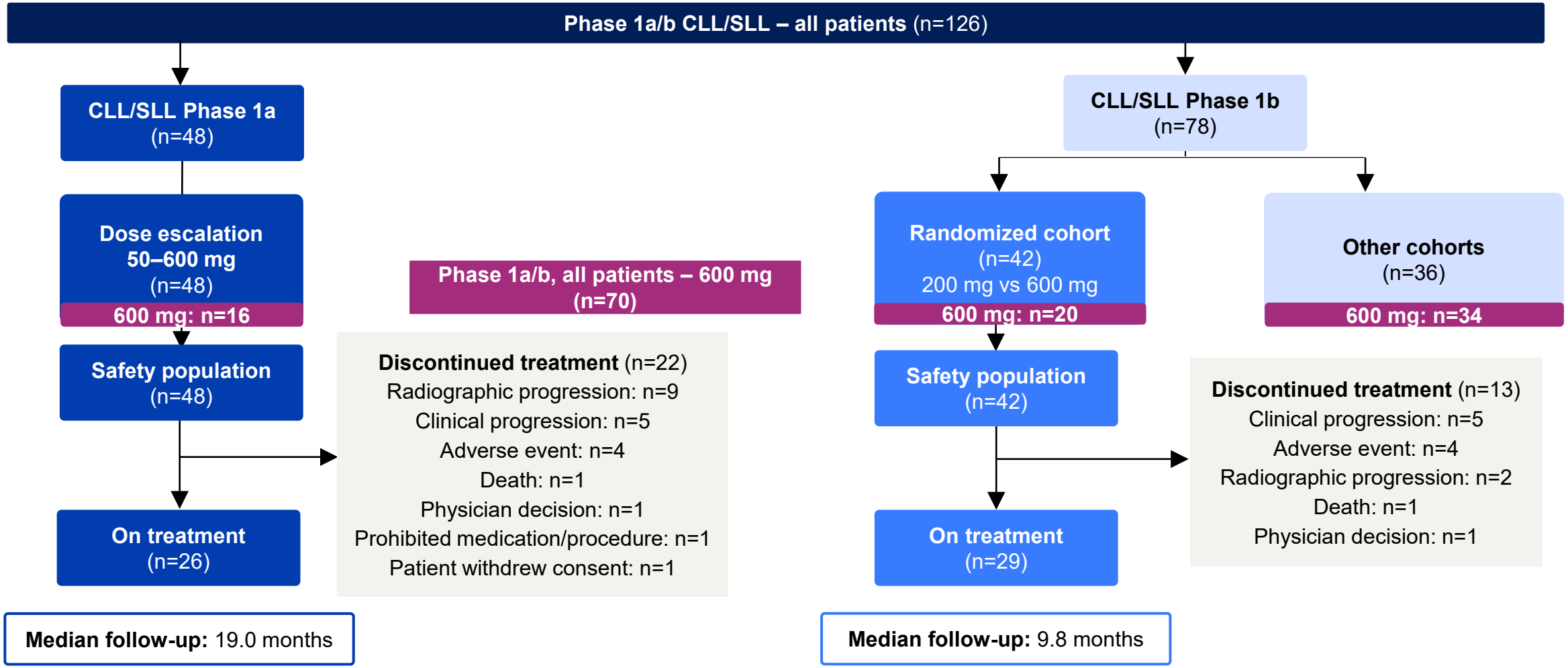


***CLL**, chronic lymphocytic leukemia; **SLL**, small lymphocytic lymphoma*

Data cutoff: 19 Sep 2025

Demographics in Overall Population (Phase 1a/b)

Population representative of CLL/SLL demographics

Characteristics	Phase 1a/b – all patients (n=126)
Median age, years (range)	69.0 (35–88)
Sex, n (%)	
Female	42 (33.3)
Male	84 (66.7)
Ethnicity, n (%)	
Hispanic or Latino	5 (4.0)
Not Hispanic or Latino	114 (90.5)
Not reported	5 (4.0)
Unknown	2 (1.6)
Race, n (%)	
Black or African American	8 (6.3)
White	110 (87.3)
Not reported	7 (5.6)
Other	1 (0.8)

***CLL**, chronic lymphocytic leukemia; **SLL**, small lymphocytic lymphoma*

Data cutoff: 19 Sep 2025

Baseline Disease Characteristics in Phase 1a/b and 1a

Multiple prior lines of therapy and a high prevalence of baseline mutations

Characteristics	Phase 1a/b – all patients (n=126)	Phase 1a (n=48)
ECOG PS, n (%)		
0	45 (35.7)	19 (39.6)
1	81 (64.3)	29 (60.4)
CNS involvement, n (%)	5 (4.0)	5 (10.4)
Median prior lines of therapy, n (range)	3.0 (1–17)	4.0 (2–12)
Previous treatments,[a] n (%)		
BTKi	108 (85.7)	47 (97.9)
cBTKi	106 (84.1)	47 (97.9)
ncBTKi	34 (27.0)	13 (27.1)
BCL2i	78 (61.9)	40 (83.3)
BTKi and BCL2i	75 (59.5)	39 (81.3)
CAR-T therapy	9 (7.1)	3 (6.3)
Bispecific antibody	5 (4.0)	1 (2.1)
PI3Ki	26 (20.6)	14 (29.2)
Chemo/chemo-immunotherapies	84 (66.7)	35 (72.9)
Mutation status,[b] n (%)	(n=111)	(n=47)
BTK	44 (39.6)	18 (38.3)
TP53	44 (39.6)	21 (44.7)
PLCG2	9 (8.1)	7 (14.9)
BCL2	8 (7.2)	6 (12.8)

[a]Patients could have received multiple prior treatments; [b]Mutations presented here were centrally sequenced

Data cutoff: 19 Sep 2025

***BCL2**, B-cell lymphoma 2; **BCL2i**, BCL2 inhibitor; **BTK**, Bruton's tyrosine kinase; **BTKi**, BTK inhibitor; **cBTKi**, covalent BTKi; **CAR-T**, chimeric antigen receptor T cell; **CNS**, central nervous system; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **ncBTKi**, non-covalent BTKi; **PI3Ki**, phosphoinositide 3-kinase inhibitor; **PLCG2**, phospholipase C gamma 2*

Overall Safety Summary in Phase 1a/b 600 mg Group vs All Patients

Tolerable safety profile, consistent between the RP2D 600 mg and overall study population

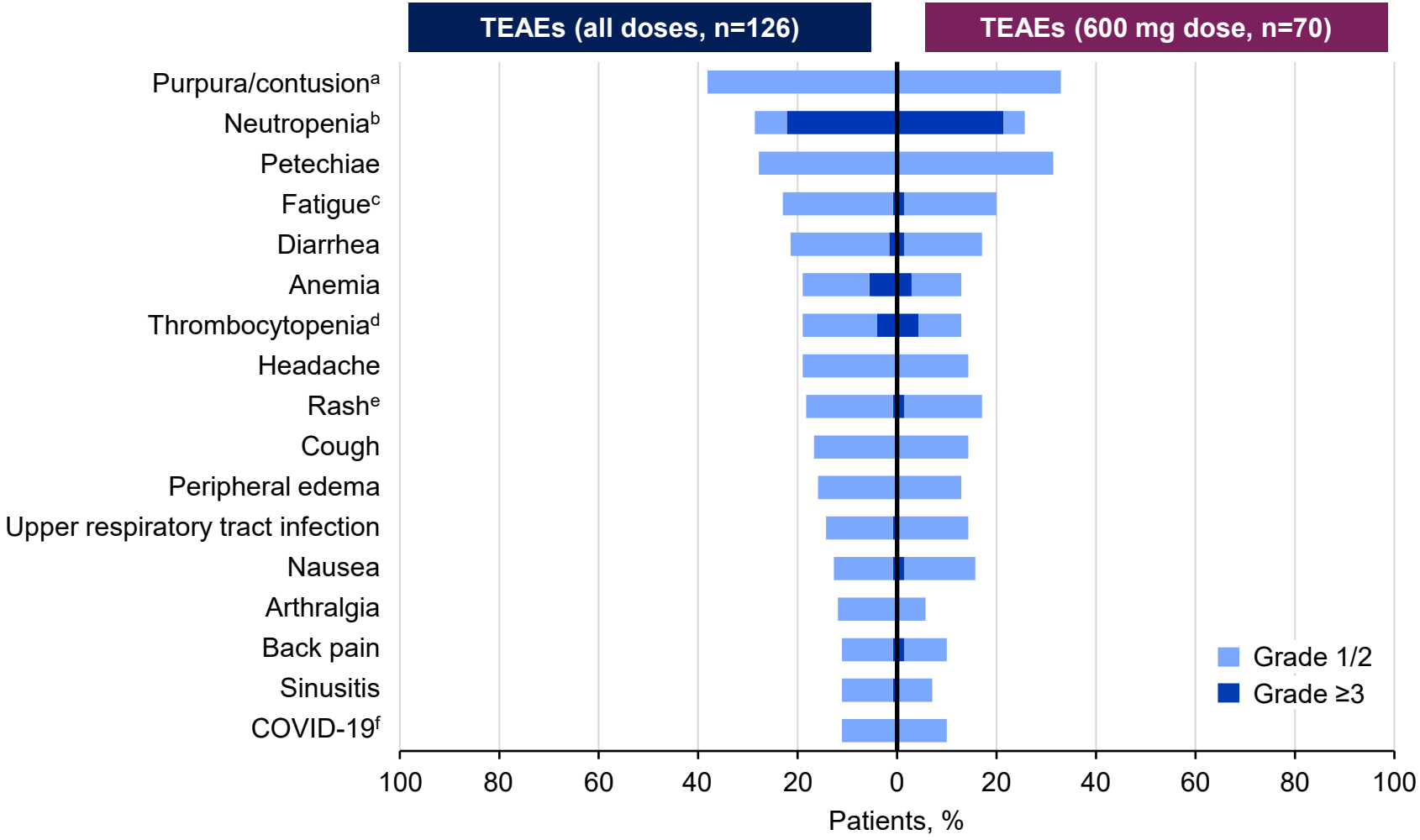
	Phase 1a/b – all patients (n=126)	Phase 1a/b 600 mg (n=70)
Any TEAE, n (%)	114 (90.5)	60 (85.7)
Treatment related	95 (75.4)	51 (72.9)
Grade ≥3	62 (49.2)	31 (44.3)
Treatment-related	31 (24.6)	18 (25.7)
SAE	27 (21.4)	10 (14.3)
Treatment-related	7 (5.6)	3 (4.3)
Grade 5[a]	3 (2.4)	1 (1.4)
Treatment-related	0	0
Leading to treatment discontinuation	8 (6.3)	4 (5.7)
Treatment-related	5 (4.0)	2 (2.9)
DLT	0	0
Median duration of treatment, months (range)	7.1 (0.0–32.3)	3.6 (0.0–18.0)

[a]*Grade 5 AEs: pulmonary embolism; death not otherwise specified; pneumonia*
***AE**, adverse event; **DLT**, dose-limiting toxicity; **RP2D**, recommended Phase 2 dose; **SAE**, serious AE; **TEAE**, treatment-emergent AE*

Data cutoff: 19 Sep 2025

TEAEs in ≥10% in Phase 1a/b 600 mg Group vs All Patients

Comparable AE profile for patients at the RP2D 600mg dose and overall population



- Tolerable safety profile consistent with prior disclosures
- No dose-limiting toxicities
- No systemic fungal infections or Grade 4 infections of any kind reported
- Single event of new onset atrial fibrillation consistent with the rate in the age-matched general population
- 3 Grade 5 AEs (death not otherwise specified; pulmonary embolism; pneumonia; all deemed not related to bexobrutideg)

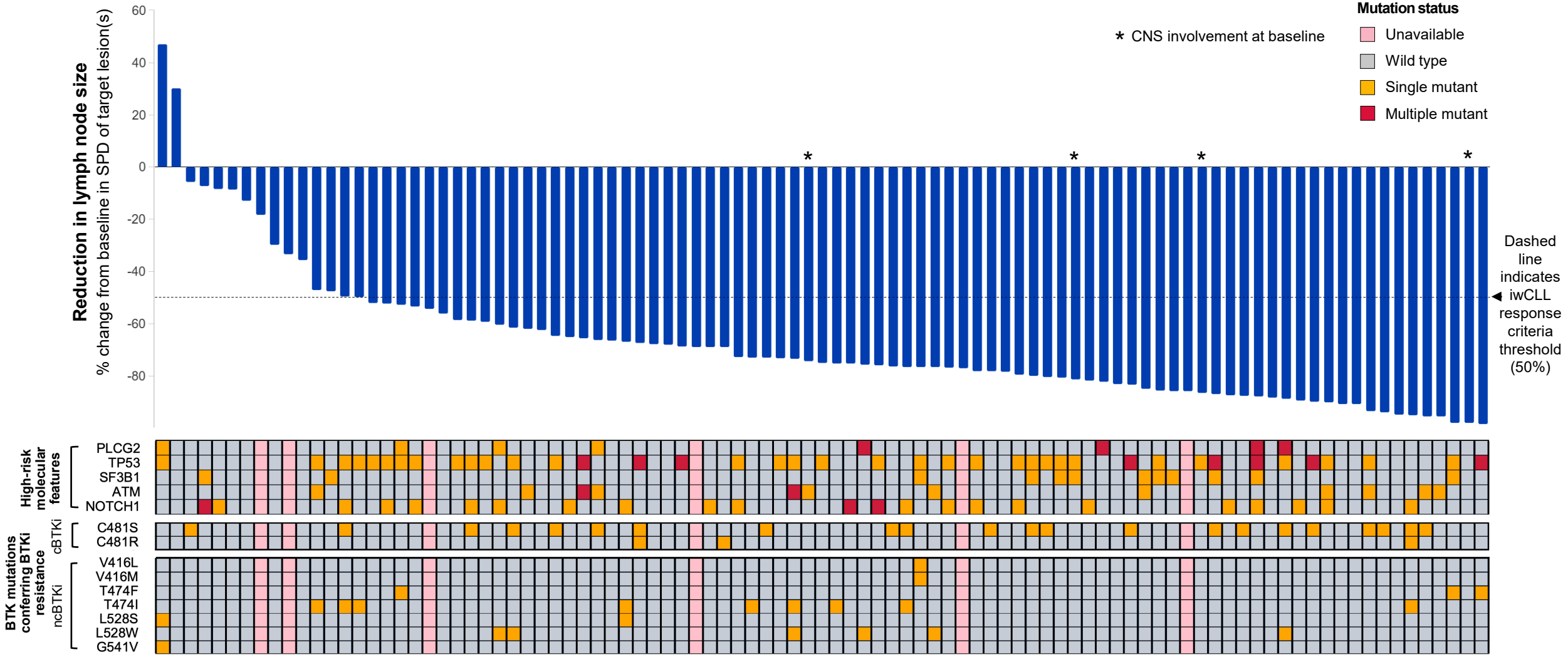
[a]Purpura/contusion includes episodes of contusion or purpura; [b]Aggregate of 'neutrophil count decreased' or 'neutropenia'; [c]Fatigue was transient; [d]Aggregate of 'thrombocytopenia' and 'platelet count decreased'; [e]Aggregate of 'rash' and 'rash maculopapular' and 'rash pustular'; [f]Aggregate of 'COVID-19' and 'COVID-19 pneumonia'

Data cutoff: 19 Sep 2025

***AE**, adverse event; **NOS**, not otherwise specified; **RP2D**, recommended Phase 2 dose; **TEAE**, treatment-emergent adverse event*

Reduction in Lymph Node Size in Phase 1a/b Overall Population[a]

Clinical activity across patients with BTK mutations,[b] high-risk molecular features and/or CNS involvement



[a]*Waterfall plot includes patients with measurable lymph node status (n=93); mutations were reported at VAF >5%;* [b]*Patients could have no mutations, a single mutation, or multiple mutations*

***ATM**, ataxia-telangiectasia mutated; **BTK**, Bruton's tyrosine kinase; **BTKi**, BTK inhibitor; **cBTKi**, covalent BTKi; **CLL**, chronic lymphocytic leukemia; **CNS**, central nervous system; **iwCLL**, International Workshop on CLL; **ncBTKi**, non-covalent BTKi; **NOTCH1**, neurologic locus notch homolog protein 1; **PLCG2**, phospholipase C gamma 2; **SPD**, sum of products diameters*

Data cutoff: 19 Sep 2025

Overall Response Rate in Phase 1a Across All Dose Levels (n=47)

Encouraging ORR and long median duration of response

Response-evaluable patients	Phase 1a (n=47)
Objective response rate (ORR),[a] % (95% CI)	**83.0 (69.2–92.4)**
Disease control rate (DCR),[b] % (95% CI)	95.7 (85.5–99.5)
Best response,[c] n (%)	
Complete response (CR)	2 (4.3)
Nodal partial response (nPR)	1 (2.1)
Partial response (PR/PR-L)	36 (76.6)
Stable disease (SD)	6 (12.8)
Progressive disease (PD)	2 (4.3)
Median follow-up,[d] months (range)	19.0 (13.5–32.3)
Median duration of response, months (95% CI)	20.1 (12.2–NE) (n=39)

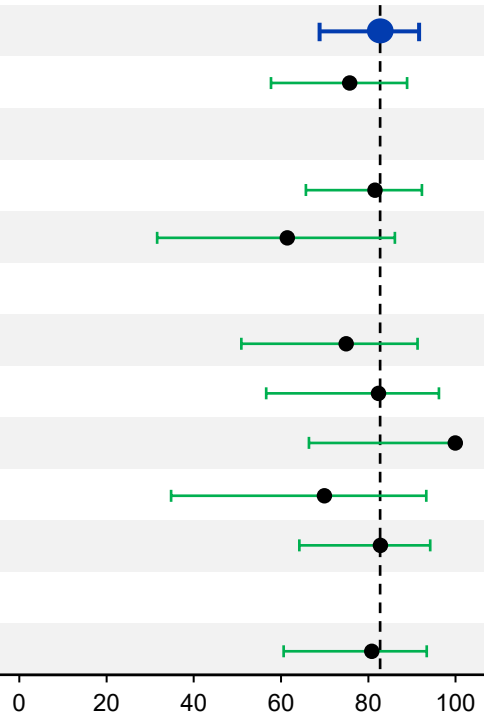
[a]Objective response rate includes CR + nPR + PR + PR-L; [b]Disease control rate includes CR + nPR + PR/PR-L + SD; [c]Percentages are based on the number of patients dosed who had at least one post-baseline disease assessment or documented clinical PD; [d]Time from treatment start to data cutoff
***CI**, confidence interval; **PR-L**, partial response with lymphocytosis*

Data cutoff: 19 Sep 2025

Overall Response Rate by Subgroup in Phase 1a (n=47)

Clinically meaningful response rate observed across difficult-to-treat subgroups

Subgroup	Number of patients with a response/total number[a]	Objective response rate, % (95% CI)
ORR in Phase 1a population	39/47	83 (69–92)
Discontinued due to PD on any prior BTKi	25/33	76 (58−89)
Prior therapy		
Prior BCL2i and BTKi	31/38	82 (66−92)
Prior non-covalent BTKi	8/13	62 (32−86)
Mutations		
TP53 mutation	15/20	75 (51−91)
Any baseline BTK mutation	14/17	82 (57−96)
C481 BTK mutation	9/9	100 (66−100)
L528/T474/V416/G541 BTK mutation	7/10	70 (35−93)
Wild-type BTK	24/29	83 (64−94)
Prior lines of systemic therapies received		
≥4 prior lines	21/26	81 (61−93)



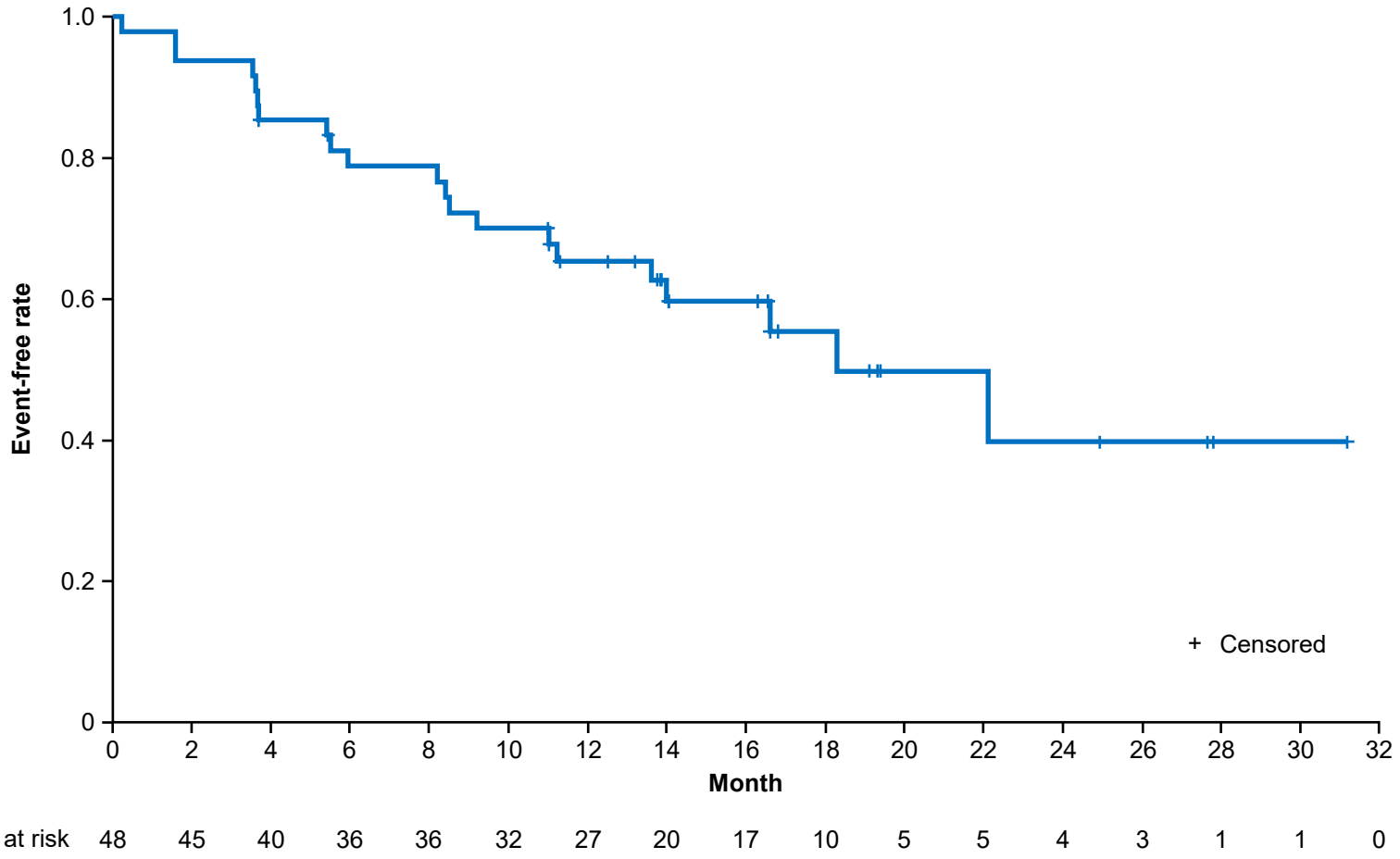
[a]*Total number of response-evaluable patients*

***BCL2i**, B-cell lymphoma 2 inhibitor; **BTK**, Bruton's tyrosine kinase; **BTKi**, BTK inhibitor; **CI**, confidence interval; **ORR**, objective response rate; **PD**, progressive disease*

Data cutoff: 19 Sep 2025

PFS in Phase 1a Across All Dose Levels (n=48)

Median PFS of 22.1 months in study population with longest follow-up



PFS summary	
	n=48
Median PFS, months (95% CI)	22.1 (11.2–NE)
Median PFS follow-up, months (95% CI)	16.6 (14.0–19.3)

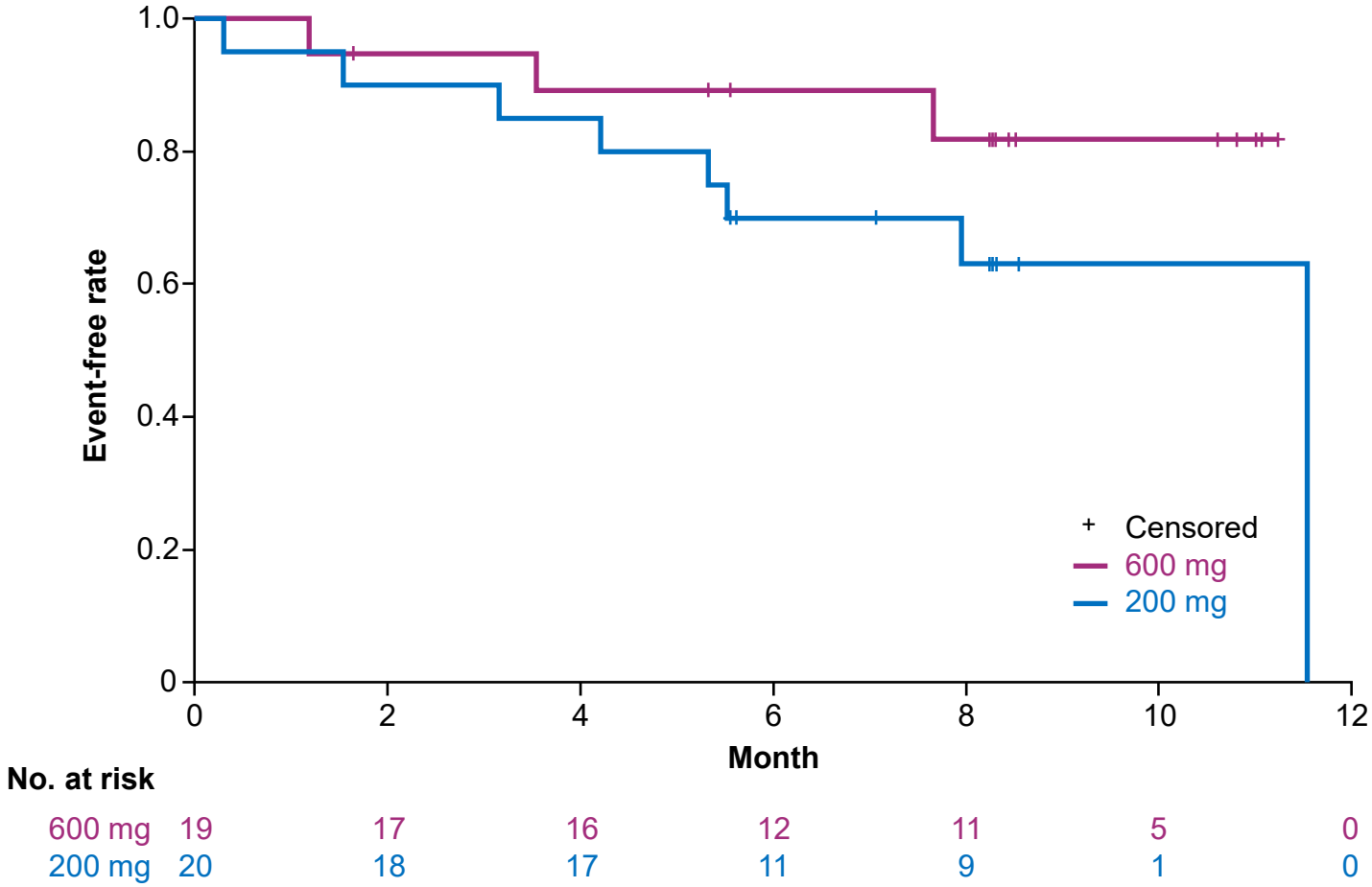
Median for PFS by Kaplan–Meier method; median PFS follow-up is by reverse Kaplan–Meier method;
***CI**, confidence interval; **NE**, not evaluable; **PFS**, progression-free survival*

Data cutoff: 19 Sep 2025

Preliminary Efficacy in Phase 1b Randomized Cohort of 200 mg vs 600 mg

Higher ORR and PFS at the RP2D 600 mg dose

Response-evaluable patients	200 mg (n=19)	600 mg (n=18)
Objective response rate,[a] % (95% CI)	73.7 (48.8–90.9)	83.3 (58.6–96.4)
Disease control rate,[b] % (95% CI)	94.7 (74.0–99.9)	100.0 (81.5–100.0)



[a]*Objective response rate includes CR + nPR + PR + PR-L;* [b]*Disease control rate includes CR + nPR + PR/PR-L + SD*
***CI**, confidence interval; **CR**, complete response; **nPR**, nodal partial response; **ORR**, objective response rate; **PFS**, progression-free survival; **PR**, partial response; **PR-L**, partial response with lymphocytosis; **RP2D**, recommended Phase 2 dose*

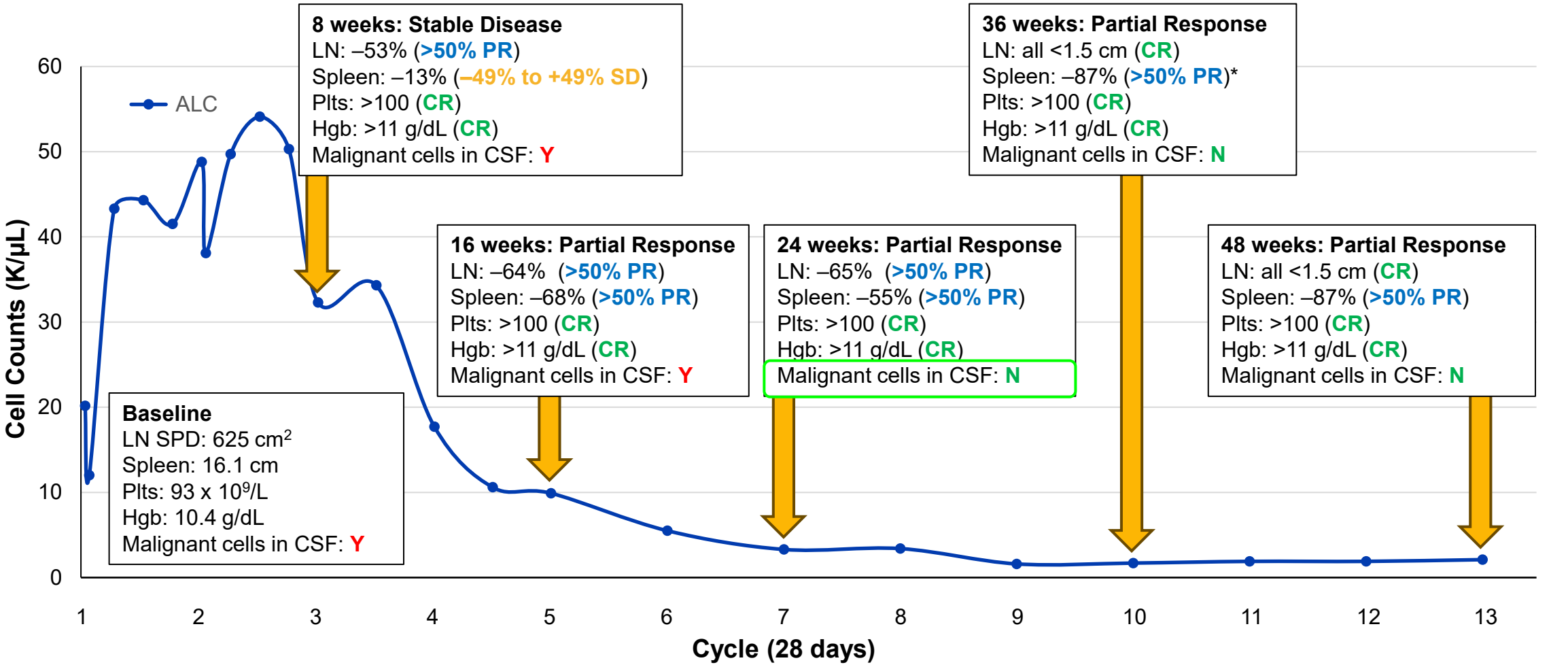
Data cutoff: 19 Sep 2025

Conclusions

- In this Phase 1a/b trial, bexobrutideg (NX-5948), a novel BTK degrader with high selectivity for BTK, was well tolerated in a heavily pretreated population of patients with relapsed/refractory CLL/SLL:
  - Tolerable safety profile consistent with prior disclosures, and consistent between the RP2D 600 mg and overall trial population
- In the Phase 1a portion of the trial with a median follow-up of 19 months:
  - Bexobrutideg demonstrated an ORR of 83% with a CR rate of 4.3%
  - Median DOR was 20.1 months
  - Median PFS was 22.1 months across all doses (50–600 mg) with data continuing to mature
  - High response rates were observed in the overall population including those in difficult-to-treat subgroups with baseline BTK mutations, high-risk molecular features and CNS involvement
- In the Phase 1b portion of the trial:
  - A randomized cohort, conducted in accordance with Project Optimus, was fully enrolled:
    - ✓ higher ORR and superior PFS were observed at the 600 mg dose, underpinning its selection as the RP2D
  - Non-randomized cohorts in CLL subsets of interest, treated at the RP2D dose, are ongoing
- **Based on the totality and consistency of safety and efficacy findings, including the Phase 1b randomized controlled cohort, the RP2D of 600 mg has been selected. Bexobrutideg will be evaluated in the ongoing pivotal Phase 2 DAYBreak CLL-201 and planned Phase 3 DAYBreak CLL-306 trials**

***BTK**, Bruton's tyrosine kinase**; CLL,** chronic lymphocytic leukemia; **CNS**, central nervous system; **CR**, complete response; **DOR**, duration of response; **ORR**, objective response rate; **RP2D**, recommended Phase 2 dose; **PFS**, progression-free survival; **SLL**, small lymphocytic lymphoma*

Patient with CLL with CNS Involvement Treated with Bexobrutideg Showed Deepening Response over Time Approaching Complete Response



Dose escalated to 600 mg, patient remains on study as of September 19, 2025

**Normal spleen: 13 cm; 36-48 week: 13.4 cm*
The overall response assessments are from the investigators while the individual parameter response assessment criteria are calculated per iwCLL from the data entered
ALC, Absolute lymphocyte count; CSF, cerebrospinal fluid; Hgb, hemoglobin; LN, lymph nodes; Plts, platelets

NX-5948-301 Ph1a/b clinical study
Data cutoff: 10 June 2024

Bexobrutideg (NX-5948), a Novel Bruton's Tyrosine Kinase (BTK) Degrader, Shows High Clinical Activity and Tolerable Safety in Patients with Waldenström Macroglobulinemia: Updated Results from an Ongoing Phase 1a/b Study

[1]Nirav N. Shah, [2]Scott Huntington, [3]David Lewis, [4]Tahla Munir, [5]Graham P. Collins, [6]Alvaro Alencar, [7]Kim Linton, [8]Zulfa Omer, [9]Dima El-Sharkawi, [10,11]Mary Gleeson, [12]Pam McKay, [13]Jeanette K. Doorduijn, [14]Jeffery Smith, [15]Daniel Morillo, [16]Pau Abrisqueta, [17]Sarah Injac, [18]Astrid Pulles

[1]Medical College of Wisconsin, Milwaukee, WI, USA; [2]Yale School of Medicine, New Haven, CT, USA; [3]Derriford Hospital, Plymouth, UK; [4]St. James's Hospital, Leeds, UK; [5]Oxford Cancer and Haematology Centre, Churchill Hospital, Oxford, UK; [6]Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL, USA; [7]Division of Cancer Sciences, The University of Manchester, Manchester, UK; [8]University of Cincinnati, Cincinnati, OH, USA; [9]Royal Marsden NHS Foundation Trust, Sutton, UK; [10]Guy's and St Thomas' NHS Foundation Trust, London, UK; [11]Sarah Cannon Research Institute, London, UK; [12]Beatson West of Scotland Cancer Centre, Glasgow, Scotland; [13]Erasmus MC Cancer Institute, University Medical Center Rotterdam, Department of Hematology, The Netherlands, on behalf of the Lunenburg Lymphoma Phase I/II Consortium – HOVON/LLPC; [14]The Clatterbridge Cancer Centre, Liverpool, UK; [15]Fundación Jiménez Díaz University Hospital, START Madrid-FJD Early Phase Unit, Madrid, Spain; [16]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [17]Nurix Therapeutics, Inc., San Francisco, CA, USA; [18]UMC Utrecht Cancer Center, University Medical Center Utrecht, The Netherlands, on behalf of the Lunenburg Lymphoma Phase I/II Consortium – HOVON/LLPC

ASH 2025 Annual Meeting, Orlando, 6–9 December 2025

Bexobrutideg Phase 1a/b (NX-5948-301) Trial Design

Phase 1a/b clinical trial in adults with relapsed/refractory B-cell malignancies

Phase 1a
Standard 3+3 dose escalation
(N = up to 66 patients)

CLL/SLL
- 600 mg QD
- 450 mg QD
- 300 mg QD
- 200 mg QD
- 100 mg QD
- 50 mg QD

NHL/WM
- 600 mg QD
- 450 mg QD
- 300 mg QD
- 200 mg QD
- 100 mg QD
- 50 mg QD

Recommended dose(s) for Phase 1b Part 1

Phase 1b part 1
Safety expansion
(N = up to 280 patients)

CLL cohorts

- **Cohort 1** Prior BTKi and BCL2i — 200 mg QD; 600 mg QD
- **Cohort 2** Non-C481S BTK mutations
- **Cohort 3** Prior non-covalent BTKi
- **Cohort 4** TP53 or 17p deletion, 2L, prior BTKi
- **Cohort 5** 2L+, prior BTKi
- **Cohort 15** BTK-naïve
- **Cohort 16** With wAIHA, prior BTKi
- **Cohort 17** With CNS involvement, prior BTKi

NHL cohorts

- **Cohort 6**: MCL
- **Cohort 7**: MZL
- **Cohort 8**: WM 3L+, prior BTKi
- **Cohort 9**: WM 2L, prior BTKi
- **Cohort 10**: DLBCL
- **Cohort 11**: FL
- **Cohort 12**: PCNSL 3L+/2L+ Prior BTKi or SCNSL (**including Bing-Neel**)
- **Cohort 13**: PCNSL 2L, BTK-naïve
- **Cohort 14**: TN WM, CIT unfit

- As of 19 September 2025, 31 patients with WM had been enrolled and treated at four daily dose levels: 200 mg (n=1), 300 mg (n=3), 450 mg (n=2), 600 mg (n=25)
- Of these, 22 (71%) remain on treatment and 9 have discontinued treatment

Data cutoff: 19 Sep 2025

BTKi, *Bruton's tyrosine kinase inhibitor;* ***CNS****, central nervous system;* ***DLBCL****, diffuse large B-cell lymphoma;* ***FL****, follicular lymphoma;* ***MCL,*** *mantle cell lymphoma;* ***MZL****, marginal zone lymphoma;* ***NHL,*** *non-Hodgkin's lymphoma;* ***PCNSL****, primary CNS lymphoma;* ***QD****, once daily;* ***SCNSL****, secondary CNS lymphoma;* ***WM****, Waldenström macroglobulinemia*

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High-Risk WM Population with Extensive Prior Therapy Exposure

Baseline demographics/disease characteristics

Characteristics	Patients with WM (n=31)
Median age, years (range)	71.0 (49–88)
Male, n (%)	24 (77.4)
ECOG PS, n (%) 0 1	 13 (41.9) 18 (58.1)
CNS involvement, n (%)	3 (9.7)
Median prior lines of therapy, n (range)	3 (1–7)
Previous treatments,[a] n (%) BTKi Pirtobrutinib BCL2i BTKi and BCL2i Chemo/chemo-immunotherapies	 31 (100.0) 4 (12.9) 4 (12.9) 4 (12.9) 28 (90.3)
Mutation status,[b] n (%) *MYD88* *CXCR4*	 24 (77.4) 6 (19.4)

[a]Patients could have received multiple prior treatments; [b]Mutation status was gathered from historic patient records

Data cutoff: 19 Sep 2025

***BTKi**, Bruton's tyrosine kinase inhibitor; **BCL2i**, B-cell lymphoma 2 inhibitor; **CAR-T**, chimeric antigen receptor T-cell; **CNS**, central nervous system; **ECOG PS**, Eastern Cooperative Oncology Group (ECOG) performance status; **PI3Ki**, PI3 kinase inhibitor; **WM**, Waldenström macroglobulinemia*

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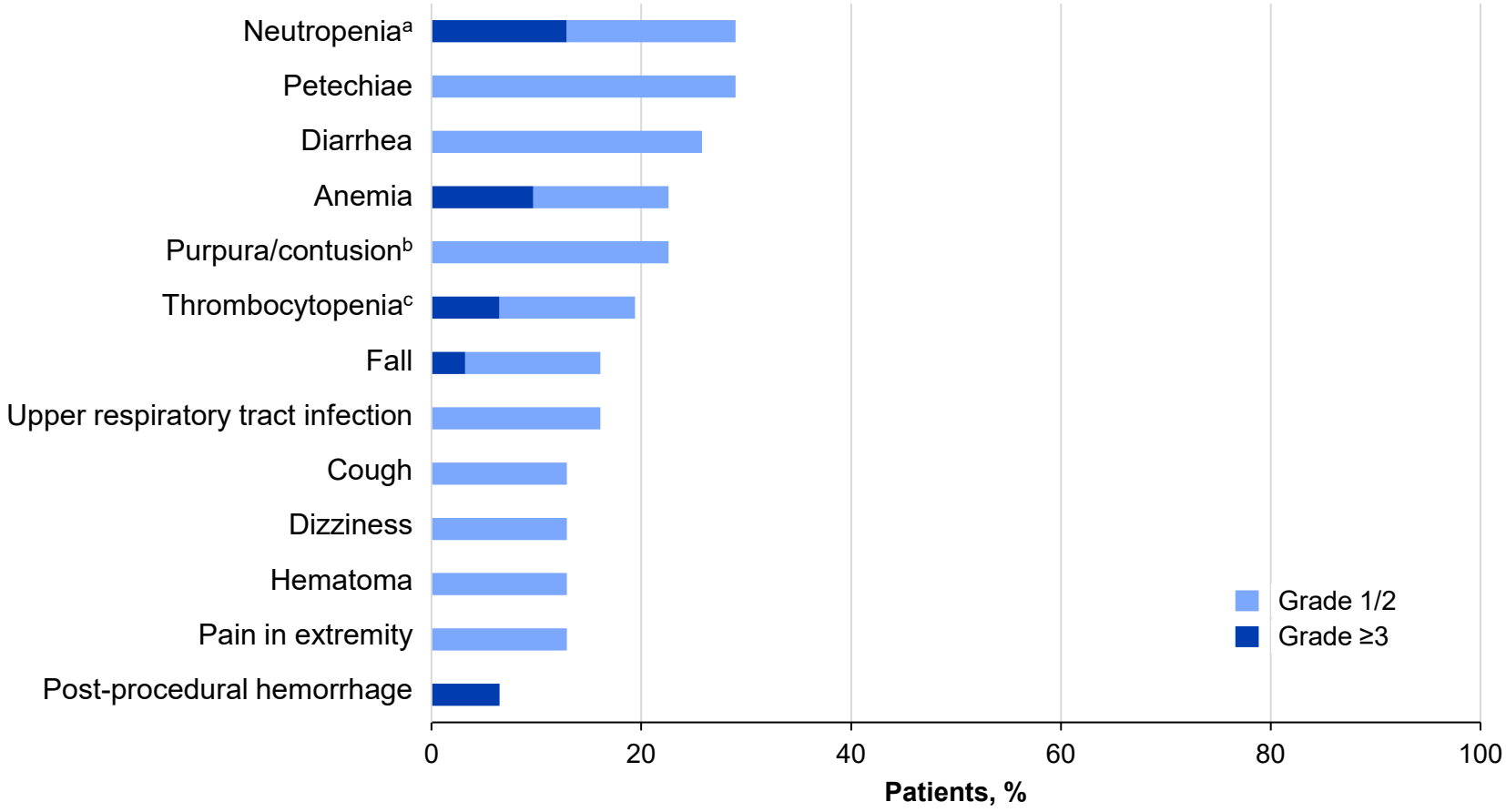
Safety Profile Aligns with Prior Clinical Experience Across Indications

TEAEs in ≥10% of WM population or Grade ≥3 TEAEs in >1 patient



- Tolerable safety profile consistent between the WM population, the overall population, and previous reports
- No dose-limiting toxicities
- 2 TEAEs leading to treatment discontinuation
- No Grade 5 AEs

[a]Aggregate of 'neutrophil count decreased' or 'neutropenia'; [b]Purpura/contusion includes episodes of contusion or purpura; [c]Aggregate of 'thrombocytopenia' and 'platelet count decreased'
***TEAE**, treatment-emergent AE; **WM**, Waldenstrom's macroglobulinemia*

Data cutoff: 19 Sep 2025

High Overall Response Rate in WM Patients Treated with Bexobrutideg

Bexobrutideg overall response assessment (IWWM-6) in patients with WM: Phase 1a/1b

	Primary efficacy analysis All response evaluable patients (n=28)[c]	**Exploratory efficacy analysis** Patients with ≥2 response assessments (n=23)[d]
Objective response rate (95% CI),[a] %	75.0 (55.1–89.3)	82.6 (61.2–95.0)
Major response rate (95% CI),[b] %	60.7 (40.6–78.5)	69.6 (47.1-86.8)
Best response, n (%)		
Complete response (CR)	0 (0.0)	0 (0.0)
Very good partial response (VGPR)	3 (10.7)	3 (13.0)
Partial response (PR)	14 (50.0)	13 (56.5)
Minor response (MR)	4 (14.3)	3 (13.0)
Stable disease (SD)	6 (21.4)	4 (17.4)
Progressive disease (PD)	1 (3.6)	0 (0.0)

[a]Objective response rate includes CR + VGPR + PR + MR; [b]Major response rate includes CR + VGPR + PR; [c]Includes patients who dosed and had at least one post-baseline disease assessment or documented clinical PD; [d]Includes patients who dosed and had at least two post-baseline disease assessment or documented clinical PD

CI, *confidence interval*

Data cutoff: 19 Sep 2025

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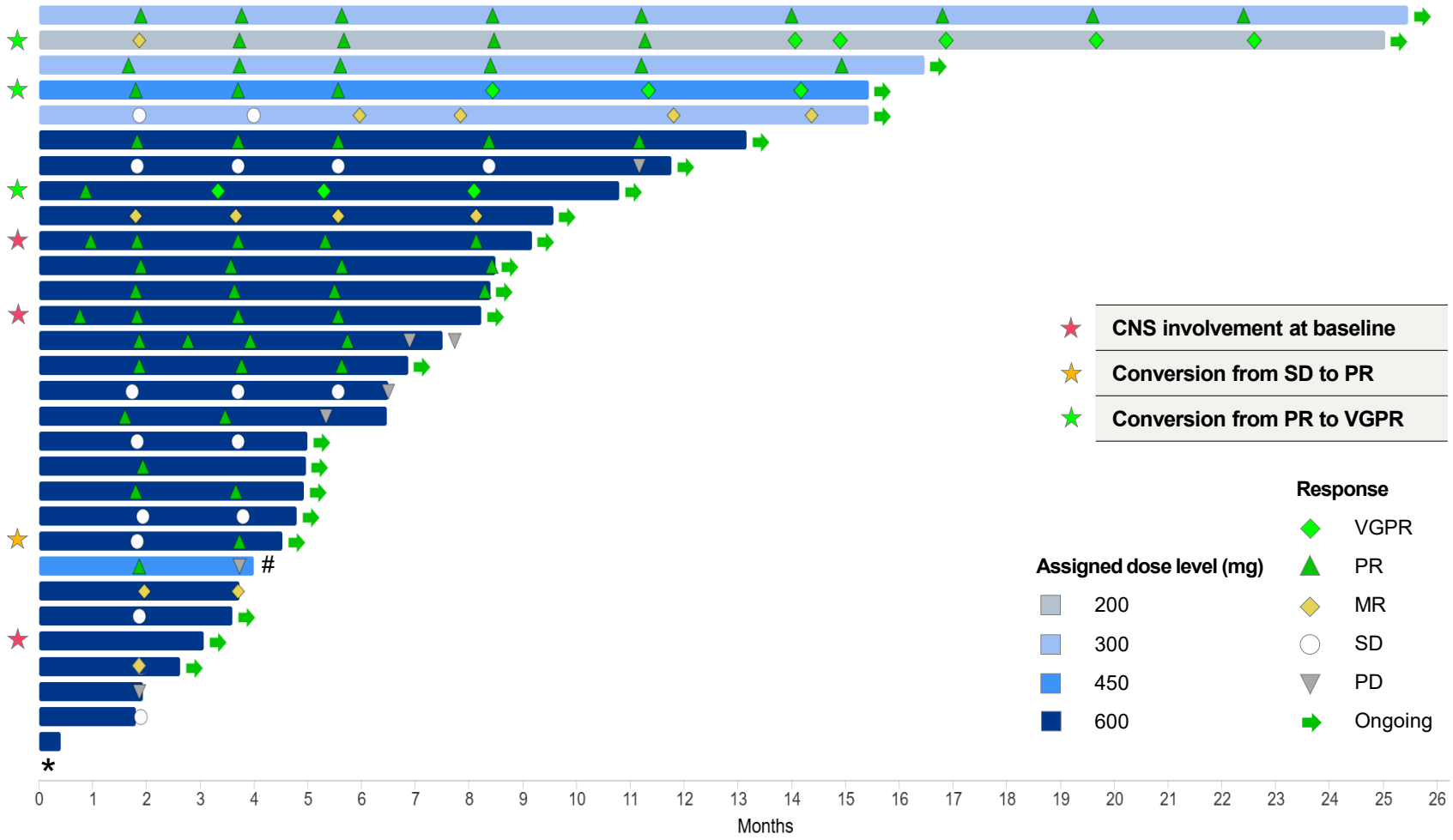
Durable Responses Regardless of Prior Therapy or Mutation Status (n=31)

Select prior therapies			Select mutations[a]	
BTKi	BCL2i	Pirto	*CXCR4*	*MYD88*
			NA	
			NA	
			NA	
			NA	
			NA	
			NA	
			NA	
			NA	
			NA	
			NA	NA
			NA	
			NA	NA
			NA	NA
			NA	
			NA	NA



[a]*Mutation data taken from patients' medical histories*
**Ineligible, identified post 1st dose; #Transformed to DLBCL*

***BTKi**, Bruton's tyrosine kinase inhibitor; **BCL2i**, B-cell lymphoma 2 inhibitor; **MR**, minor response; **NA**, not available; **Pirto**, pirtobrutinib; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease; **VGPR**, very good partial response; **WM**, Waldenström macroglobulinemia*

Data cutoff: 19 Sep 2025

Conclusions

- Bexobrutideg is a novel small molecule BTK degrader that can overcome treatment-emergent BTKi resistance mutations and disrupt BTK scaffolding.
- In the ongoing WM portion of the phase 1 NX-5948-301 study as of the 19 September 2025 data cut:
  - Median follow-up was 8.1 months, and most patients were still on treatment.
  - In the WM safety population (31 patients), bexobrutideg was well tolerated, which is consistent with the overall study population and previous disclosures:
    - AEs were predominantly low grade; the most common AEs were neutropenia, petechiae, diarrhea, anemia, purpura/contusion, and thrombocytopenia. No atrial fibrillation was observed.
    - No DLTs were noted; two TEAEs led to drug discontinuation. There were no Grade 5 AEs.
  - In 28 response-evaluable patients, durable and deepening responses were observed in a heavily pre-treated (3 median lines of treatment) population of patients with WM, irrespective of CNS involvement, MYD88 or CXCR4 mutations:
    - A MRR of 60.7% and ORR of 75.0% was observed (including 3 VGPR and 14 PR), with 3 responses deepening from PR to VGPR with longer duration on treatment, and only one PD (3.6%) as best overall response.
    - Out of 3 patients with CNS involvement (2 with systemic disease), 2 have responded and none progressed.
    - A steady reduction in IgM levels occurred in most patients starting from the first IgM assessment (4 weeks), which continued to deepen at 8 weeks and beyond (data shown on the poster).
    - The median duration of response was not reached. 14 patients continued on treatment for more than 6 months.

AEs, *adverse events;* ***BTKi****, Bruton's tyrosine kinase inhibitor;* ***CNS****, central nervous system;* ***DLTs****, dose-limiting toxicities;* ***IgM,*** *immunoglobulin M;* ***MRR****, major response rate;* ***ORR****, objective response rate;* ***PD****, progressive disease;* ***PR****, partial response;* ***VGPR****, very good partial response;* ***TEAE****, treatment-emergent AE;* ***WM****, Waldenström macroglobulinemia*

Data cutoff: 19 Sep 2025

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Bexobrutideg: Driving Clinical Momentum and Competitive Leadership

Paula G. O’Connor, M.D.
Chief Medical Officer, Nurix Therapeutics

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Positioned for Success – Recent Key Program Updates

Advancing bexobrutideg as a potential best-in-class BTK degrader

- ✓ 600 mg dose selected per Project Optimus
  - ✓ Cleared to move ahead globally (FDA, MHRA, EMA)
- ✓ Pivotal Phase 2 trial initiated – DAYBreak CLL-201
- ✓ Confirmatory Phase 3 trial initiation planned for H1 2026
- ✓ New best-in-class *in vitro* potency and selectivity data
- ✓ Bexobrutideg clinical update at ASH 2025

NEW information:

- Bexobrutideg data from Phase 1a in CLL patients demonstrate **ORR of 83.0%**, **median DOR of 20.1 months**, and **median PFS of 22.1 months**

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Current CLL Results for Bexobrutideg Are Highly Differentiated From Pirtobrutinib

- Bexobrutideg maturing data from Phase 1a in CLL patients demonstrates **ORR of 83.0%**, **median DOR of 20.1 months**, and **median PFS of 22.1 months**
- ORR, DOR, and PFS data for bexobrutideg are **highly differentiated from pirtobrutinib** based on results from the BRUIN-321 study of pirtobrutinib vs. BR/IR
  - Pirtobrutinib ORR was 65% (69% by investigator) with a DOR of 13.8 months (13.9 by investigator)
  - Pirtobrutinib mPFS was 14.0 months overall and 11.4 months in patients with prior cBTKi & BCL-2i (double exposed)
- **Superior ORR, DOR, and PFS** for bexobrutideg compared to pirtobrutinib **despite less favorable baseline characteristics:**
  - More prior lines of therapy (median of 4 vs. 3)
  - More patients with 4+ lines of prior therapy (56.3% vs. 33%)
  - Prior exposure to ncBTKi (27% vs. 0%)
  - More patients exposed to prior BCL-2i (83.3% vs. 50%)

***DOR**, duration of response; **ORR**, objective response rate; **PFS**, progression-free survival*
Bexobrutideg: NX-5948-301 study data cut off Sept 19, 2025
Pirtobrutinib: Sharman et al, JCO 43: 2538-2549, June 2025

Data cutoff: 19 Sep 2025

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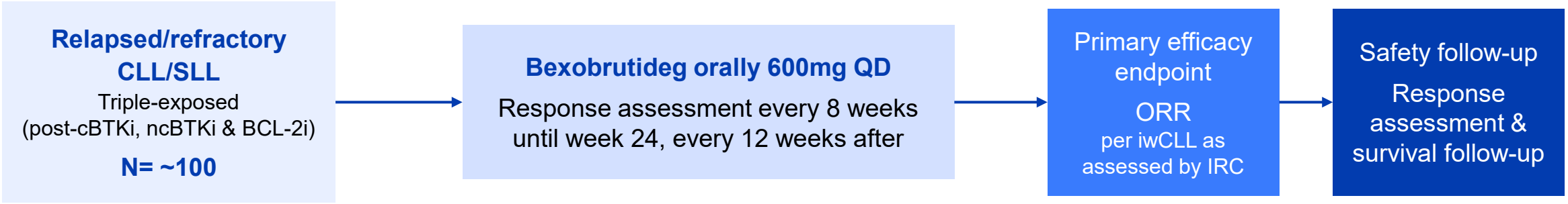
Phase 2 Single-Arm Study Designed to Support Accelerated Approval

DAYBreak CLL-201

Triple-exposed CLL patients who progressed on, did not respond to, or discontinued prior therapy



- Potential to address a current and anticipated future unmet medical need
  - Pirtobrutinib recently gained full approval
- 600 mg cleared for pivotal studies in r/r CLL
- First patient dosed in October 2025

***CLL**, chronic lymphocytic leukemia; **ORR,** objective response rate; **iwCLL,** International Workshop on CLL; **IRC,** Independent Review Committee; **QD,** once daily; **SLL,** small lymphocytic lymphoma; **cBTKi,** covalent BTK inhibitor; **ncBTKi,** non-covalent BTK inhibitor; **BCL-2i,** BCL-2 inhibitor*

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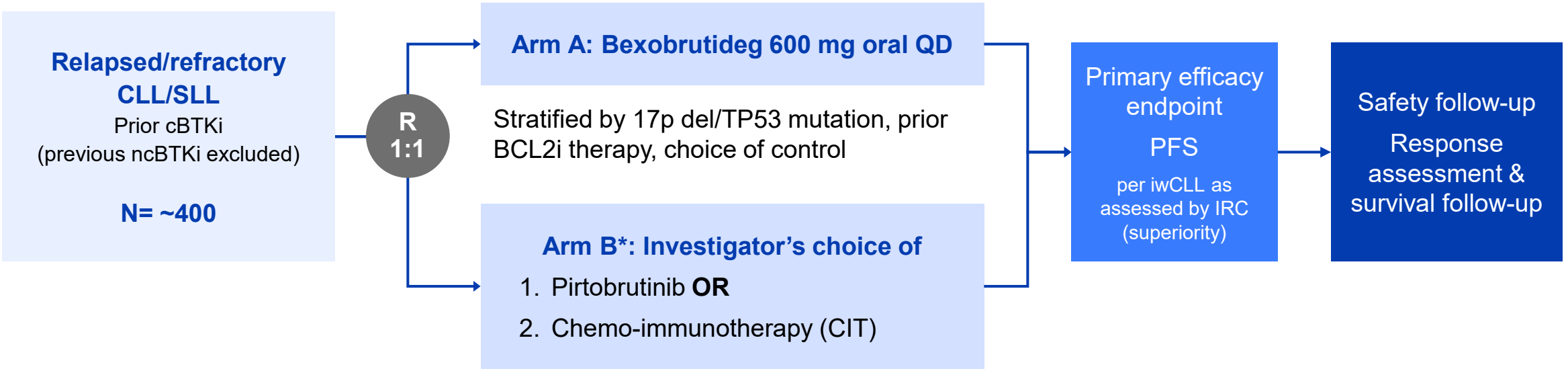
Confirmatory Phase 3 Trial for Full Approval*

DAYBreak CLL-306

2L+ CLL patients who have been exposed to prior covalent BTK inhibitor



- Trial designed to support global registrational strategy
- Anticipate initiation in H1 2026
- Based on the emerging durability results for bexobrutideg, Nurix believes that bexobrutideg will outperform all components of the investigator's choice arm

***CLL**, chronic lymphocytic leukemia; **PFS,** progression-free survival; **iwCLL,** International Workshop on CLL; **IRC,** Independent Review Committee; **QD,** once daily; **SLL,** small lymphocytic lymphoma; ncBTKi, non-covalent BTK inhibitor*

** Trial design subject to change based on changing standards of care and regulatory review*

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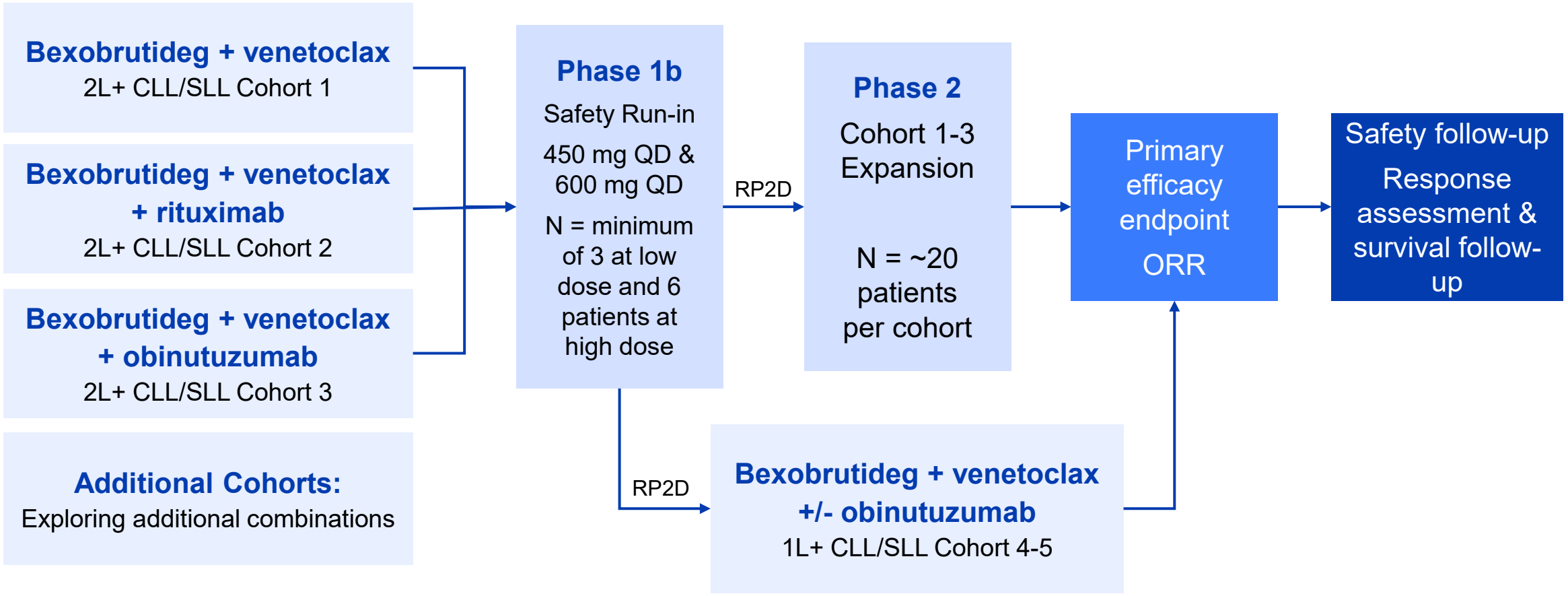
Phase 1b/2 Combination Study to Address Emerging Treatment Standards in CLL

DAYBreak CLL-203

Combination regimen of bexobrutideg + BCL-2i maximizes 2L market share opportunity and provides potential path to 1L CLL



***CLL**, chronic lymphocytic leukemia; **SLL**, small lymphocytic lymphoma; **ORR**, objective response rate; **QD**, once daily; **RP2D**, recommended Phase 2 dose*

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Bexobrutideg Clinical Conclusions

Robust clinical activity and well tolerated across all B-cell malignancies tested

CLL

- 83% ORR with a 20.1 month median duration of response
- Well tolerated with low rate of discontinuation
- Progression free survival tracking well above standard of care with a current estimate of 22.1 months

WM

- 75% ORR, with responses deepening over time including 3 VGPRs
- Median duration of response was not reached, with 14 patient on treatment for more than 6 months

NHL

- 130 NHL patients treated to date in NX-5948-301
- Multiple CR/CMRs have been observed in all cohorts (DLBCL, MCL, FL, MZL, PCNSL)

Anticipate future bexobrutideg clinical updates throughout 2026, targeting European Hematology Association (EHA) in June and American Society of Hematology (ASH) in December

Data cutoff: 19 Sep 2025

CR, complete response; CMR, complete metabolic response, CLL, chronic lymphocytic leukemia, DLBCL, diffuse large B-cell lymphoma, FL, follicular lymphoma; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; NHL, non-Hodgkin lymphoma, ORR, objective response rate; PCNSL, primary CNS lymphoma; VGPR, very good partial response

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Bexobrutideg and Beyond: Building the Next Generation of TPD Therapies

Arthur T. Sands, M.D., Ph.D.
Chief Executive Officer, Nurix Therapeutics

NURIX

2025: A Breakthrough Year as Nurix Hit Several Meaningful Milestones

Clinical Execution Excellence

- Secured 600mg dose per Project Optimus
- Initiated DAYBreak CLL-201 Phase 2 study designed to support Accelerated Approval
- Presented compelling update at ASH: 83% ORR and 22.1-month median PFS

Pipeline & Partnership Momentum

- Partner Gilead initiated GS-6791 Phase 1 SAD/MAD study
- Secured STAT6 + one additional degrader program license with Sanofi
- Initiated healthy volunteer studies with new bexobrutideg formulation for I&I
- Presented clinical proof of concept for CBL-B inhibitor NX-1607

Strengthened Financial Position

- Strengthened our balance sheet with a $250M follow-on offering
- Earned $47M in non-dilutive capital through our discovery partnerships
- Well capitalized with pro forma cash/investments of $663.8 million*
- Expected cash runway into 2028

*Cash balance as of August 31, 2025, plus the net proceeds from the October 2025 registered direct offering

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2026: Accelerating the Next Phase of Leadership in Protein Degradation

1	**Building Evidence with Clinical Data Readouts**	▪ Bexobrutideg Phase 1b CLL cohorts ▪ Bexobrutideg Phase 1a/b NHL cohorts ▪ Bexobrutideg Phase 1 SAD/MAD study
2	**Advancing Degrader Programs in I&I**	▪ Potential GS-6791 IRAK4 degrader Phase 1 results* ▪ Potential NX-3911 STAT6 degrader IND filing by Sanofi* ▪ Bexobrutideg IND filing in I&I
3	**Executing Pivotal Development Pathway**	▪ Initiate bexobrutideg confirmatory Phase 3 study in r/r CLL ▪ Initiate bexobrutideg combination study in CLL

** Nurix estimate for partnered programs using industry standard timelines based on current stage of development (not official guidance of partners).*

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Q&A


NURIX™