

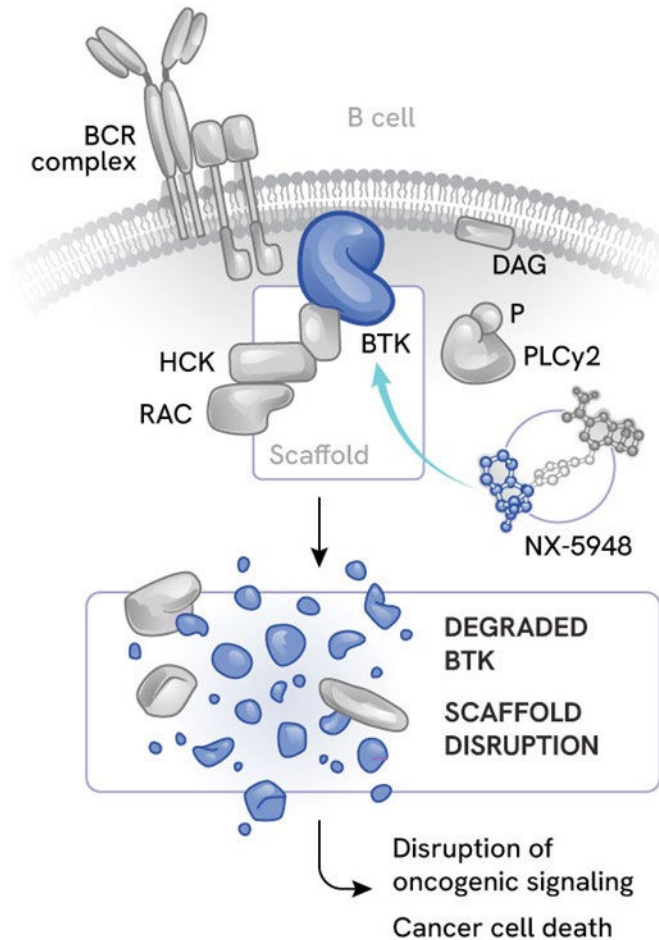
Updated efficacy and safety data from an ongoing phase 1a/b trial of the BTK degrader bexobrutideg (NX-5948) in patients with CLL/SLL across lines of therapy

¹Talha Munir, ²Zulfa Omer, ³Sebastian Grosicki, ⁴Michal Kwiatek, ⁵Alexey Danilov, ⁶Nirav N. Shah, ⁷Francesco Forconi, ⁸Alvaro Alencar, ^{9,10}Mary Gleeson, ¹¹Laura Samples, ¹²Graham P. Collins, ¹³Jane Robertson, ¹⁴Jonathon B. Cohen, ¹⁵William Wierda, ¹⁶Danielle Brander, ¹⁷Shuo Ma, ¹⁸Allison Winter, ¹⁹Krzysztof Giannopoulos, ²John C. Byrd, ²⁰Sarah Injac, ²¹Wojciech Jurczak

¹St. James's Hospital, Leeds, UK; ²University of Cincinnati, Cincinnati, OH, USA; ³Medical University of Silesia, Katowice, Poland; ⁴AidPort Hospital, Skórzewo (Poznan), Poland; ⁵City of Hope National Medical Center, Duarte, CA, USA; ⁶Medical College of Wisconsin, Milwaukee, WI, USA; ⁷University Hospital Southampton NHS Trust, Southampton, UK; ⁸Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL, USA; ⁹Guy's and St Thomas' NHS Foundation Trust, London, UK; ¹⁰Sarah Cannon Research Institute, London, UK; ¹¹Fred Hutchinson Cancer Center, Seattle, WA, USA; ¹²Oxford Cancer and Haematology Centre, Churchill Hospital, Oxford, UK; ¹³The Christie Hospital NHS Foundation Trust, Manchester, UK; ¹⁴Emory University Winship Cancer Institute, Atlanta, GA, USA; ¹⁵MD Anderson Cancer Center, Houston, TX, USA; ¹⁶Duke Cancer Institute, Durham, NC, USA; ¹⁷Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; ¹⁸Cleveland Clinic Foundation, Cleveland, OH, USA; ¹⁹Medical University of Lublin, Lublin, Poland; ²⁰Nurix Therapeutics, Inc., Brisbane, CA, USA; ²¹Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland

Bexobrutideg (NX-5948)

A novel CNS-penetrant BTK degrader that addresses BTK scaffolding and overcomes BTK resistance mutations



✓ Active against not only wildtype BTK but also treatment emergent BTK-inhibitor resistance mutations^{1,2}

✓ Addresses both BTK scaffolding and kinase functions, unlike current BTK inhibitors³

✓ Acts catalytically, driving degradation at low free-drug plasma concentrations

✓ Crosses the blood-brain barrier and demonstrates clinical activity in the CNS⁴

✓ Demonstrates robust clinical activity in difficult-to-treat B-cell malignancies⁵⁻⁷

BCR, B-cell receptor; **BTK**, Bruton's tyrosine kinase; **CNS**, central nervous system; **DAG**, diacylglycerol; **HCK**, hematopoietic cell kinase; **PLCγ2**, phospholipase gamma 2; **RAC**, Ras-related C3 botulinum toxin substrate GTPase

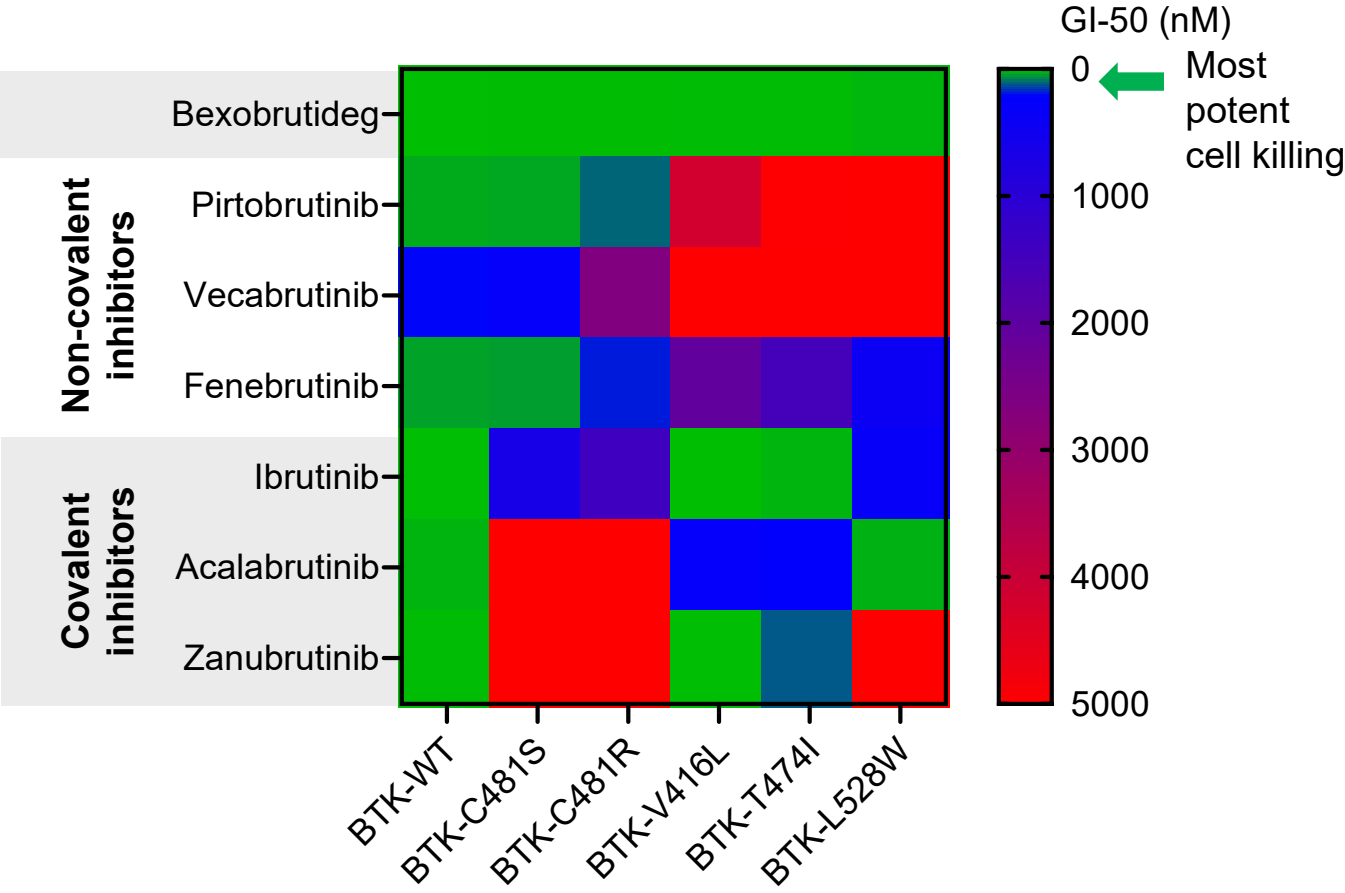
1. Noviski et al. 20th Biennial International Workshop on CLL, Boston, MA, USA, Oct 6–9, 2023; 2. Hansen. Presented at TPD Basel, Switzerland, Sept 19, 2023; 3. Montoya et al. *Science* 2024;383: eadi5798;

4. Noviski. 8th TPD & Induced Proximity Summit, Boston, MA, USA, Oct 29, 2025; 5. Shah et al. *Blood* (2024) 144 (Supplement 1): 884; 6. Danilov et al. Oral presentation at 18th ICML congress, Lugano, Switzerland, Jun 17–21, 2025;

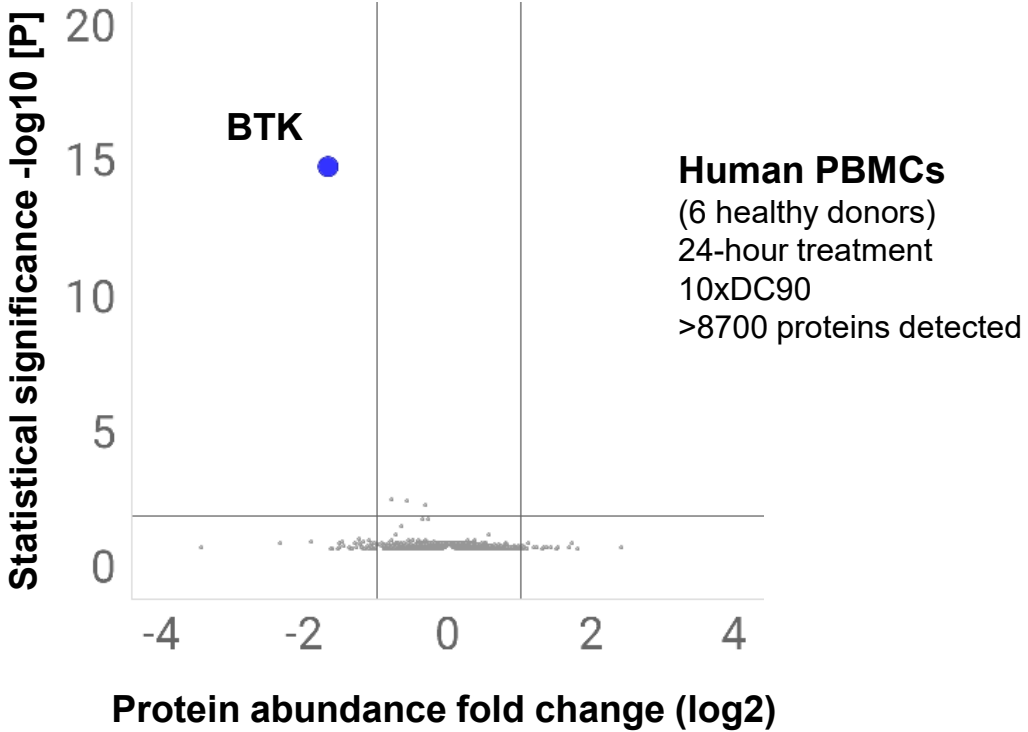
7. Omer et al. Poster presentation at the EHA Congress 2025, Milan, Italy, Jun 12–15, 2025

Bexobrutideg Shows Superior Mutation Coverage and Highly Selective BTK Degradation

Bexobrutideg shows superior cell killing across mutations compared with BTK inhibitors*



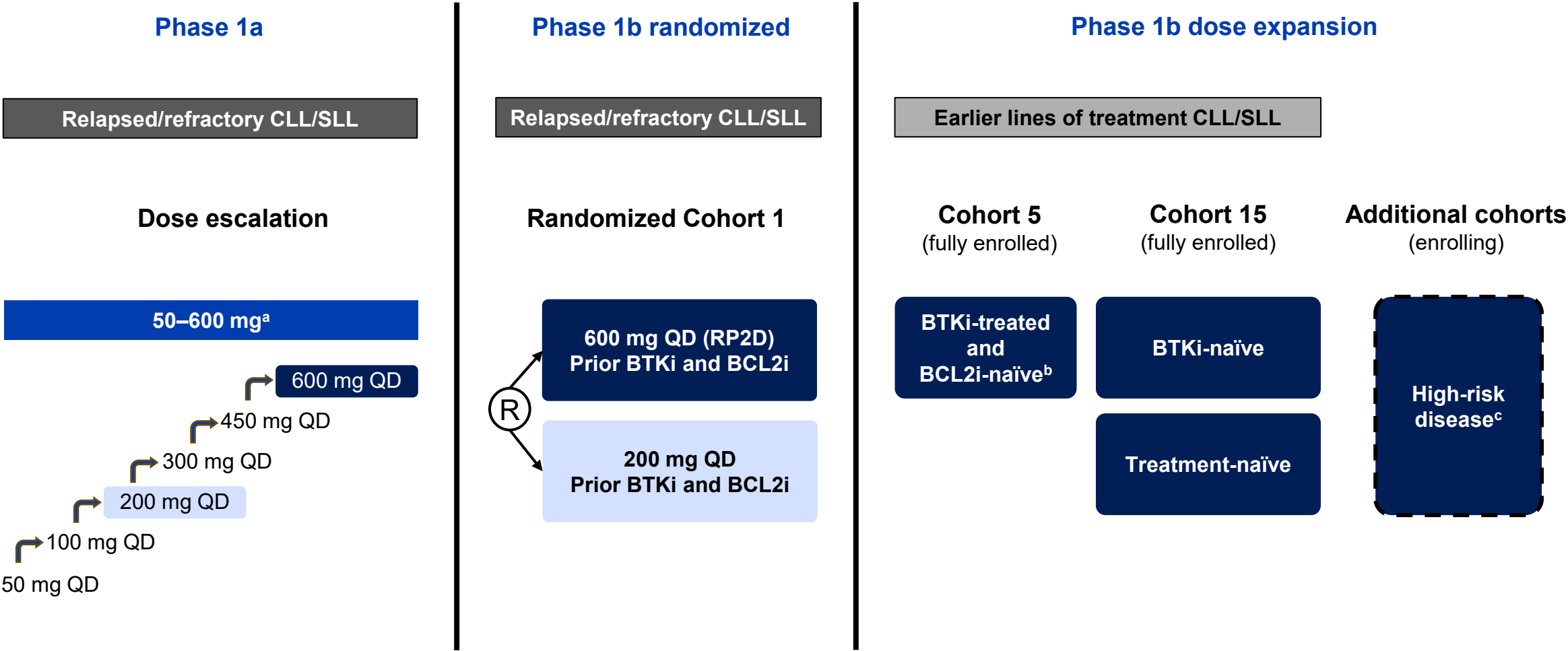
Global proteomics using bexobrutideg show selective degradation of BTK at clinically relevant exposures



BTK, Bruton's tyrosine kinase; GI-50, growth inhibition 50%; PBMCs, peripheral blood mononuclear cells
*In CRISPR-engineered TMD8 cells

Bexobrutideg Trial Design (NX-5948-301, CLL/SLL Cohorts, Phase 1a/b)

Including Phase 1b cohorts with BTKi-treated and BCL2i-naïve; BTKi-naïve (including treatment-naïve)



BCL2i, B-cell lymphoma 2 inhibitor; **BTKi**, Bruton's tyrosine kinase inhibitor; **CLL**, chronic lymphocytic leukemia; **ncBTKi**, non-covalent BTKi; **QD**, once daily; **RP2D**, recommended Phase 2 dose; **SLL**, small lymphocytic lymphoma
^aStarting dose; ^bAll patients at 600 mg except one patient on 200 mg dose; ^cIncluding: non-C418S mutations; prior ncBTKi; TP53 mutations; warm autoimmune hemolytic anemia; CNS involvement with prior BTKi

Bexobrutideg Safety Summary: All CLL/SLL Patients (Phase 1a/b)

TEAEs consistent between overall population and patients receiving 600 mg dose

n (%)	All patients with CLL/SLL (n=142)	600 mg dose patients (n=86)	50–450 mg dose patients (n=56)
Any TEAE	134 (94.4)	79 (91.9)	55 (98.2)
Treatment related	110 (77.5)	65 (75.6)	45 (80.4)
Grade 3+	73 (51.4)	39 (45.3)	34 (60.7)
Treatment related	35 (24.6)	22 (25.6)	13 (23.2)
SAE	33 (23.2)	16 (18.6)	17 (30.4)
Treatment related	9 (6.3)	5 (5.8)	4 (7.1)
Grade 5*	3 (2.1)	1 (1.2)	2 (3.6)
Treatment related	0	0	0
Leading to treatment discontinuation	8 (5.6)	5 (5.8)	3 (5.4)
Treatment related	6 (4.2)	3 (3.5)	3 (5.4)
DLT	0	0	0
Median exposure time, months (range)	7.3 (0.03–35.8)	5.1 (0.03–21.5)	12.5 (0.2–35.8)

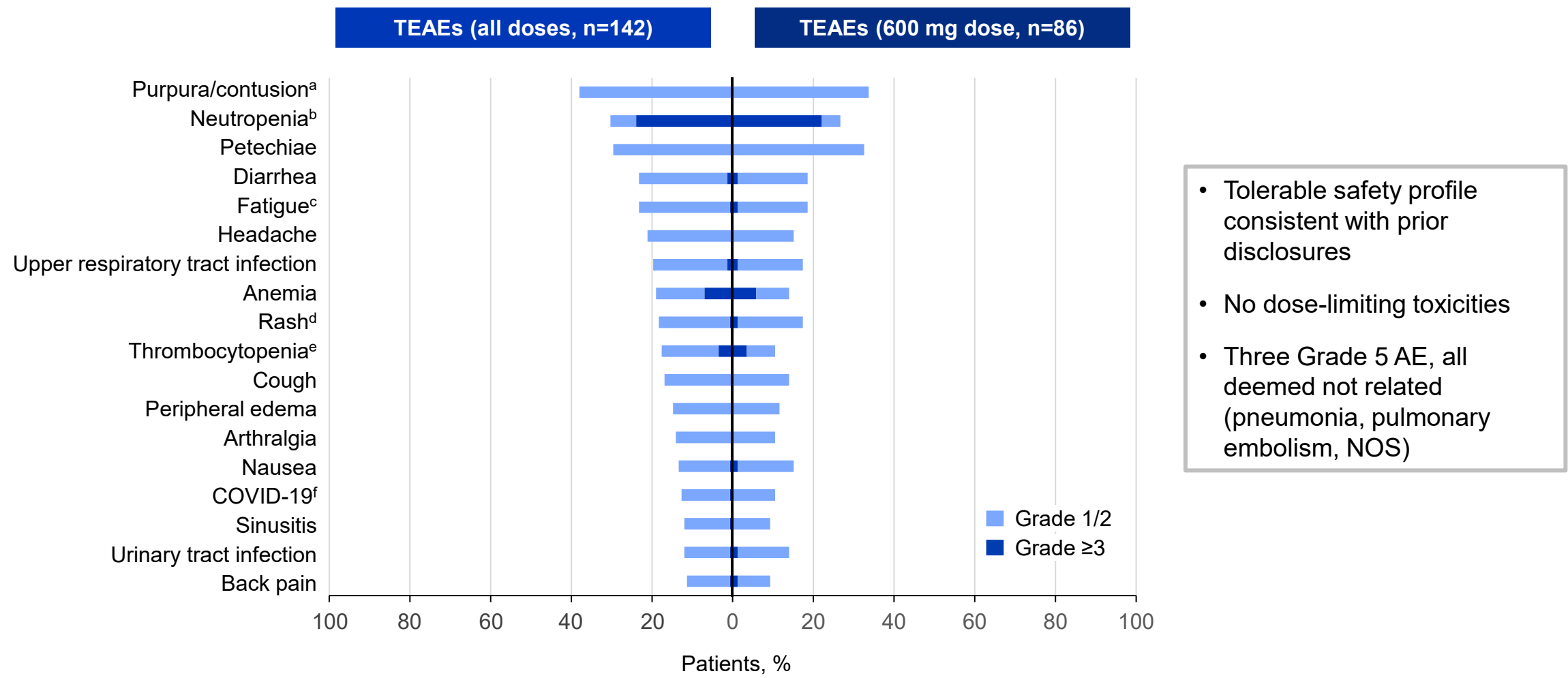
CLL, chronic lymphocytic leukemia; DLT, dose-limiting toxicity; SAE, serious adverse event; SLL, small lymphocytic lymphoma; TEAE, treatment-emergent adverse event

*Grade 5 AEs: pulmonary embolism, death not otherwise specified; pneumonia

Data cutoff: 1 Jan 2026

TEAEs in ≥10% of Patient Population (Phase 1a/b)

Tolerable AE profile: comparable between overall population and patients receiving 600 mg dose



AE, adverse event; CLL, chronic lymphocytic leukemia; NOS, not otherwise specified; RP2D, recommended Phase 2 dose; SLL, small lymphocytic lymphoma; TEAE, treatment-emergent adverse event

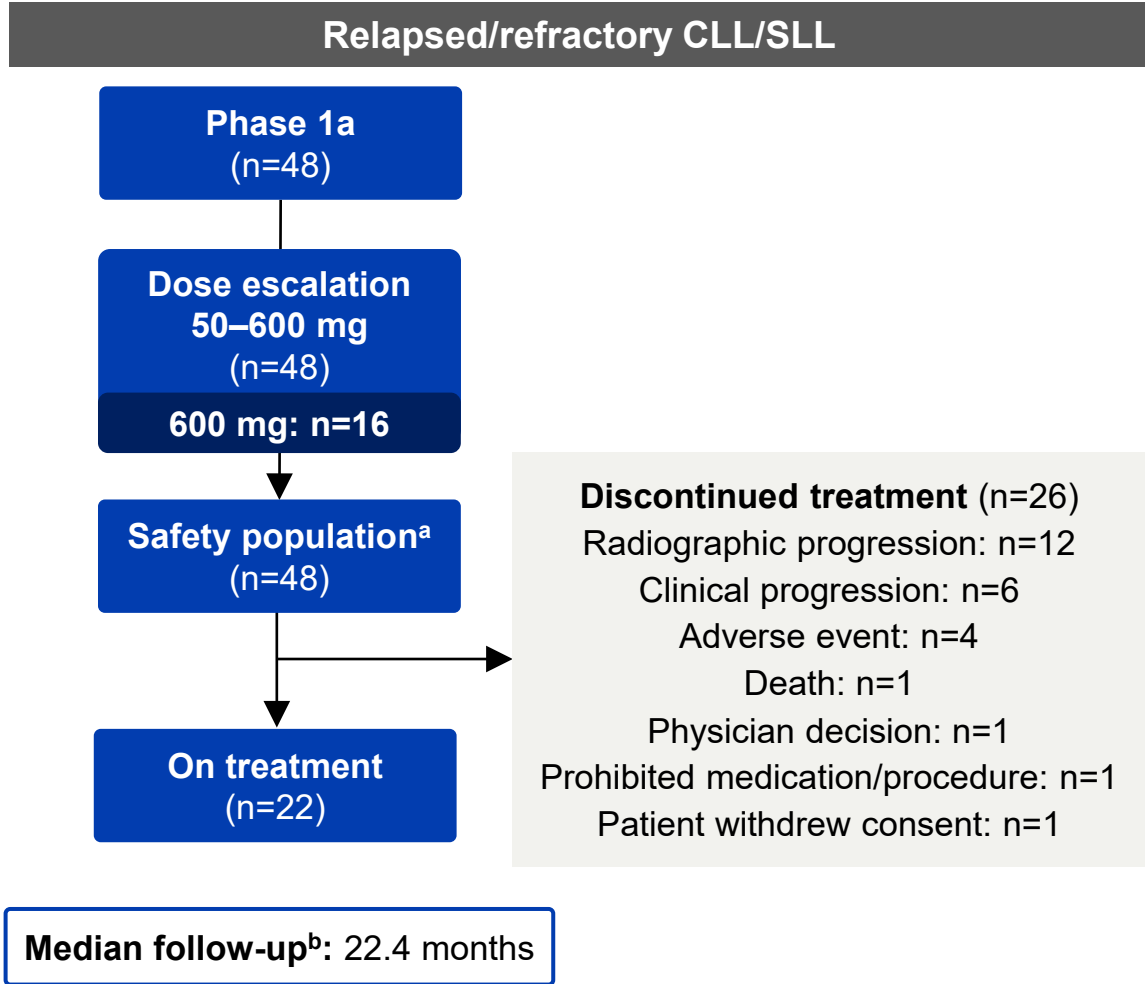
^aPurpura/contusion includes episodes of contusion or purpura; ^bAggregate of 'neutrophil count decreased' or 'neutropenia'; ^cFatigue was transient; ^dAggregate of 'rash' and 'rash maculopapular' and 'rash pustular';

^eAggregate of 'thrombocytopenia' and 'platelet count decreased'; ^fAggregate of 'COVID-19' and 'COVID-19 pneumonia'

Data cutoff: 1 Jan 2026

Patient Disposition and Baseline Characteristics (Phase 1a)

Patients with relapsed/refractory CLL/SLL



Characteristics	Relapsed/refractory CLL/SLL
	Phase 1a: Dose escalation 50–600 mg* (n=48)
Median age, years (range)	68.5 (35.0–88.0)
Male, n (%)	32 (66.7)
White, n (%)	42 (87.5)
ECOG PS 0/1, n (%)	19 (39.6) / 29 (60.4)
CNS involvement, n (%)	5 (10.4)
Median prior lines of therapy, n (range)	4.0 (2–12)
Previous treatments, ^c n (%)	
BTKi	47 (97.9)
cBTKi / ncBTKi	47 (97.9) / 13 (27.1)
BCL2i	40 (83.3)
BTKi and BCL2i	39 (81.3)
cBTKi, ncBTKi and BCL2i	11 (22.9)
Chemo/chemo-immunotherapies	35 (72.9)
Mutation status, ^d n (%)	(n=47)
BTK	18 (38.3)
TP53	21 (44.7)
PLCG2	7 (14.9)
BCL2	6 (12.8)
IGHV (unmutated)	29 (85.3), n=34

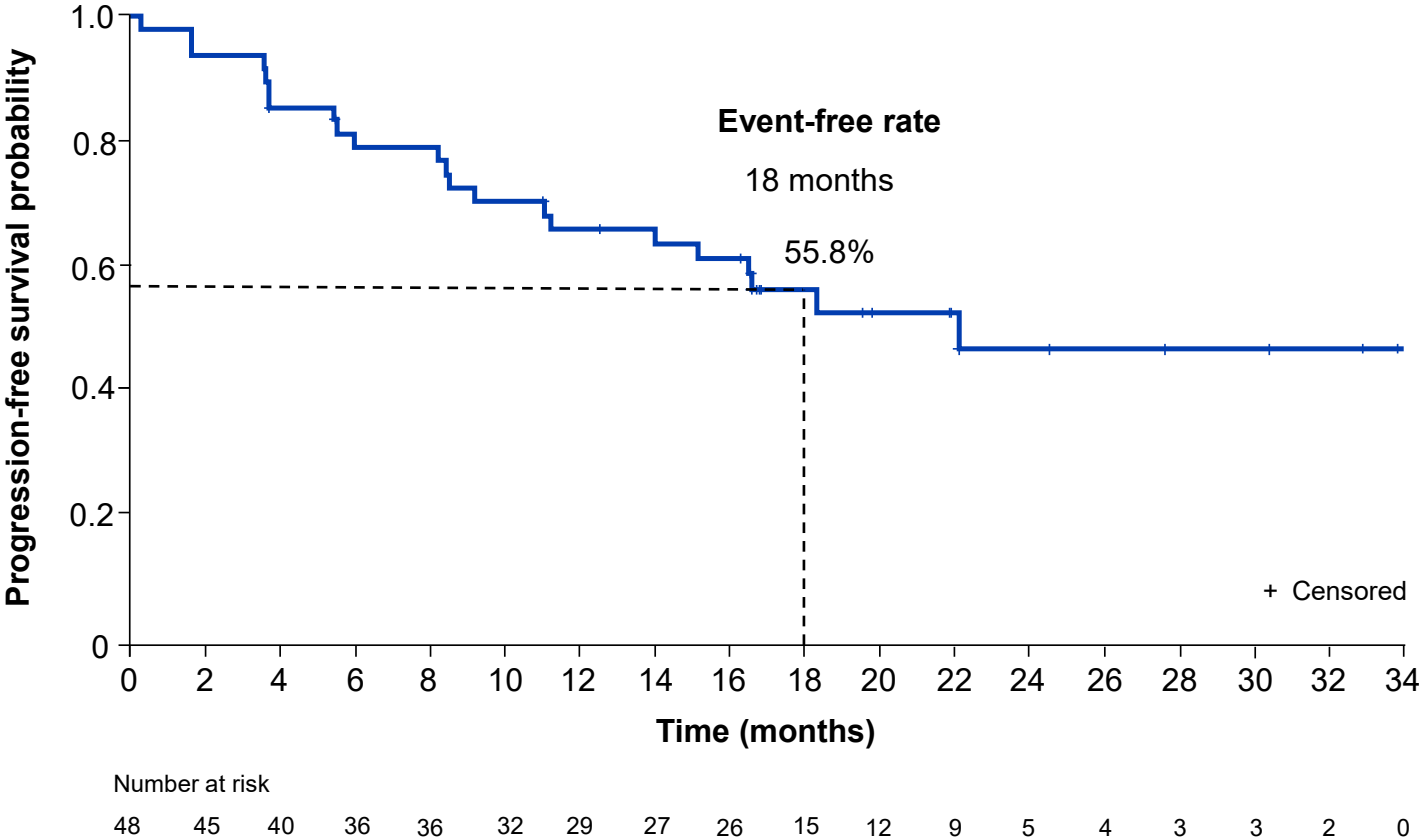
BCL2i, B-cell lymphoma 2 inhibitor; *BTKi*, Bruton's tyrosine kinase inhibitor; *cBTKi*, covalent BTKi; *CLL*, chronic lymphocytic leukemia; *CNS*, central nervous system; *ECOG PS*, Eastern Cooperative Oncology Group Performance Status; *ncBTKi*, non-covalent BTKi; *SLL*, small lymphocytic lymphoma

^aSafety and efficacy populations are identical; ^bTime from treatment start to data cutoff; ^cPatients could have received multiple prior treatments; ^dPatients could have multiple mutations (which are reported at VAF >5%)

*Starting dose

Bexobrutideg PFS and ORR in Relapsed/Refractory Patients (Phase 1a)

PFS remains durable with a median of 22.1 months



Relapsed/refractory CLL/SLL	
PFS summary	
n=48	
Median PFS ^a , months (95% CI)	22.1 (14.0–NR)
ORR summary	
n=47 ^b	
ORR, % (95% CI) ^c	83.0 (69.2–92.4)
CR	2 (4.3)
nPR	1 (2.1)
PR	36 (76.6)
SD	6 (12.8)
PD	2 (4.3)
Median follow-up, ^d months (range)	22.4 (16.9–35.7)

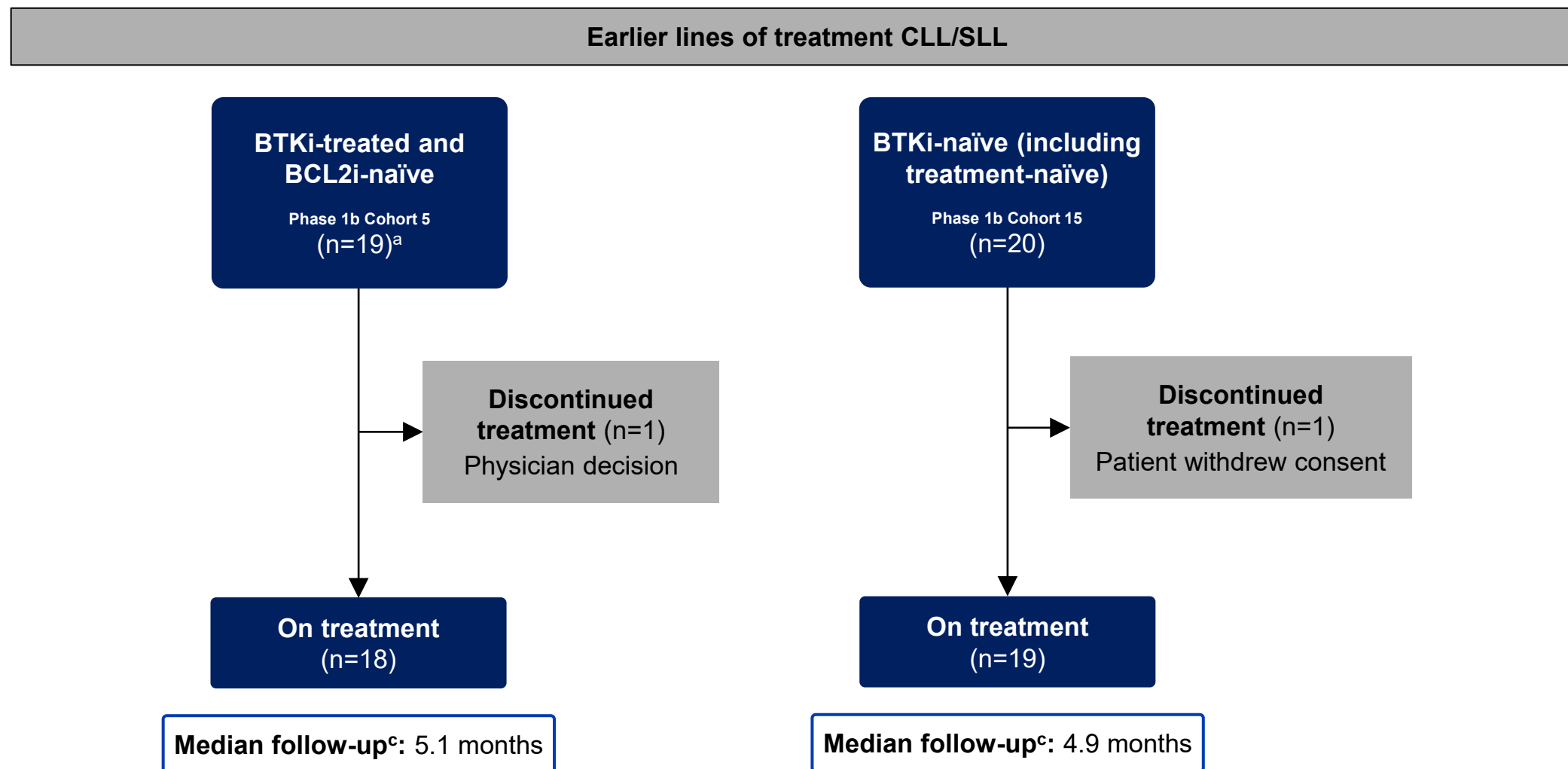
CI, confidence interval; CLL, chronic lymphocytic leukemia; CR, complete response; nPR, nodal partial response; NR, not reached; ORR, objective response rate; PD, progressive disease;

PFS, progression-free survival; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease; SLL, small lymphocytic lymphoma

^aMedian for PFS by Kaplan–Meier method; ^bExcludes 1 patient who was not evaluable for response; ^cObjective response rate includes CR + nPR + PR + PR-L; ^dTime from treatment start to data cutoff

Patient Disposition (Phase 1b Cohorts 5 and 15)

Patients with CLL/SLL in earlier lines of treatment



BCL2i, B-cell lymphoma 2 inhibitor; *BTKi*, Bruton's tyrosine kinase inhibitor; *CLL*, chronic lymphocytic leukemia; *SLL*, small lymphocytic lymphoma

^aOne patient in Cohort 5 was enrolled at 200 mg prior to selection of 600 mg as the go-forward dose; all other patients at 600 mg; ^cTime from treatment start to data cutoff

Data cutoff: 1 Jan 2026

Baseline Characteristics (Phase 1b Cohorts 5 and 15)

Patients in earlier lines of treatment

Characteristics	Earlier lines of treatment CLL/SLL	
	BTKi-treated and BCL2i-naïve Phase 1b Cohort 5 (n=19)	BTKi-naïve (including treatment-naïve) Phase 1b Cohort 15 (n=20)
Median age, years (range)	71.0 (48.0–79.0)	69.5 (41.0–87.0)
Male, n (%)	16 (84.2)	10 (50.0)
White, n (%)	18 (94.7)	19 (95.0)
ECOG PS 0/1, n (%)	12 (63.2) / 7 (36.8)	5 (25.0) / 15 (75.0)
Number of prior lines of therapy, n (%)		
0	0	10 (50.0)
1	8 (42.1)	9 (45.0)
≥2	11 (57.9)	1 (5.0)
Previous treatments, ^a n (%)		
BTKi	19 (100.0)	0
cBTKi / ncBTKi	19 (100.0) / 1 (5.3)	0 / 0
BCL2i	0	2 (10.0)
Chemo/chemo-immunotherapies	9 (47.4)	8 (40.0)
Mutation status, ^b n (%)	(n=19)	(n=20)
BTK	10 (52.6)	0
TP53	9 (47.4)	3 (15.0)
PLCG2	3 (15.8)	0
BCL2	1 (5.3)	0
IGHV (unmutated)	14 (93.3), n=15	0 , n=2

BCL2i, B-cell lymphoma 2 inhibitor; *BTKi*, Bruton's tyrosine kinase inhibitor; *cBTKi*, covalent BTKi; *CLL*, chronic lymphocytic leukemia; *CNS*, central nervous system; *ECOG PS*; Eastern Cooperative Oncology Group Performance Status; *ncBTKi*, non-covalent BTKi; *SLL*, small lymphocytic lymphoma

^aPatients could have received multiple prior treatments; ^bPatients could have multiple mutations (which are reported at VAF >5%)

Data cutoff: 1 Jan 2026

ORR in Earlier Lines of Treatment (Phase 1b Cohorts 5 and 15)

Promising response rates in BCL2i-naïve, BTKi-naïve and treatment-naïve patients

	Earlier lines of treatment CLL/SLL	
	BTKi-treated and BCL2i-naïve	BTKi-naïve (including treatment-naïve)
	Phase 1b Cohort 5 (n=14)	Phase 1b Cohort 15 (n=19)
ORR, % (95% CI) ^a	92.9 (66.1–99.8)	84.2 (60.4–96.6)
PR/PR-L	13 (92.9)	16 (84.2)
SD	0	3 (15.8)
PD	0	0
NE	1 (7.1)	0
Median follow-up, ^b months (range)	5.2 (1.9–7.7)	4.9 (2.9–5.8)

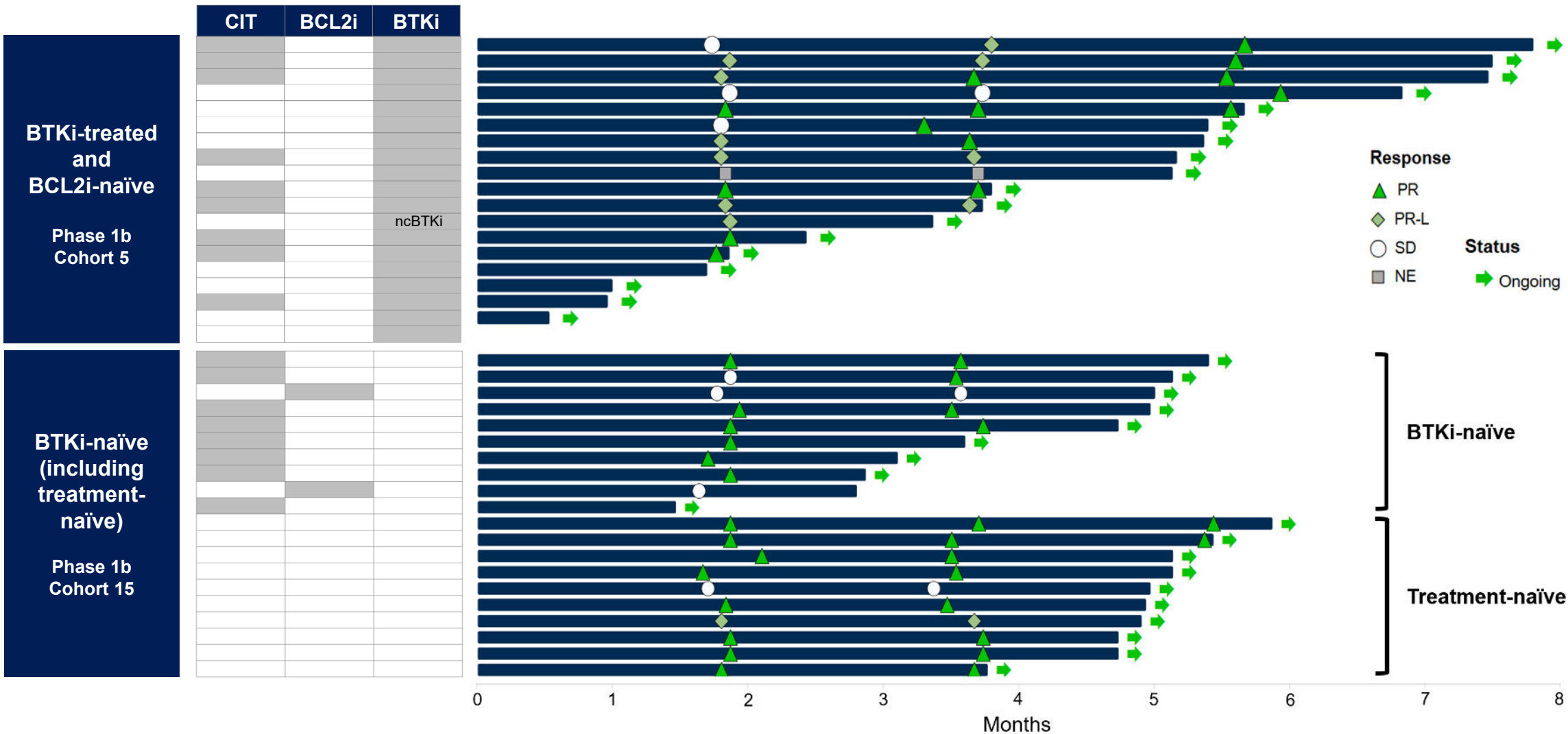
BCL2i, B-cell lymphoma 2 inhibitor; *BTKi*, Bruton's tyrosine kinase inhibitor; *CI*, confidence interval; *CLL*, chronic lymphocytic leukemia; *NE*, non-evaluable; *nPR*, nodal partial response; *ORR*, objective response rate; *PD*, progressive disease; *PR*, partial response; *PR-L*, partial response with lymphocytosis; *SD*, stable disease; *SLL*, small lymphocytic lymphoma

^aObjective response rate includes CR + nPR + PR + PR-L; ^bTime from treatment start to data cutoff

Data cutoff: 1 Jan 2026

Time on Treatment in Patients Receiving Earlier Lines of Treatment

Rapid and durable responses noted in most patients

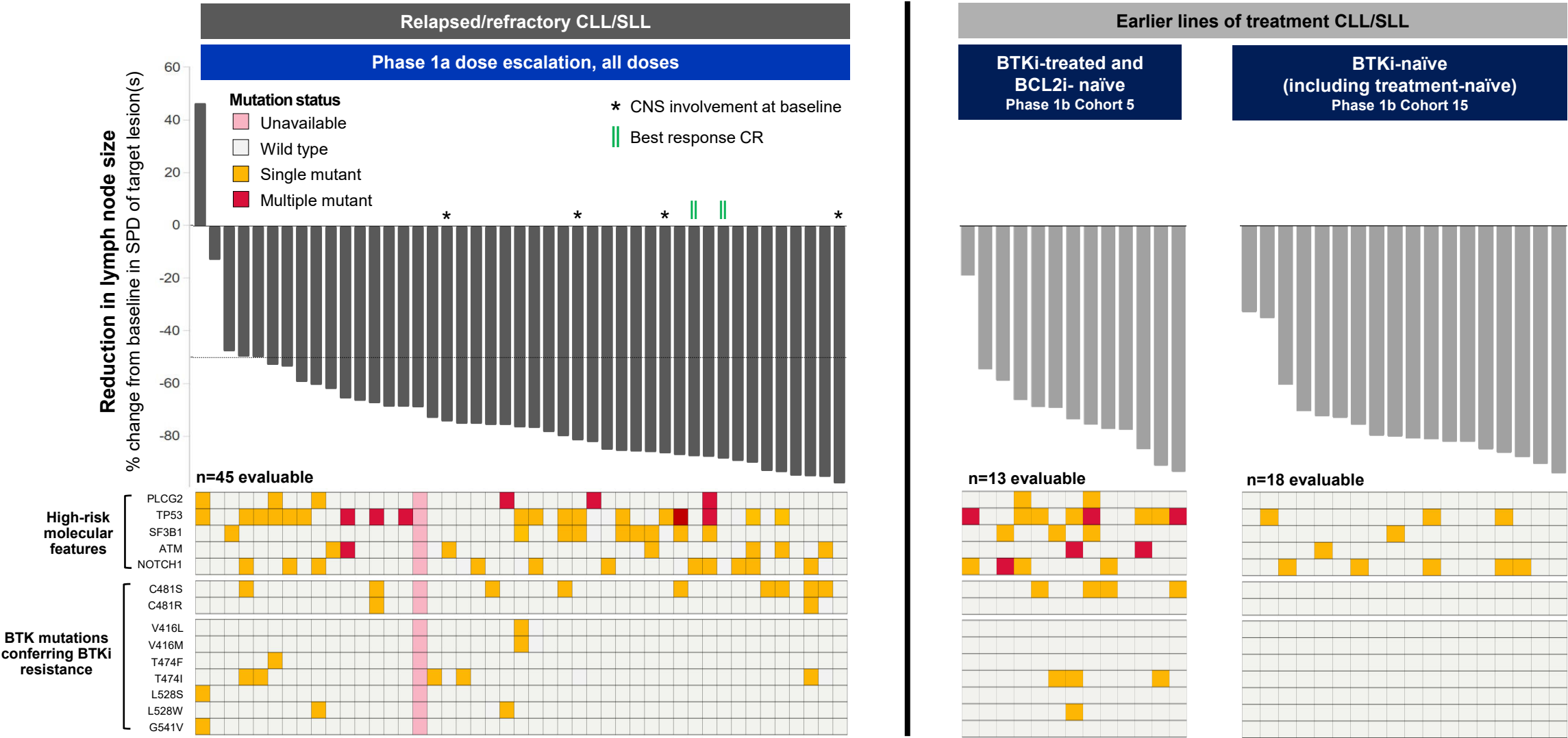


BCL2i, B-cell lymphoma 2 inhibitor; *BTKi*, Bruton's tyrosine kinase inhibitor; *CIT*, chemo-immunotherapy; *CLL*, chronic lymphocytic leukemia; *ncBTKi*, non-covalent BTKi; *NE*, non-evaluable; *PR*, partial response; *PR-L*, partial response with lymphocytosis; *SD*, stable disease; *SLL*, small lymphocytic lymphoma

Data cutoff: 1 Jan 2026

Reduction in Lymph Node Size in Patients Treated with Bexobrutideg

Bexobrutideg demonstrates broad clinical activity including in high-risk patients



ATM, ataxia-telangiectasia mutated; BTK, Bruton's tyrosine kinase; BTKi, BTK inhibitor; CLL, chronic lymphocytic leukemia; CNS, central nervous system; CR, complete response; NOTCH1, neurologic locus notch homolog protein 1; PLCG2, phospholipase C gamma 2; SLL, small lymphocytic lymphoma; SPD, sum of products diameters

Waterfall plot includes patients with measurable lymph node status; mutations were reported at VAF >5%; Patients could have no mutations, a single mutation, or multiple mutations

Data cutoff: 1 Jan 2026

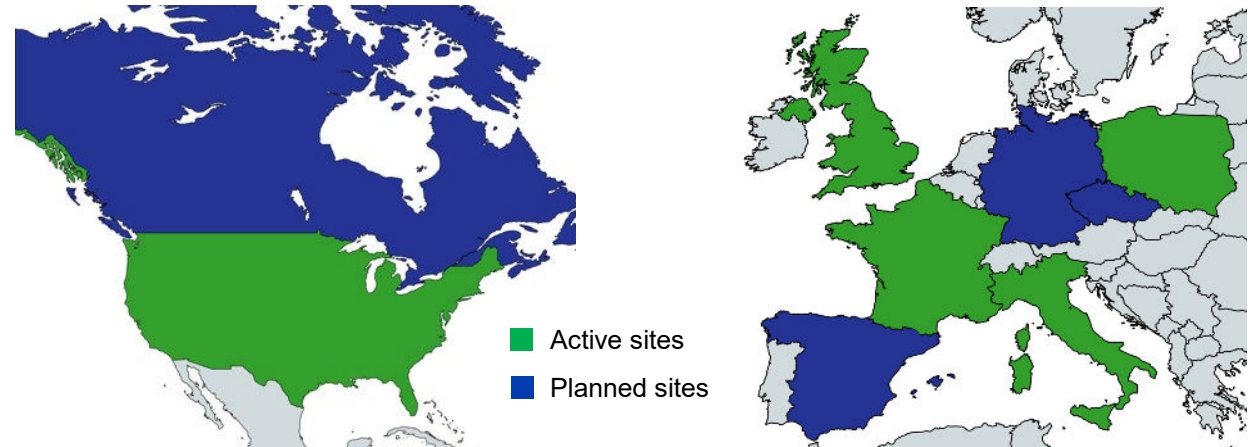
Conclusions

- Bexobrutideg is a highly selective, CNS penetrant degrader of both wild type BTK and BTKi resistance mutations that eliminates both the kinase and scaffolding functions of the BTK protein
- In the Phase 1a portion of trial NX-5948-301, bexobrutideg demonstrated an ORR of 83% with a median PFS of 22.1 months across all doses (50–600 mg)
- In the Phase 1b portion of the trial, high ORRs were observed in cohorts of patients with fewer or no prior lines of treatment (despite short follow-up period):
 - 92.9% in patients who were BTKi-treated and BCL2i-naïve (Cohort 5)
 - 84.2% in patients who were BTKi-naïve (including treatment-naïve; Cohort 15)
- Clinical responses were observed across the overall population including in difficult-to-treat subgroups with baseline BTK mutations, relapsed/refractory disease, high number of prior therapies, high-risk molecular features and CNS involvement
- Bexobrutideg was well tolerated and safety profile was consistent with prior disclosures, including in comparisons between the RP2D 600 mg and overall trial population
- **Based on the totality and consistency of safety and efficacy findings, bexobrutideg is being evaluated in the ongoing pivotal Phase 2 DAYBreak CLL-201 and planned Phase 3 DAYBreak CLL-306 trials**

Acknowledgments

- The authors are grateful to the patients who enrolled in the NX-5948-301 trial and their families
 - The authors would also like to thank:
 - All NX-5948-301 investigators and study site staff in France, Italy, the United States, the United Kingdom, the Netherlands, Poland, Spain, and Switzerland for participating in this clinical research
 - Nurix employees developing bexobrutideg and supporting the clinical trial
-

- Phase 2 clinical trial of bexobrutideg (NX-5948) – DAYBreak CLL-201 is now enrolling globally



- Bexobrutideg (NX-5948) studies are sponsored by Nurix Therapeutics, Inc.
-