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

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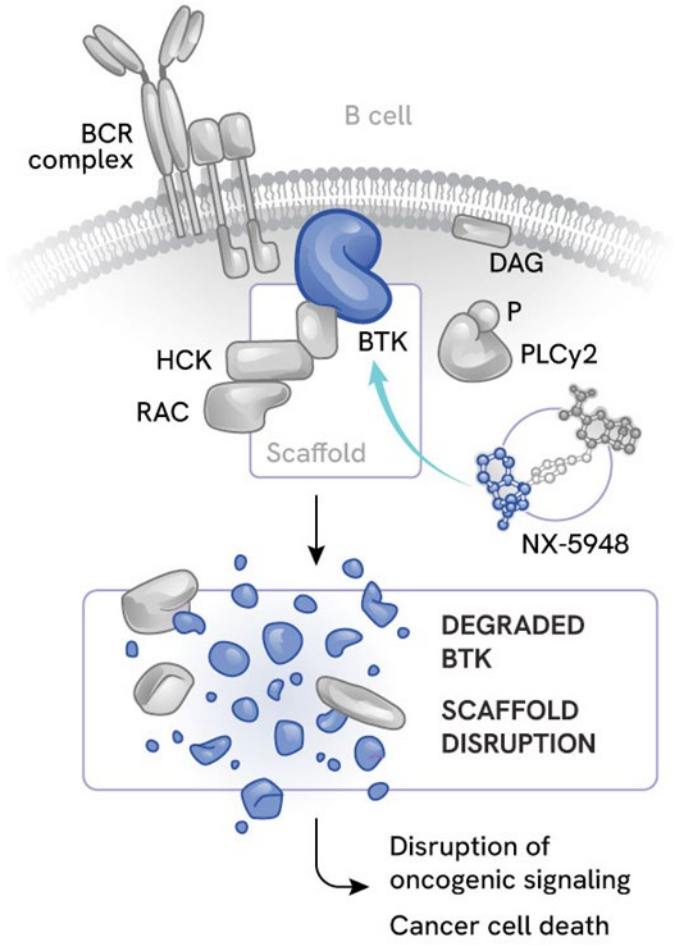
Bexobrutideg (NX-5948)

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



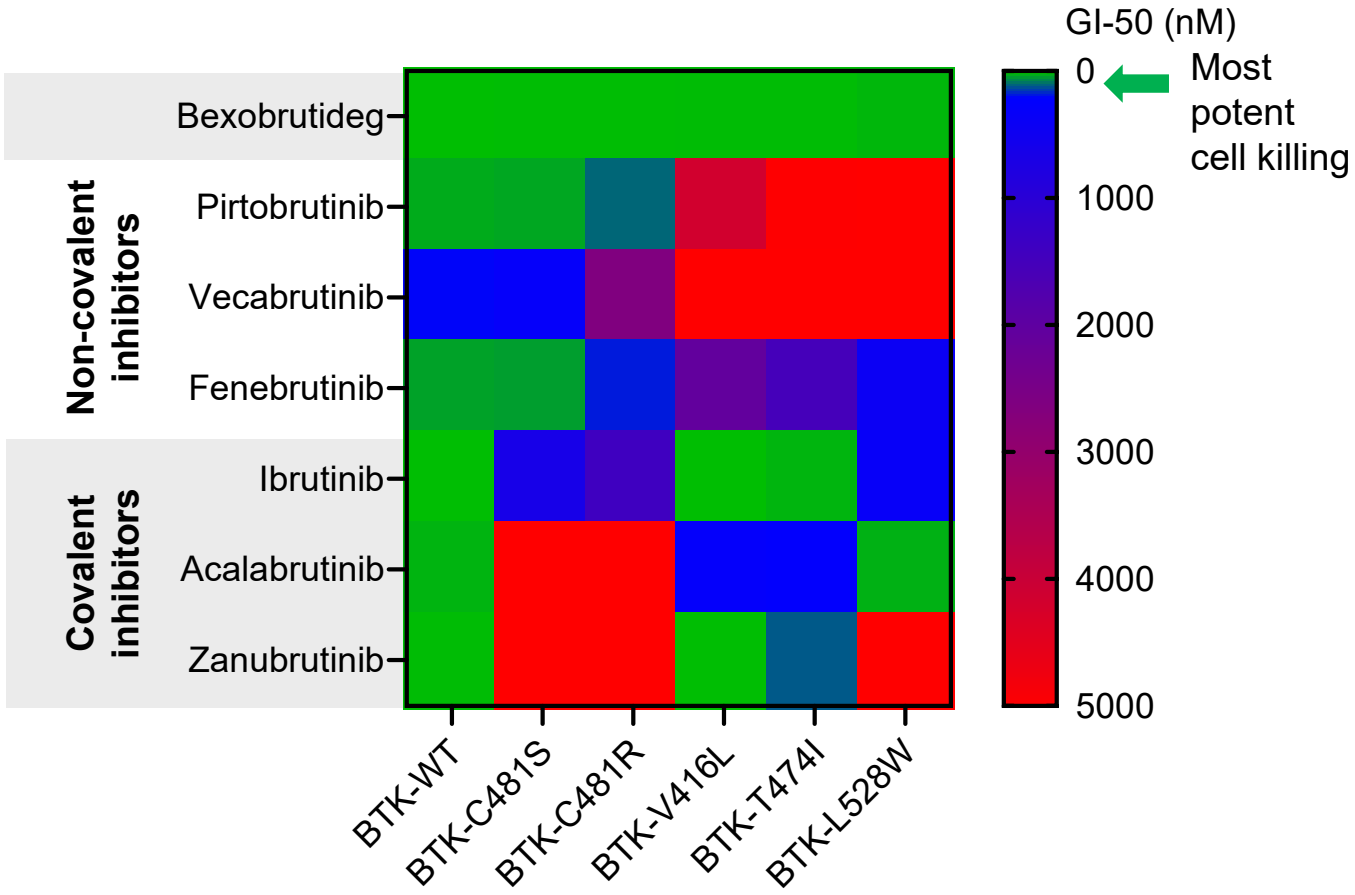
- ✓ Active against not only wildtype BTK but also treatment emergent BTK-inhibitor resistance mutations[1,2]
- ✓ Addresses both BTK scaffolding and kinase functions, unlike current BTK inhibitors[3]
- ✓ Acts catalytically, driving degradation at low free-drug plasma concentrations
- ✓ Crosses the blood-brain barrier and demonstrates clinical activity in the CNS[4]
- ✓ Demonstrates robust clinical activity in difficult-to-treat B-cell malignancies[5–7]

***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*

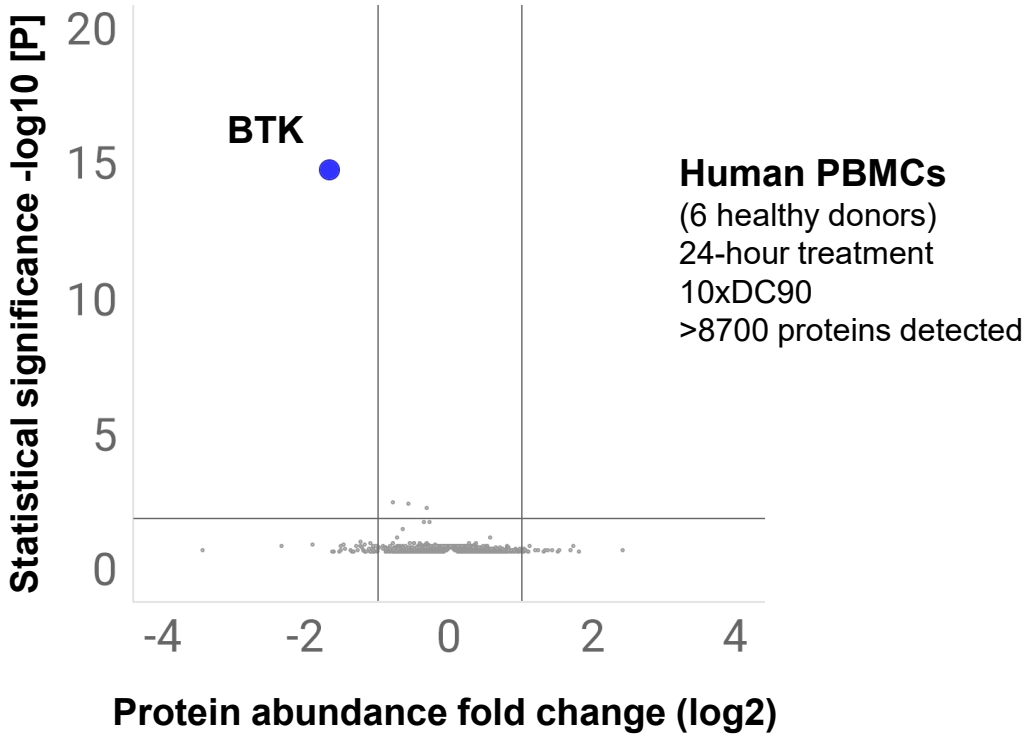
1. Noviski et al. 20th Biennial International Workshop on CLL, Boston, MA, USA. Oct 6–9, 2023; 2. Hansen. Presented at TPD Basel, Switzerland, Sept 19, 2023; 3. Montoya et al. Science 2024;383; eadi5798;
4. Noviski. 8th TPD & Induced Proximity Summit, Boston, MA, USA, Oct 29, 2025; 5. Shah et al. Blood (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)

Phase 1a

Relapsed/refractory CLL/SLL

Dose escalation

50–600 mg[a]

600 mg QD

450 mg QD

300 mg QD

200 mg QD

100 mg QD

50 mg QD

Phase 1b randomized

Relapsed/refractory CLL/SLL

Randomized Cohort 1

R

600 mg QD (RP2D)
Prior BTKi and BCL2i

200 mg QD
Prior BTKi and BCL2i

Phase 1b dose expansion

Earlier lines of treatment CLL/SLL

Cohort 5 (fully enrolled)	**Cohort 15** (fully enrolled)	**Additional cohorts** (enrolling)
BTKi-treated and BCL2i-naïve[b]	**BTKi-naïve**	**High-risk disease[c]**
	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*
[a]Starting dose;[b]All patients at 600 mg except one patient on 200 mg dose; [c]Including: 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

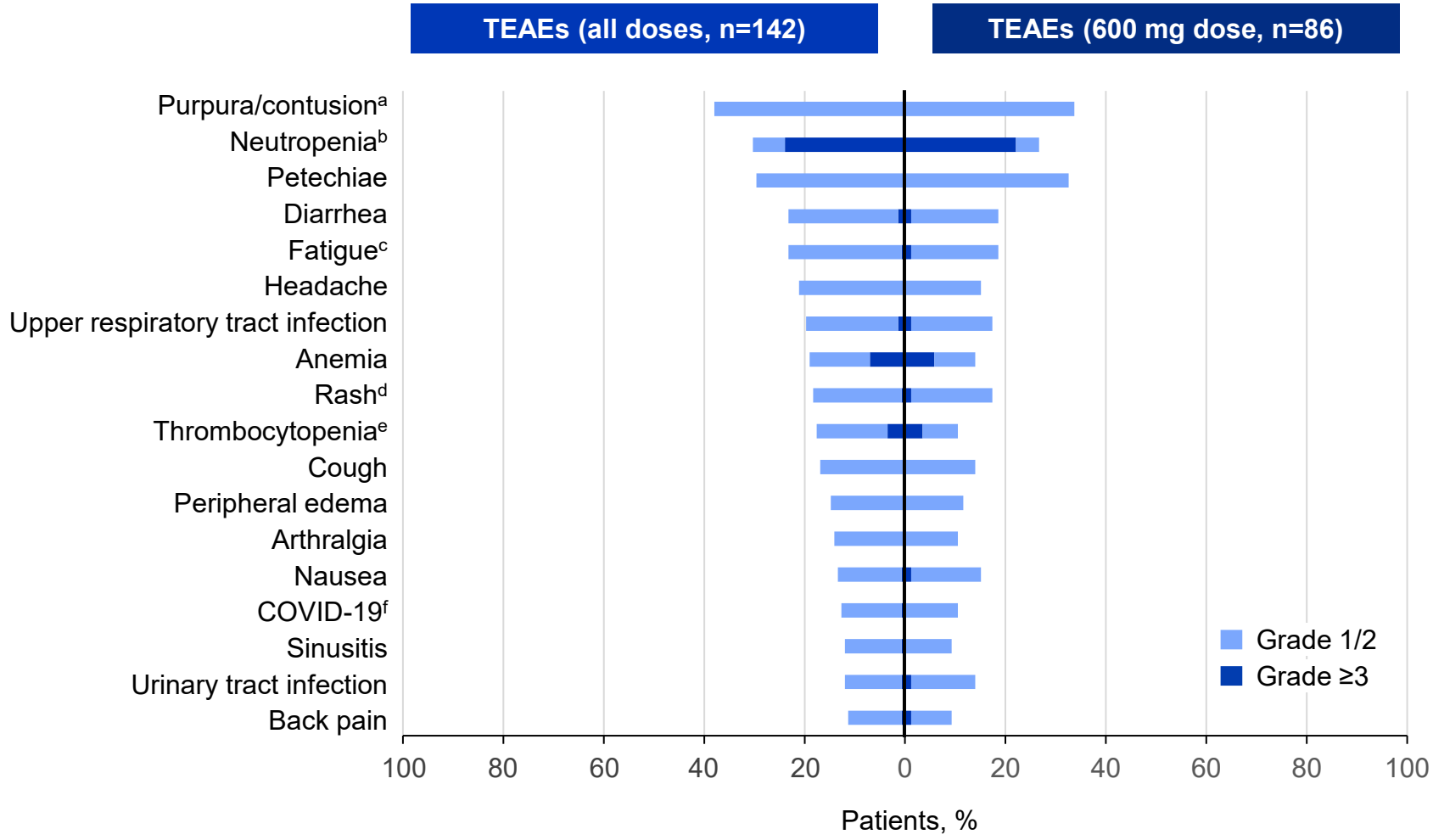
n (%)	All patients with CLL/SLL (n=142)	600 mg dose patients (n=86)	50–450 mg dose patients (n=56)
Any TEAE	134 (94.4)	79 (91.9)	55 (98.2)
Treatment related	110 (77.5)	65 (75.6)	45 (80.4)
Grade 3+	73 (51.4)	39 (45.3)	34 (60.7)
Treatment related	35 (24.6)	22 (25.6)	13 (23.2)
SAE	33 (23.2)	16 (18.6)	17 (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



- Tolerable safety profile consistent with prior disclosures
- No dose-limiting toxicities
- Three Grade 5 AE, all deemed not related (pneumonia, pulmonary embolism, NOS)

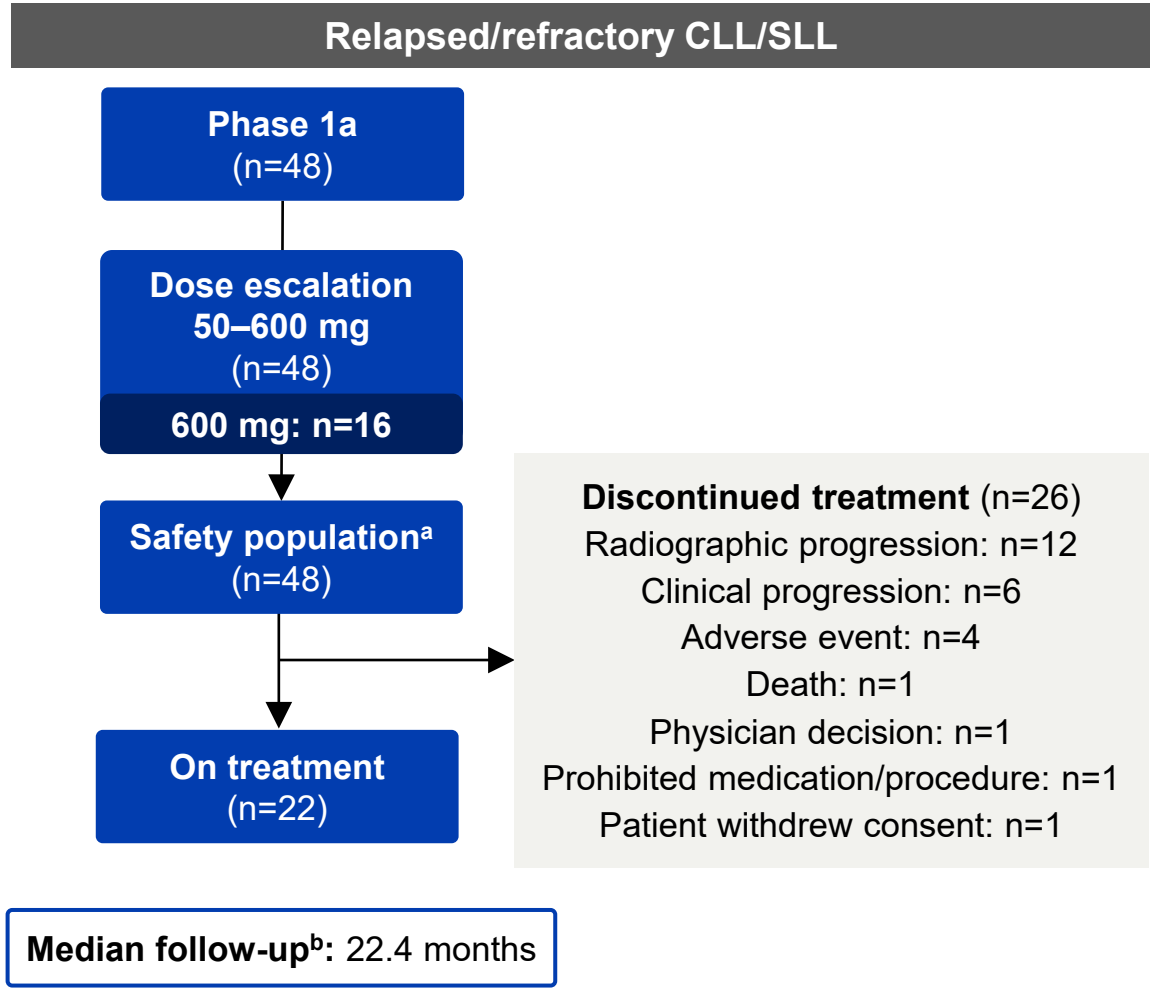
***AE**, adverse event; **CLL**, chronic lymphocytic leukemia; **NOS**, not otherwise specified; **RP2D**, recommended Phase 2 dose; **SLL**, small lymphocytic lymphoma; **TEAE**, treatment-emergent adverse event*

[a]Purpura/contusion includes episodes of contusion or purpura; [b]Aggregate of 'neutrophil count decreased' or 'neutropenia'; [c]Fatigue was transient; [d]Aggregate of 'rash' and 'rash maculopapular' and 'rash pustular'; [e]Aggregate of 'thrombocytopenia' and 'platelet count decreased'; [f]Aggregate 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 (%) *BTK* *TP53* *PLCG2* *BCL2* *IGHV (unmutated)*	(n=47) 18 (38.3) 21 (44.7) 7 (14.9) 6 (12.8) 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

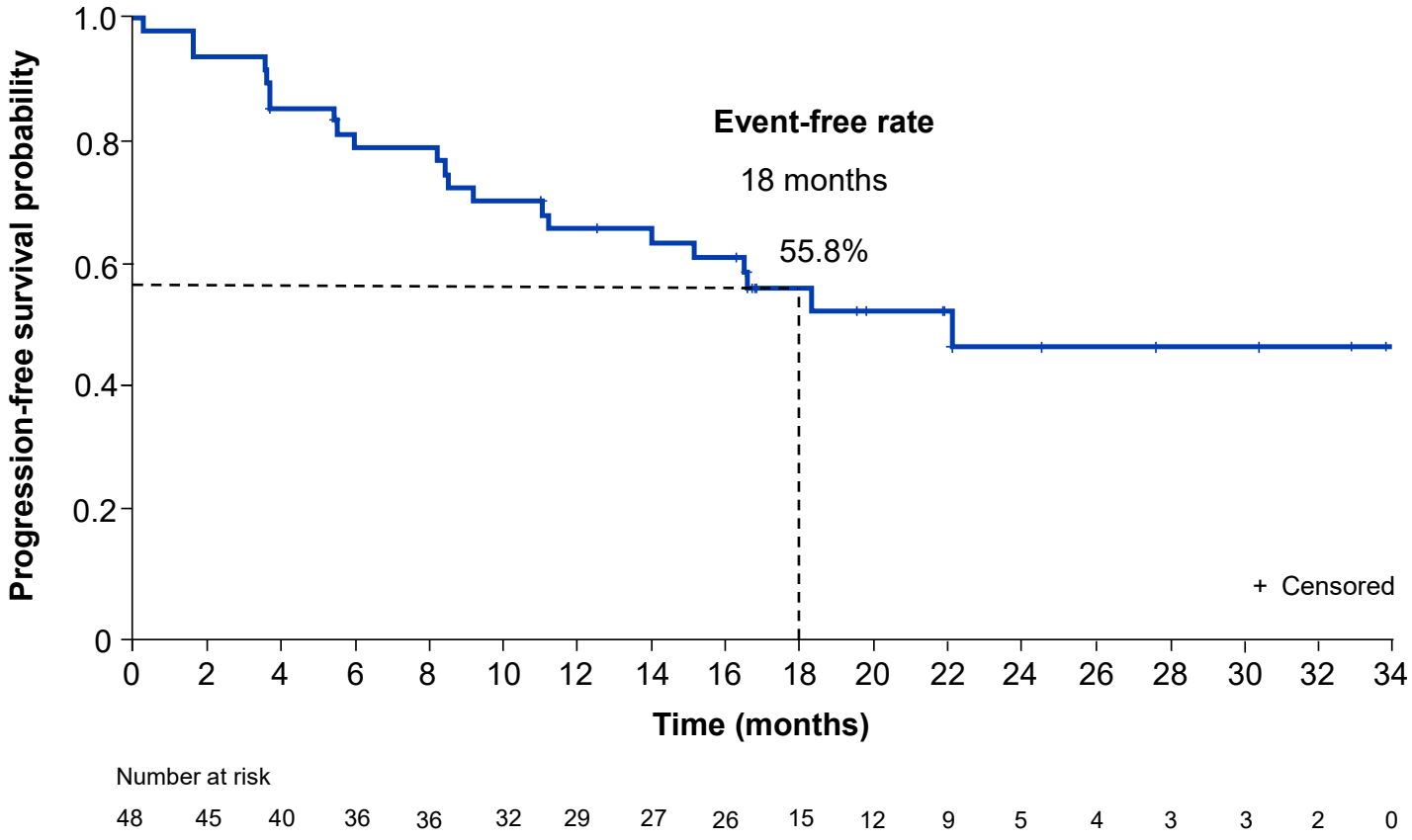
Data cutoff: 1 Jan 2026

[a]Safety and efficacy populations are identical; [b]Time from treatment start to data cutoff; [c]Patients could have received multiple prior treatments; [d]Patients 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)

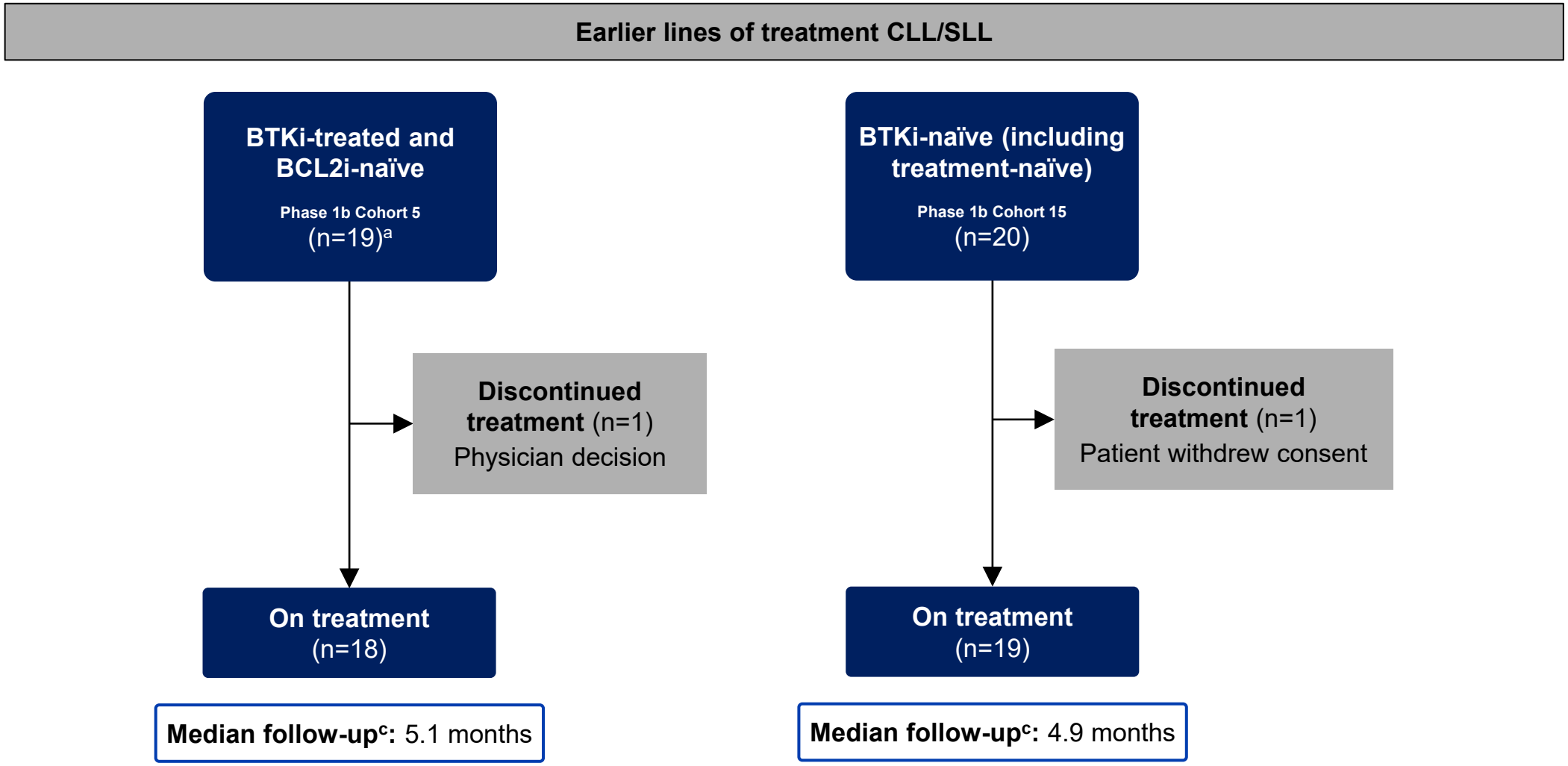
***CI**, confidence interval; **CLL**, chronic lymphocytic leukemia; **CR**, complete response; **nPR**, nodal partial response; **NR**, not reached; **ORR**, objective response rate; **PD**, progressive disease; **PFS**, progression-free survival; **PR**, partial response; **PR-L**, partial response with lymphocytosis; **SD**, stable disease; **SLL**, small lymphocytic lymphoma*

[a]Median for PFS by Kaplan–Meier method; [b]Excludes 1 patient who was not evaluable for response; [c]Objective response rate includes CR + nPR + PR + PR-L; [d]Time from treatment start to data cutoff

Data cutoff: 1 Jan 2026

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

[a]One 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; [c]Time 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 (%) *BTK* *TP53* *PLCG2* *BCL2* *IGHV (unmutated)*	(n=19) 10 (52.6) 9 (47.4) 3 (15.8) 1 (5.3) 14 (93.3), n=15	(n=20) 0 3 (15.0) 0 0 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*

[a]Patients could have received multiple prior treatments; [b]Patients 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 **Phase 1b Cohort 5** (n=14)	**BTKi-naïve (including treatment-naïve)** **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)

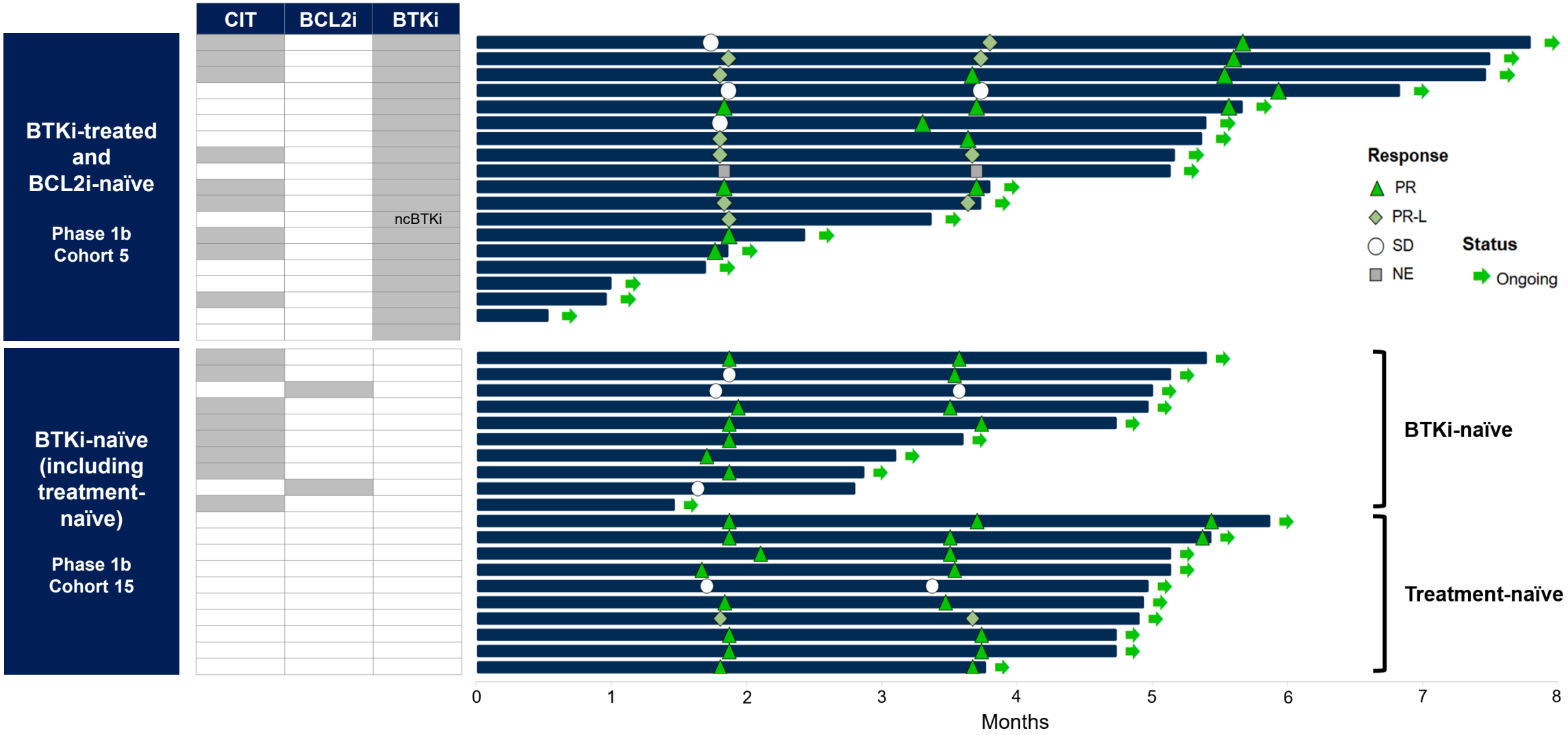
***BCL2i**, B-cell lymphoma 2 inhibitor; **BTKi**, Bruton's tyrosine kinase inhibitor; **CI**, confidence interval; **CLL**, chronic lymphocytic leukemia; **NE**, non-evaluable; **nPR**, nodal partial response; **ORR**, objective response rate; **PD**, progressive disease; **PR**, partial response; **PR-L**,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

[a]Objective response rate includes CR + nPR + PR + PR-L; [b]Time 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

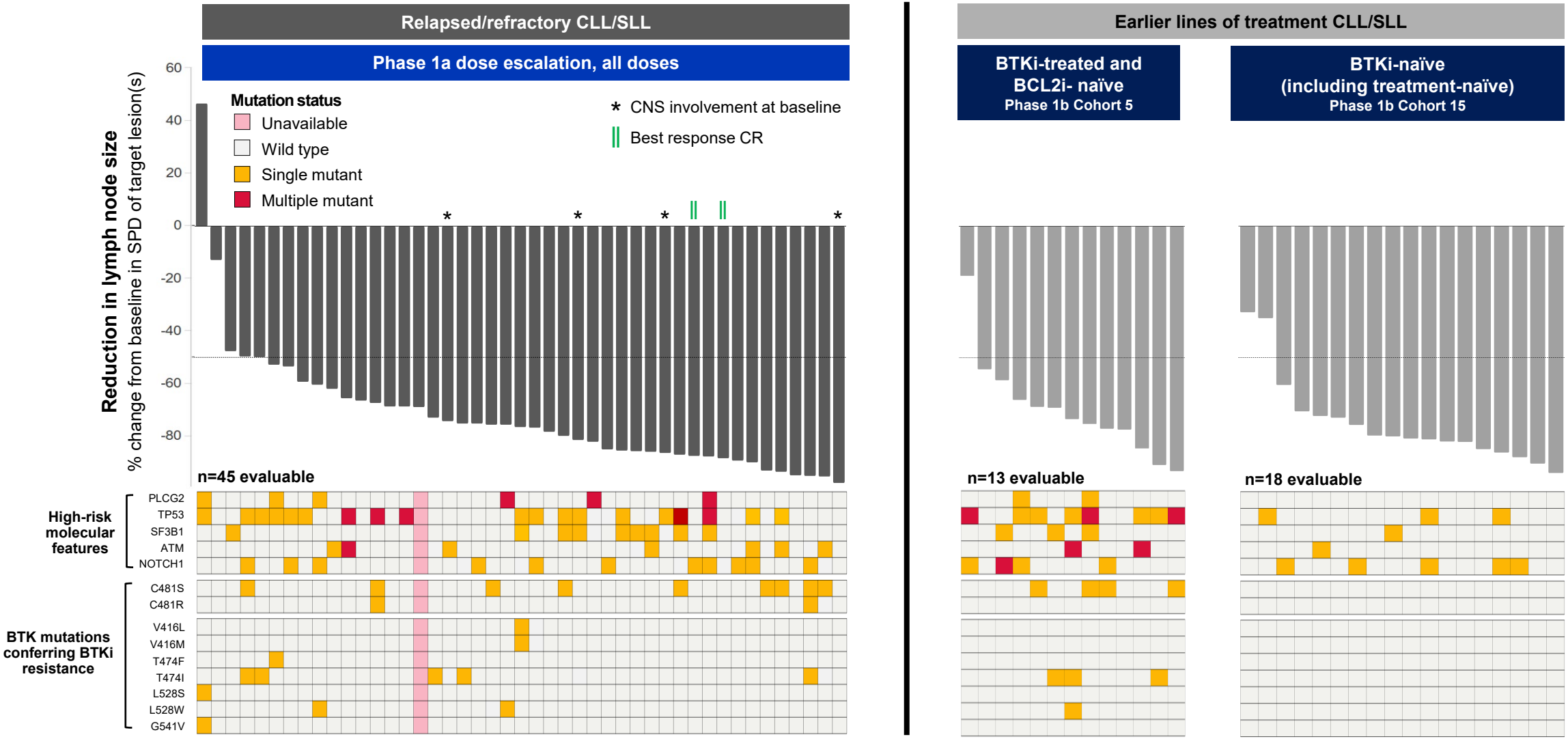


***BCL2i**, B-cell lymphoma 2 inhibitor; **BTKi**, Bruton's tyrosine kinase inhibitor; **CIT**, chemo-immunotherapy; **CLL**, chronic lymphocytic leukemia; **ncBTKi**, non-covalent BTKi; **NE**, non-evaluable; **PR**, partial response; **PR-L**, partial response with lymphocytosis; **SD**, stable disease;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

***BCL2i**, B-cell lymphoma 2 inhibitor; **BTK**, Bruton's tyrosine kinase**; BTKi**, BTK inhibitor; **CLL,** chronic lymphocytic leukemia; **CNS**, central nervous system; **ORR**, objective response rate; **PFS**, progression-free survival; **RP2D**, recommended Phase 2 dose; **SLL**, small lymphocytic lymphoma*

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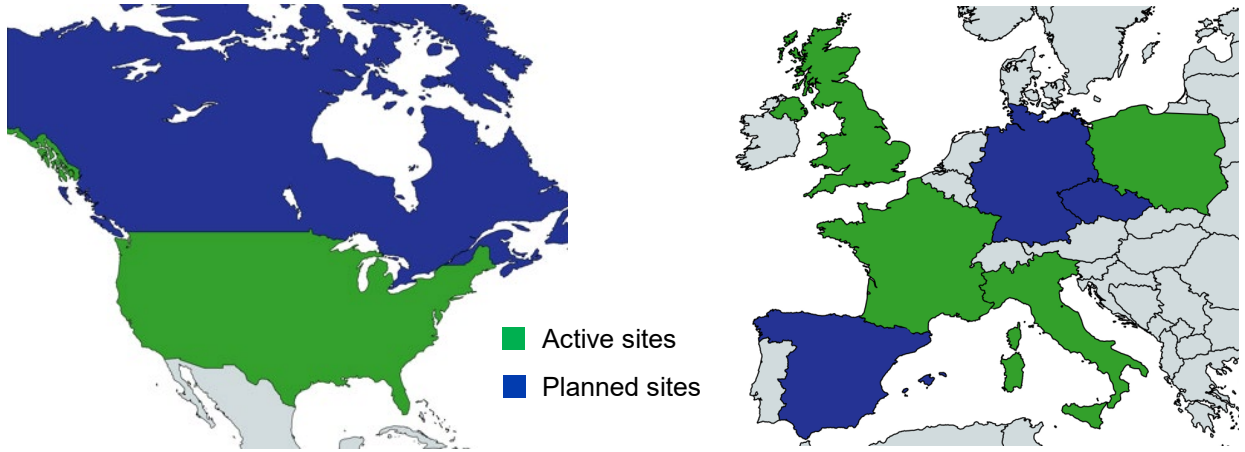
- The authors would also like to thank:
  - All NX-5948-301 investigators and study site staff in France, Italy, the United States, the United Kingdom, the Netherlands, Poland, Spain, and Switzerland for participating in this clinical research
  - Nurix employees developing bexobrutideg and supporting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

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

DAYBreak CLL-201



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