



Leader in Targeted Protein Modulation

# Nurix Therapeutics

*Blazing a New Path in Medicine*

Investor Presentation

November 2024

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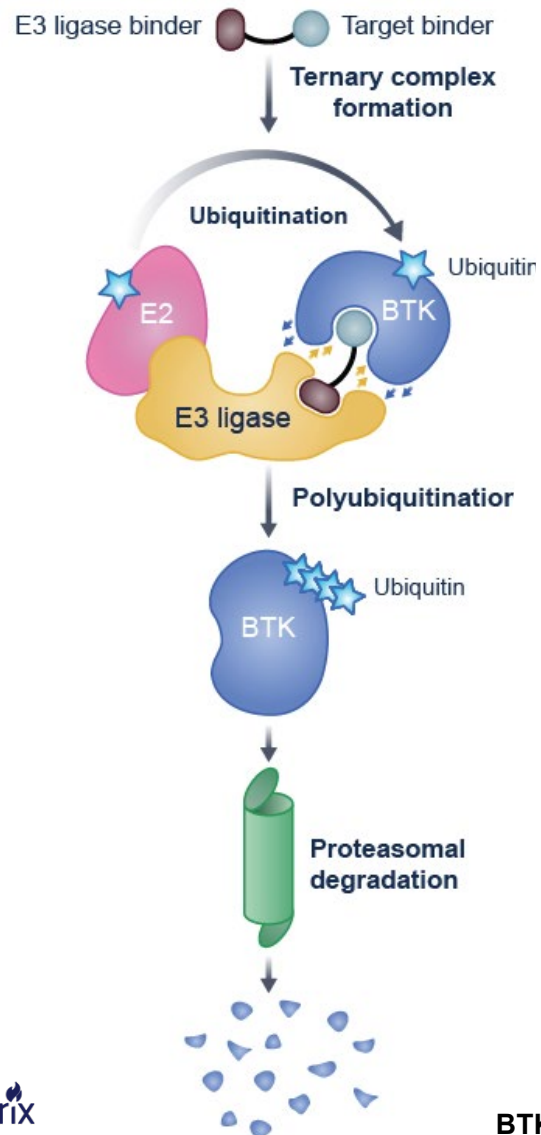
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# Nurix Is Advancing a Pipeline of Proprietary and Partnered Programs in Oncology and Inflammation & Immunology

MOA	Oncology program	Target	Therapeutic area	Discovery – Lead Op	IND enabling	Phase 1a	Phase 1b
TPD	NX-5948	BTK	B-cell malignancies				
	NX-2127	BTK-IKZF	B-cell malignancies				
TPE	NX-1607	CBL-B	Immuno-Oncology				
TPD	Multiple	Undisclosed	Undisclosed				
	Multiple	Undisclosed	Undisclosed				
	Multiple	Undisclosed	Undisclosed				
DAC	Multiple	Undisclosed	Oncology				

MOA	I&I program	Target	Therapeutic area	Discovery – Lead Op	IND enabling	Phase 1a	Phase 1b
TPD	NX-5948	BTK	Inflammation / autoimmune				
	NX-0479 / GS-6791	IRAK4	Rheumatoid arthritis and other inflammatory diseases				
	STAT6 degrader	STAT6	Type 2 inflammatory diseases				
	Undisclosed	Undisclosed	Inflammation / autoimmune				

# Why Do We Need BTK Degraders?



BTK degraders can overcome treatment-emergent resistance mutations

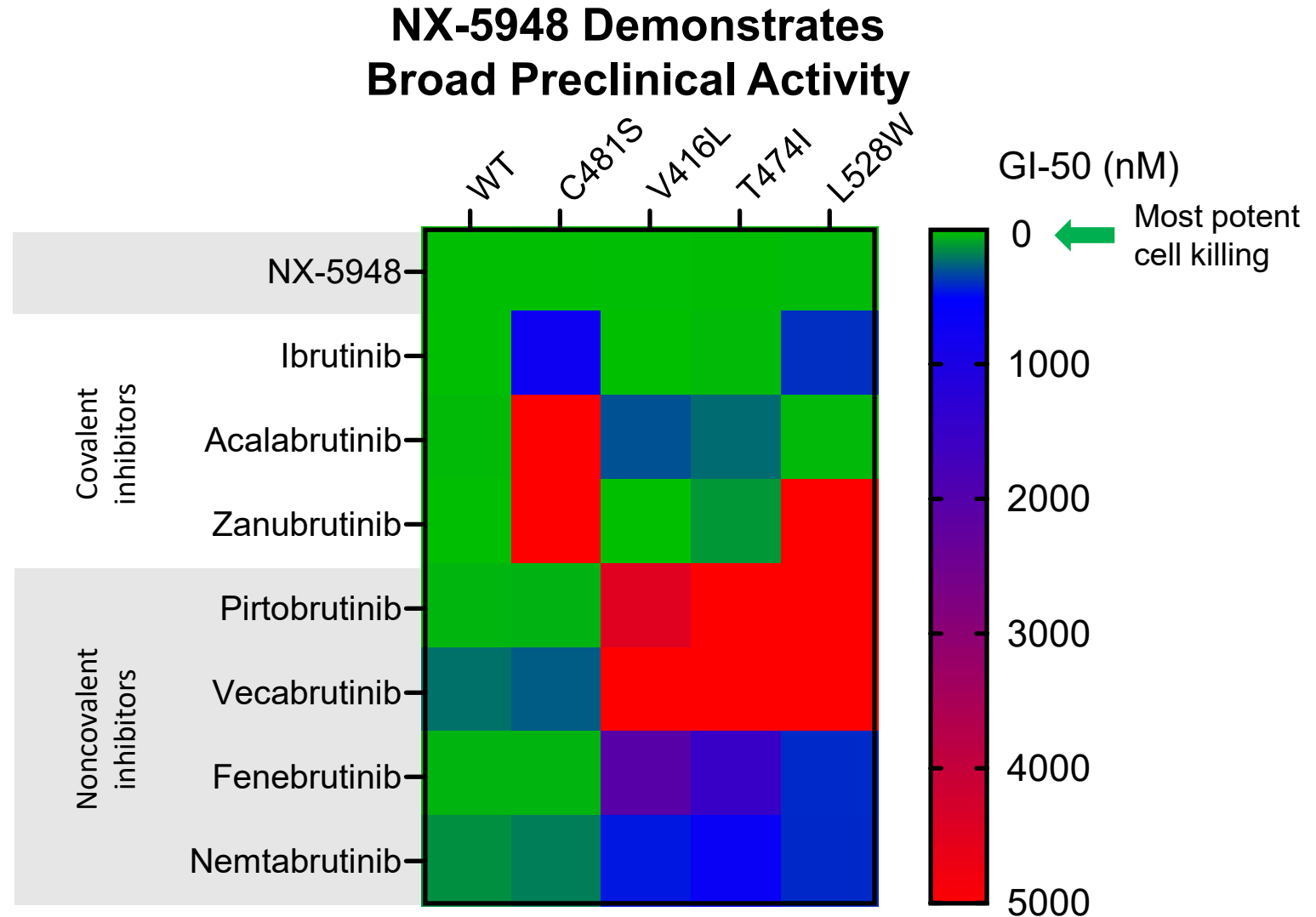
BTK degraders address BTK scaffolding function

BTK degraders show emerging activity in various B-cell malignancies

BTK degraders have the potential to replace BTK inhibitors in the clinic

# NX-5948 Is More Potent and Broadly Active Than All BTK Inhibitors Tested

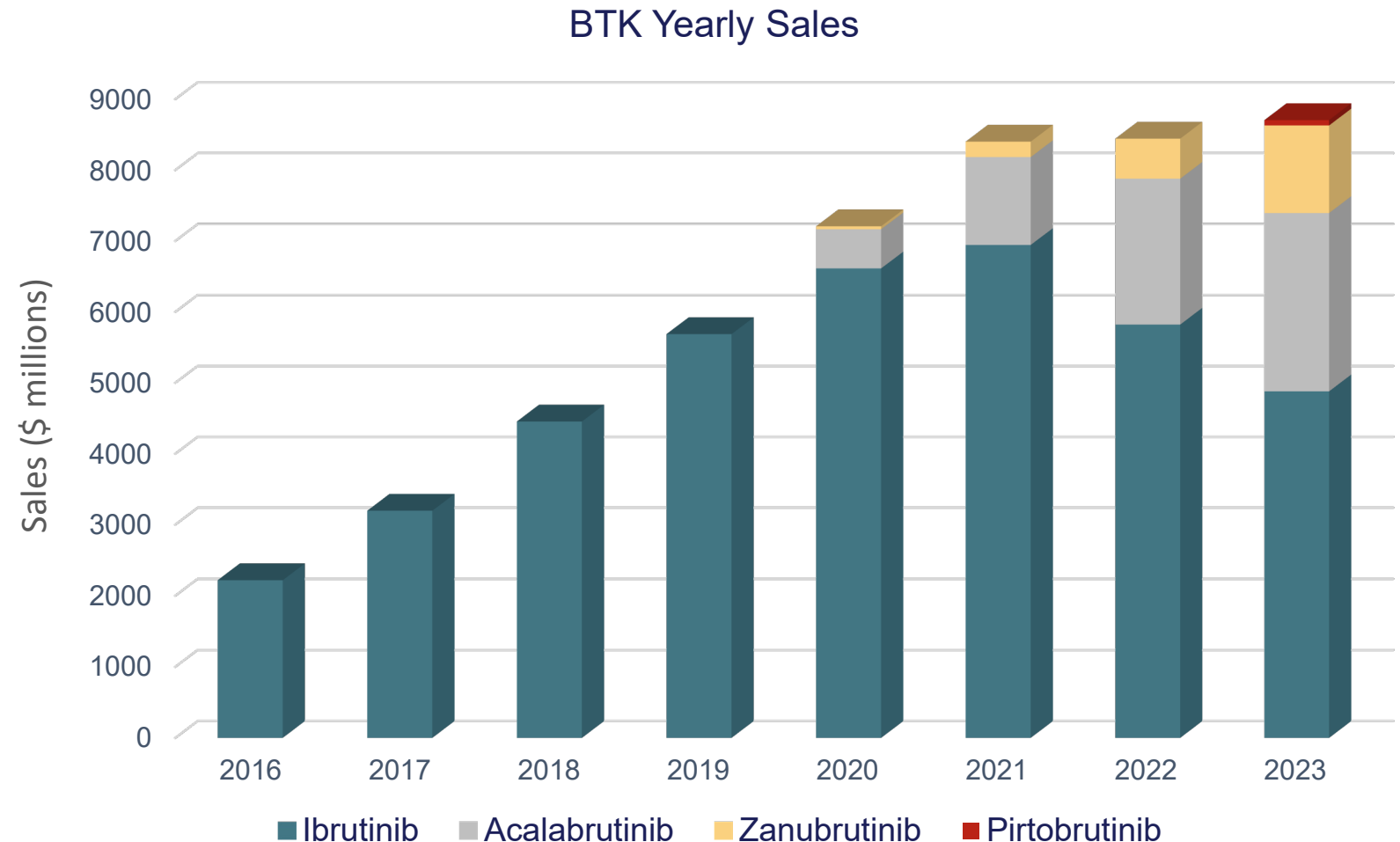
- All inhibitors have resistance mutation liabilities
- NX-5948 displays potent cell killing in the context of key resistance mutations
- We have shown that BTK degradation translates into clinical responses across key mutation classes



# Blockbuster Opportunity in BTK Market

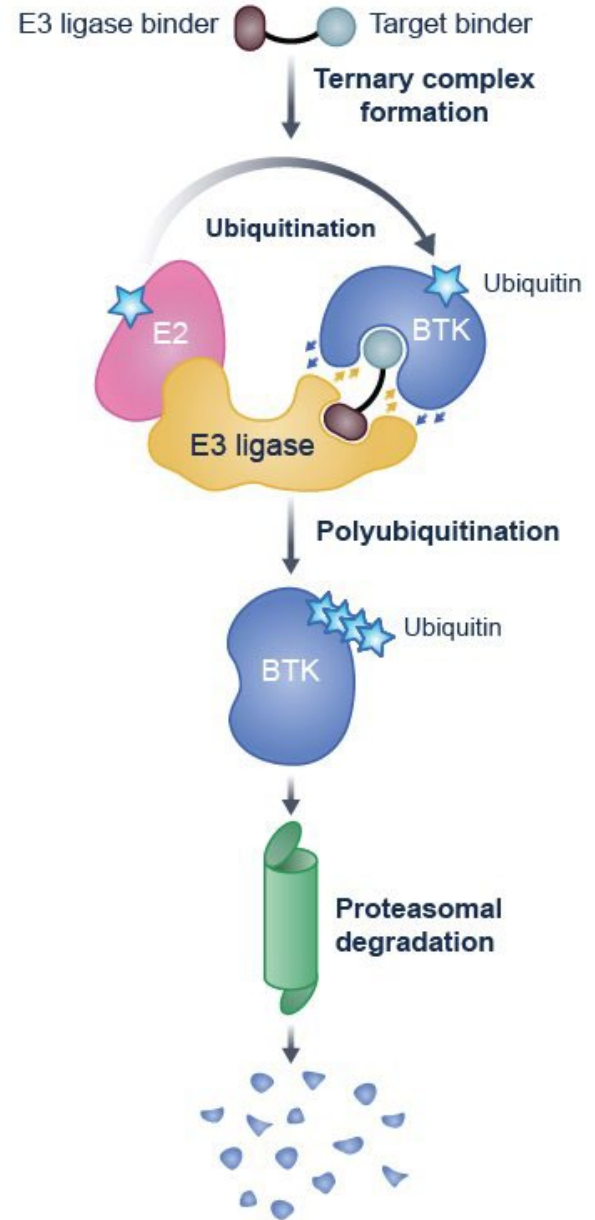
\$8.7 billion in annual sales of approved BTK inhibitors

- Next generation BTK inhibitors are currently taking market share from Imbruvica
- All BTK inhibitors share resistance mutation vulnerabilities
- Opportunity for Nurix BTK degraders to displace both covalent and non-covalent inhibitors and expand the market



# NX-5948

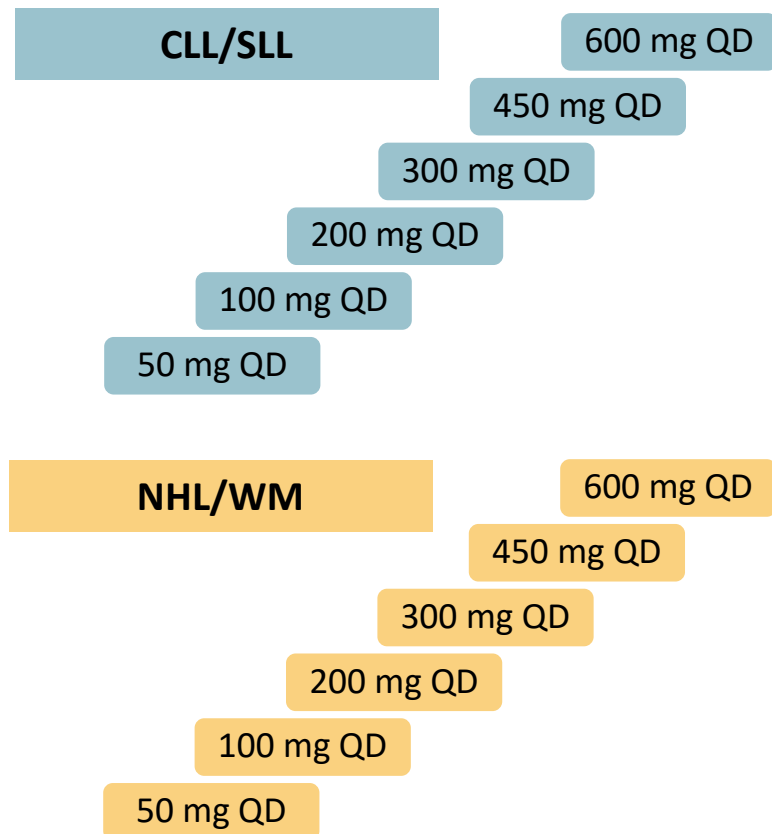
Highly selective BTK degrader



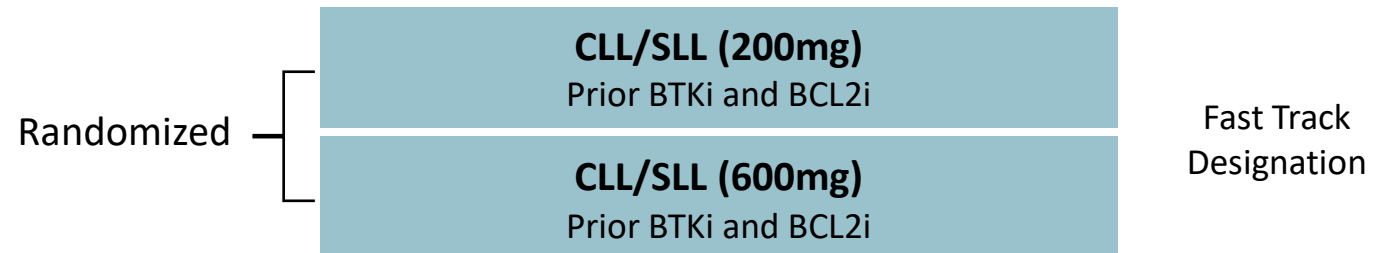
# NX-5948-301: Trial Design

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

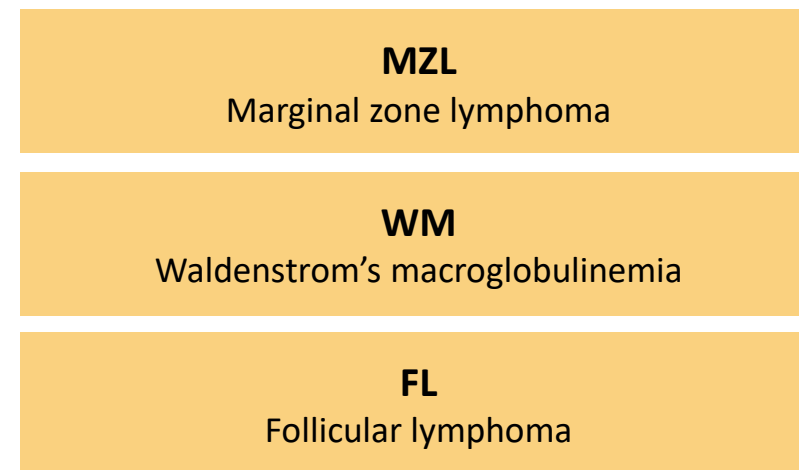
## Phase 1a dose escalation [fully enrolled]



## Ongoing CLL Phase 1b expansion cohorts



## Ongoing NHL/WM Phase 1b expansion cohorts





# Baseline Demographics/Disease Characteristics

Elderly population with multiple prior lines of targeted therapies

Characteristics	Patients with CLL (n=31)	Patients with NHL/WM (n=48)	Overall population (N=79)
<b>Median age, years (range)</b>	69.0 (35–88)	66.5 (42–87)	67.0 (35–88)
<b>Male, n (%)</b>	19 (61.3)	33 (68.8)	52 (65.8)
<b>ECOG PS, n (%)</b>			
0	13 (41.9)	13 (27.1)	26 (32.9)
1	18 (58.1)	33 (68.8)	51 (64.6)
<b>CNS involvement, n (%)</b>	2 (6.5)	10 (20.8)	12 (15.2)
<b>Median prior lines of therapy (range)</b>	4.0 (2–14)	4.0 (2–13)	4.0 (2–14)
<b>Previous treatments<sup>a</sup>, n (%)</b>			
BTKi	30 (96.8)	29 (60.4)	59 (74.7)
≥2 BTKi	11 (35.5)	NA	NA
Pirtobrutinib	7 (22.6)	7 (14.6)	14 (17.7)
BCL2i	28 (90.3)	7 (14.6)	35 (44.3)
BTKi and BCL2i	27 (87.1)	7 (14.6)	34 (43.0)
CAR-T therapy	2 (6.5)	11 (22.9)	13 (16.5)
Bispecific antibody	1 (3.2)	7 (14.6)	8 (10.1)
PI3Ki	9 (29.0)	4 (8.3)	13 (16.5)
Chemo/chemo-immunotherapies	24 (77.4)	48 (100.0)	72 (91.1)
<b>Mutation status, n (%)</b>			
TP53	14/30 (46.7)	4/42 (9.5)	18/72 (25.0)
BTK	13/30 (43.3)	0/42 (0.0)	13/72 (18.1)
PLCG2	6/30 (20.0)	2/42 (4.8)	8/72 (11.1)

# NX-5948 Is Well Tolerated

TEAEs in ≥10% of overall population or grade ≥3 TEAEs or SAEs in >1 patient

TEAEs, n (%)	Patients with CLL (n=31)			Overall population (N=79)		
	Any grade	Grade ≥3	SAEs	Any grade	Grade ≥3	SAEs
Purpura/contusion <sup>a</sup>	13 (41.9)	–	–	28 (35.4)	–	–
Thrombocytopenia <sup>b</sup>	7 (22.6)	1 (3.2)	–	21 (26.6)	7 (8.9)	–
Neutropenia <sup>c</sup>	7 (22.6)	6 (19.4)	–	16 (20.3)	12 (15.2)	–
Fatigue	7 (22.6)	–	–	14 (17.7)	2 (2.5)	–
Anemia	6 (19.4)	1 (3.2)	–	13 (16.5)	3 (3.8)	–
Petechiae	7 (22.6)	–	–	13 (16.5)	–	–
Rash <sup>d</sup>	8 (25.8)	–	1 (3.2)	13 (16.5)	1 (1.3)	1 (1.3)
Headache	6 (19.4)	–	–	12 (15.2)	–	–
Cough	4 (12.9)	–	–	11 (13.9)	1 (1.3)	–
Diarrhea	5 (16.1)	1 (3.2)	–	9 (11.4)	1 (1.3)	–
COVID-19 <sup>e</sup>	2 (6.5)	–	–	8 (10.1)	2 (2.5)	2 (2.5)
Hypertension	1 (3.2)	1 (3.2)	–	6 (7.6)	4 (5.1)	–
Pneumonia <sup>f</sup>	2 (6.5)	1 (3.2)	1 (3.2)	5 (6.3)	4 (5.1)	4 (5.1)

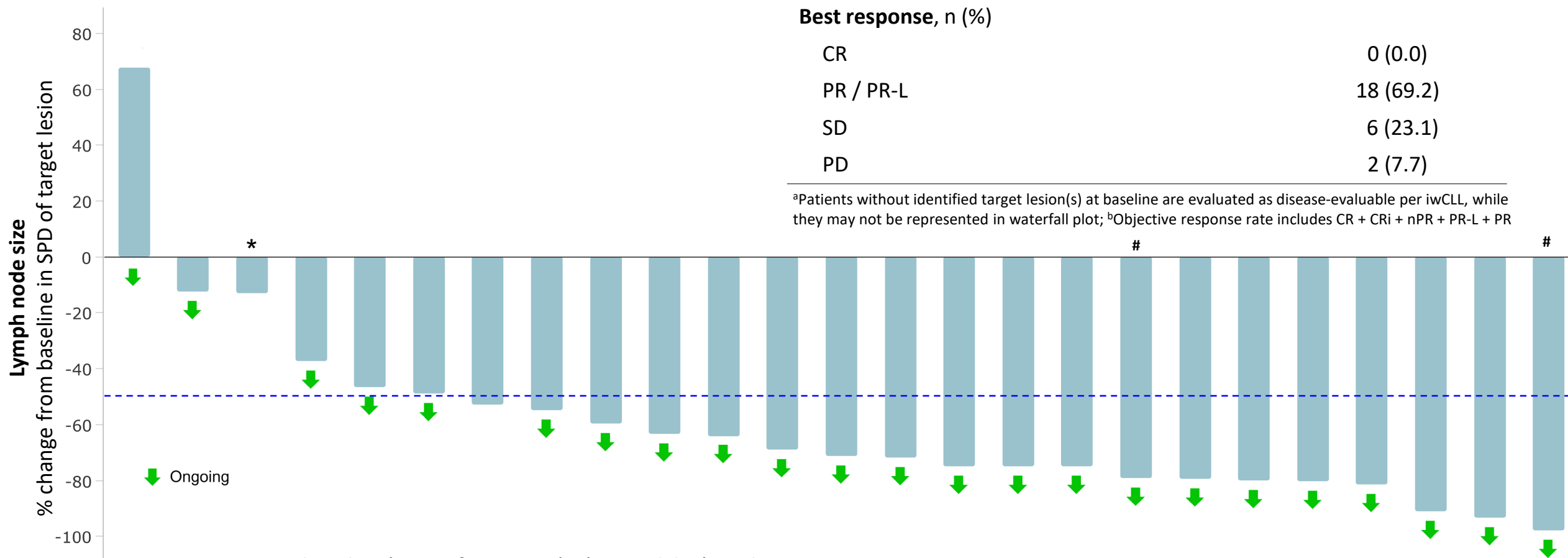
- 1 DLT (non-protocol mandated drug hold; NHL)
- 2 TEAEs resulting in drug discontinuation (both NHL)
- 1 related SAE (TLS based on labs, no clinical sequelae)
- Grade 5 AE (pulmonary embolism, not deemed NX-5948 related)
- No additional safety signal with higher doses

# NX-5948 Efficacy: Clinical Response

Broad antitumor activity in CLL as demonstrated by significant lymph node reduction and ORR

CLL disease-evaluable patients <sup>a</sup>	n=26
<b>Objective response rate (ORR)<sup>b</sup>, % (95% CI)</b>	69.2 (48.2–85.7)
<b>Best response, n (%)</b>	
CR	0 (0.0)
PR / PR-L	18 (69.2)
SD	6 (23.1)
PD	2 (7.7)

<sup>a</sup>Patients without identified target lesion(s) at baseline are evaluated as disease-evaluable per iwCLL, while they may not be represented in waterfall plot; <sup>b</sup>Objective response rate includes CR + CRi + nPR + PR-L + PR





# Case Study 1: Patient with CLL and CNS Involvement

Age, Race, M/F	59, White, M
Diagnosis	CLL, High Risk, Stage C
Initial diagnosis	May 2015
Recent progression	03 Oct 2022 (with CNS relapse)
Dose	100 mg/day → 300 mg/day
C1D1	27-Jun-23
Status	On treatment
Current cycle	12

## Relevant medical history

- Anxiety: 2015-ongoing
- Depression: 2015-ongoing
- Previous Hepatitis B infection: 2015 (on anti-viral prophylaxis but no evidence of recurrent disease)
- Recurrent lung infection: 2015-ongoing
- Face numbness: Unknown-ongoing
- Constipation: 21Jun23-ongoing

## Prior systemic therapies

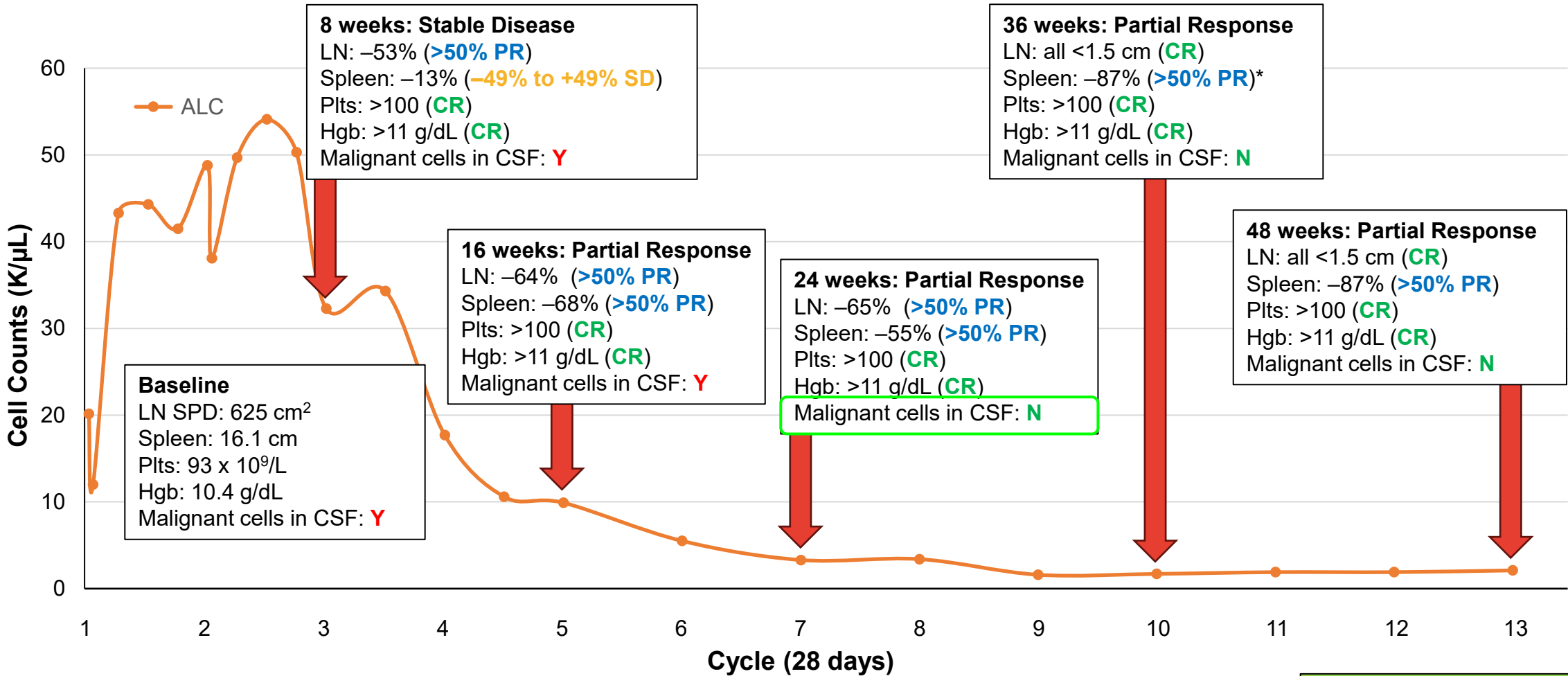
- Idelalisib: 2015-2018
- Venetoclax + Rituximab: 2018-2022
- Acalabrutinib: Oct 2022-Jun 2023

## Prior radiotherapy

- None

# Case Study 1: Patient with CLL and CNS Involvement

Deepening response over time approaching complete response criteria



\*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

Remains on study as of Oct 10, 2024

# Case Study 2: CLL Patient with Extensive Prior Treatment

Site	City of Hope
Age, M/F	61, male
Diagnosis	CLL
Initial diagnosis	2008
Prior progression	12 Sep 2023
Dose	200 mg daily
IwCLL response	PR
Status	On treatment
Current cycle	Cycle 8

## Relevant Medical History

- Atrial fibrillation: Dx Jul 2022
- Hypothyroidism: Dx May 2022
- Hypertension: Dx Jul 2022
- Fatigue: Dx Oct 2023
- Disease related cytopenias: Dx 2022-23

## Molecular, Cytogenetics and other baseline features

- Del(11q, 13q)\*, IGHV unmutated\*
- BTK T474I mutation\*\*
- Bulky disease (5 of 6 target lymph nodes >5 cm in longest diameter)
- Splenomegaly

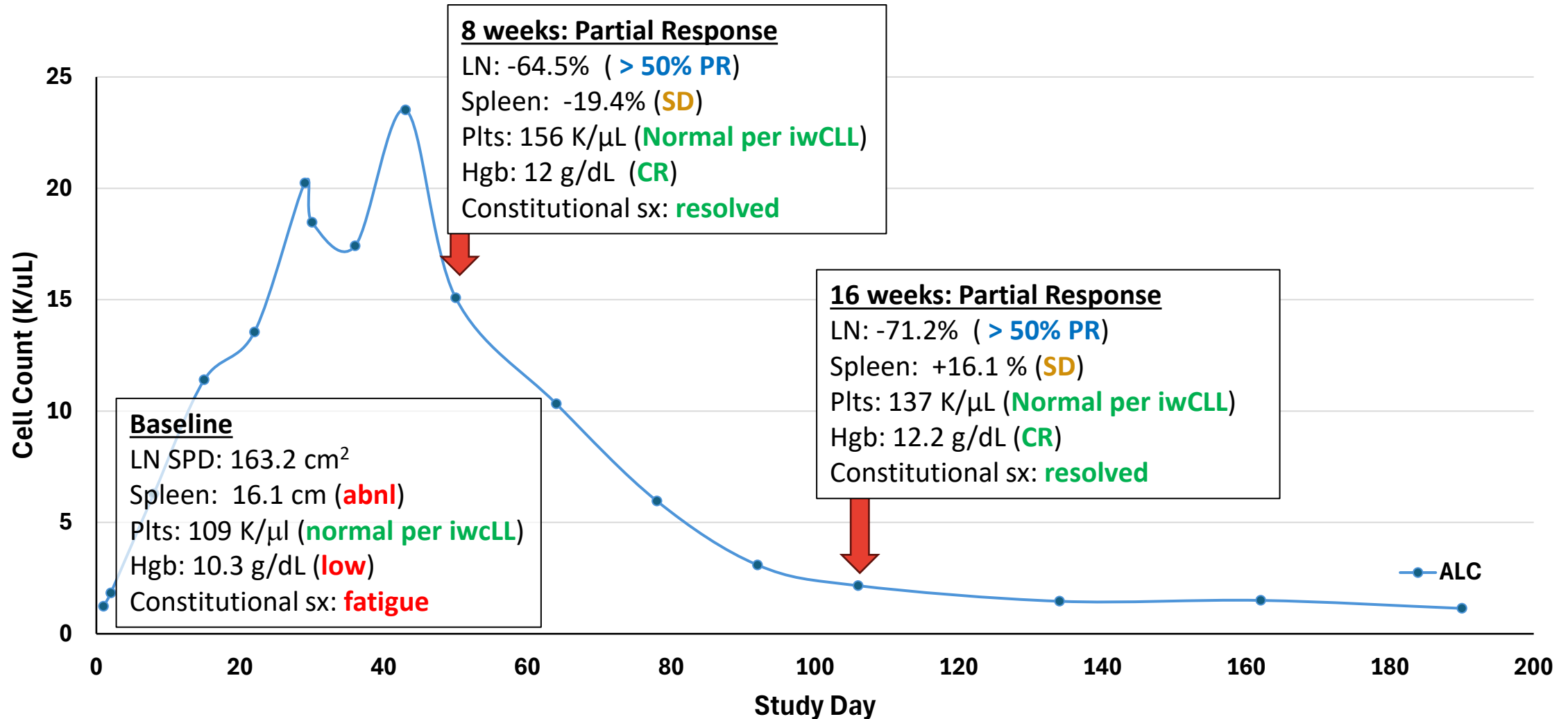
## Prior Systemic Therapies

- FCR: 2009-2010
- **Ibrutinib** + rituximab: 2012
- Venetoclax: 2018
- **Acalabrutinib**: 2021
- Chlorambucil + obinutuzumab: 2021
- **Zanubrutinib**: 2022
- Lisocabtagene maraleucel: 2022
- Duvelisib: 2022-23
- **Pirtobrutinib** + obinutuzumab: 2023
- R-CHOP: 2023
- **Pirtobrutinib** + bendamustine + obinutuzumab: 2023

*Reason for pirtobrutinib + bendamustine + obinutuzumab discontinuation: Progressive disease*

# Case Study 2: CLL Patient with Extensive Prior Treatment

Rapid and sustained lymph node reduction with improving hematologic features



The overall response assessments are from the investigators, while the individual parameter response assessment criteria are calculated per iwCLL from the data entered.



# Mutation Status and BTK Degradation

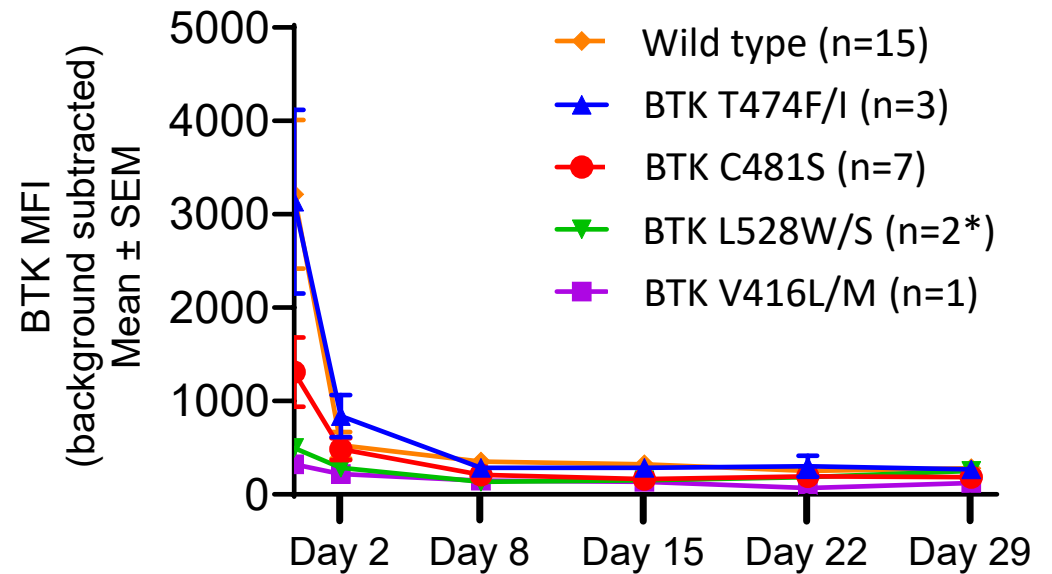
NX-5948 induces rapid and robust degradation of wild-type and mutant BTK

	Patients with CLL (n=30)
Mutation status, n (%)	
BTK <sup>a</sup>	13 (43.3)
C481S	7 (23.3)
L528 <sup>b</sup>	2 (6.7)
T474 <sup>c</sup>	3 (10.0)
V416 <sup>d</sup>	1 (3.3)
G541V	1 (3.3)

<sup>a</sup>Patients could have multiple BTK mutations; BTK mutations were tested at baseline by NGS centrally.  $\geq 5\%$  allelic frequency is reported.

<sup>b</sup>L528W, L528S; <sup>c</sup>T474F, T474I; <sup>d</sup>V416L, V416M.

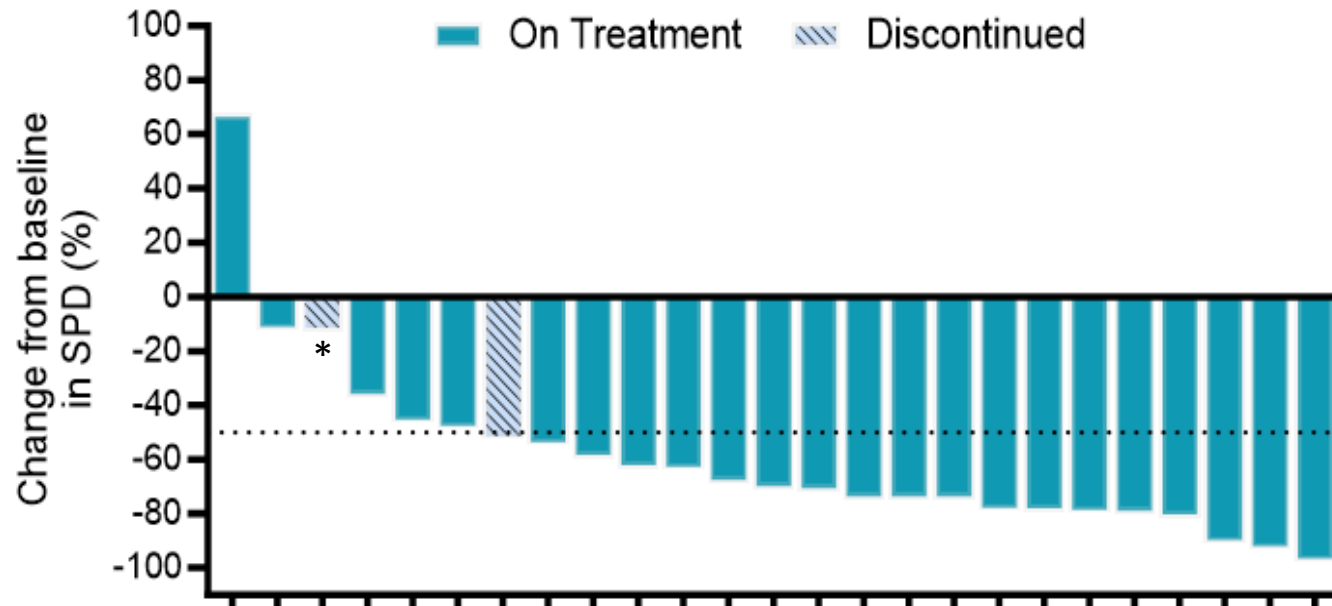
## BTK degradation in CLL with *BTK* mutations



\*1 patient has both BTK L528S and G541S

# Clinical Activity in Patients with Baseline Mutations

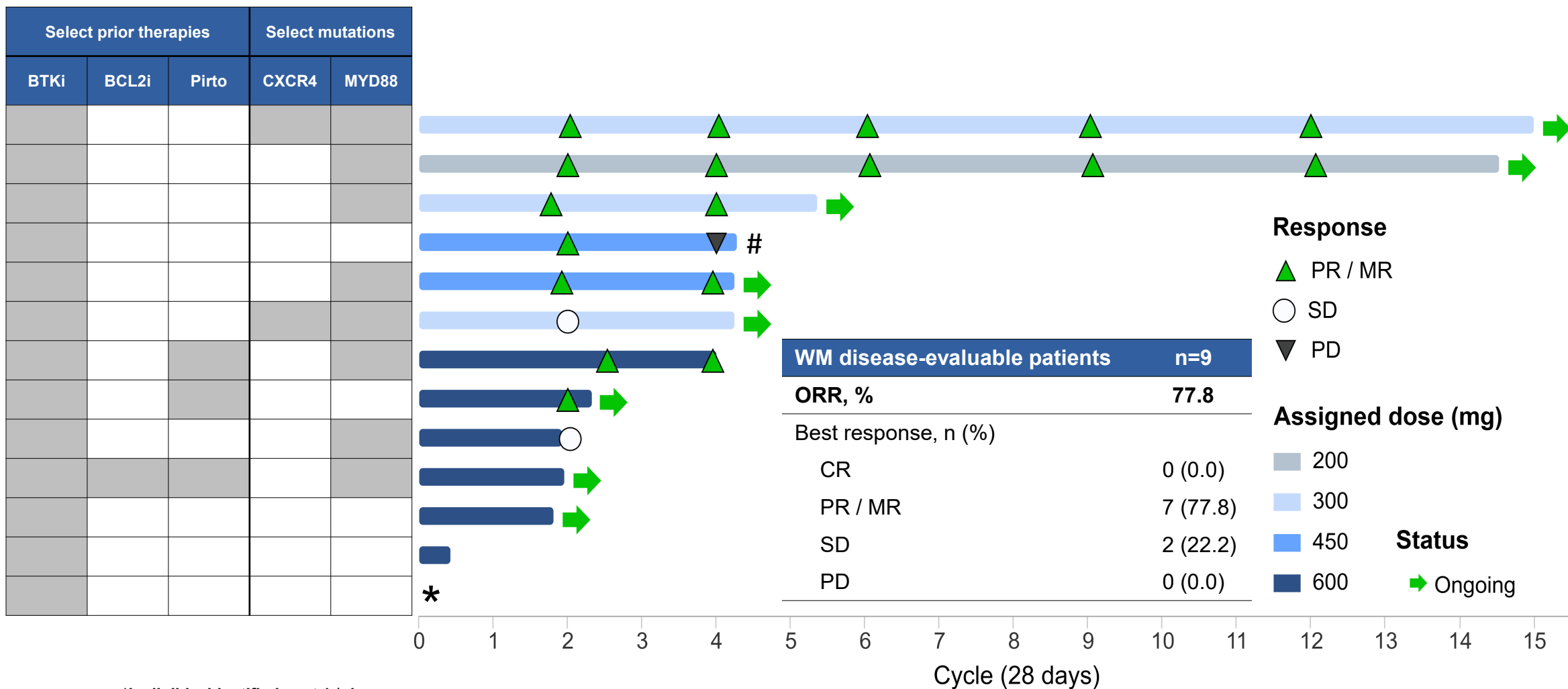
Treatment resistance and poor-prognosis genetic mutations



- Baseline treatment-resistance and poor prognosis mutations were common, indicating a genetically diverse and hard-to-treat CLL patient population
- No genotypic profile was linked to intrinsic NX-5948 resistance

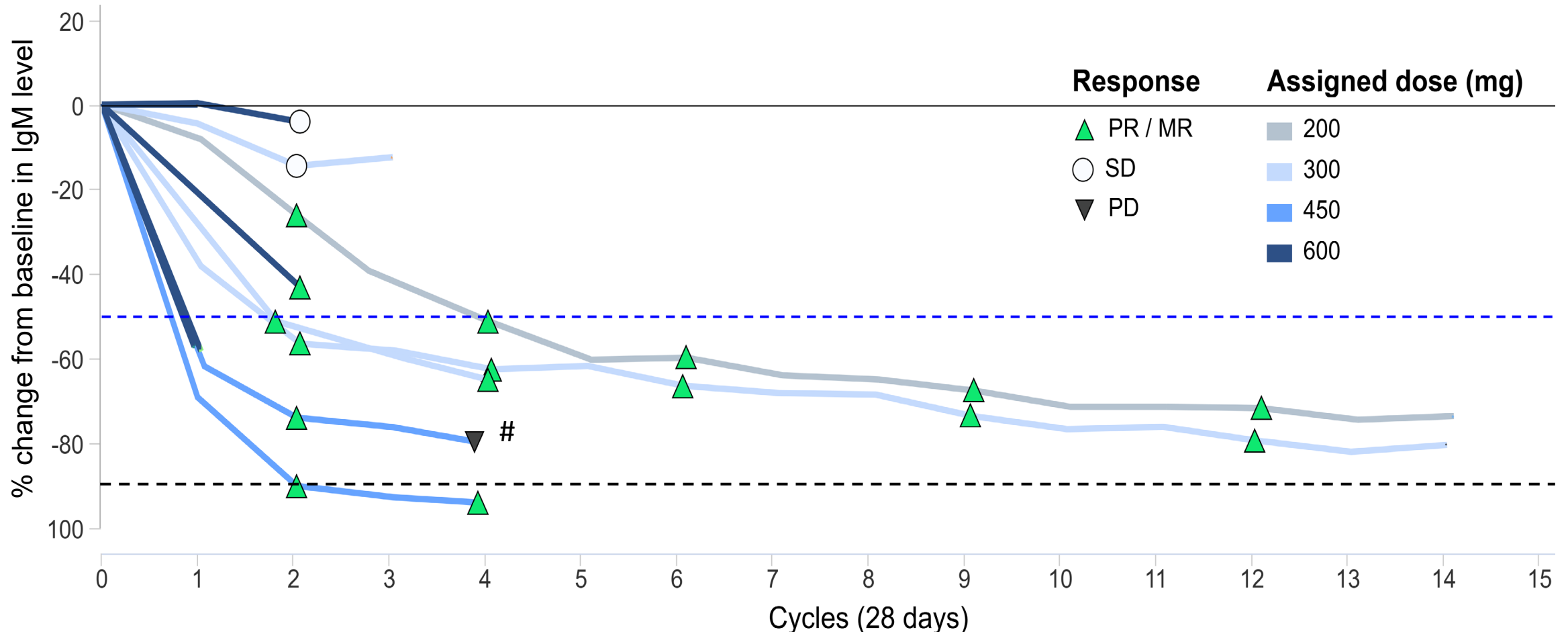


# NX-5948 Efficacy and Duration of Treatment in Patients with Waldenstrom's Macroglobulinemia (WM)



\*Ineligible, identified post 1<sup>st</sup> dose  
 #Transformed to DLBCL

# Steady Decrease in Response Marker Levels in WM Patients Treated with NX-5948



#Transformed to DLBCL

<sup>1</sup>Response criteria used: Owen RG, Kyle RA, Stone MJ, et al. VIth International Workshop on Waldenström macroglobulinaemia.

Response assessment in Waldenström macroglobulinaemia: update from the VIth International Workshop. Br J Haematol 2013;160:171-6

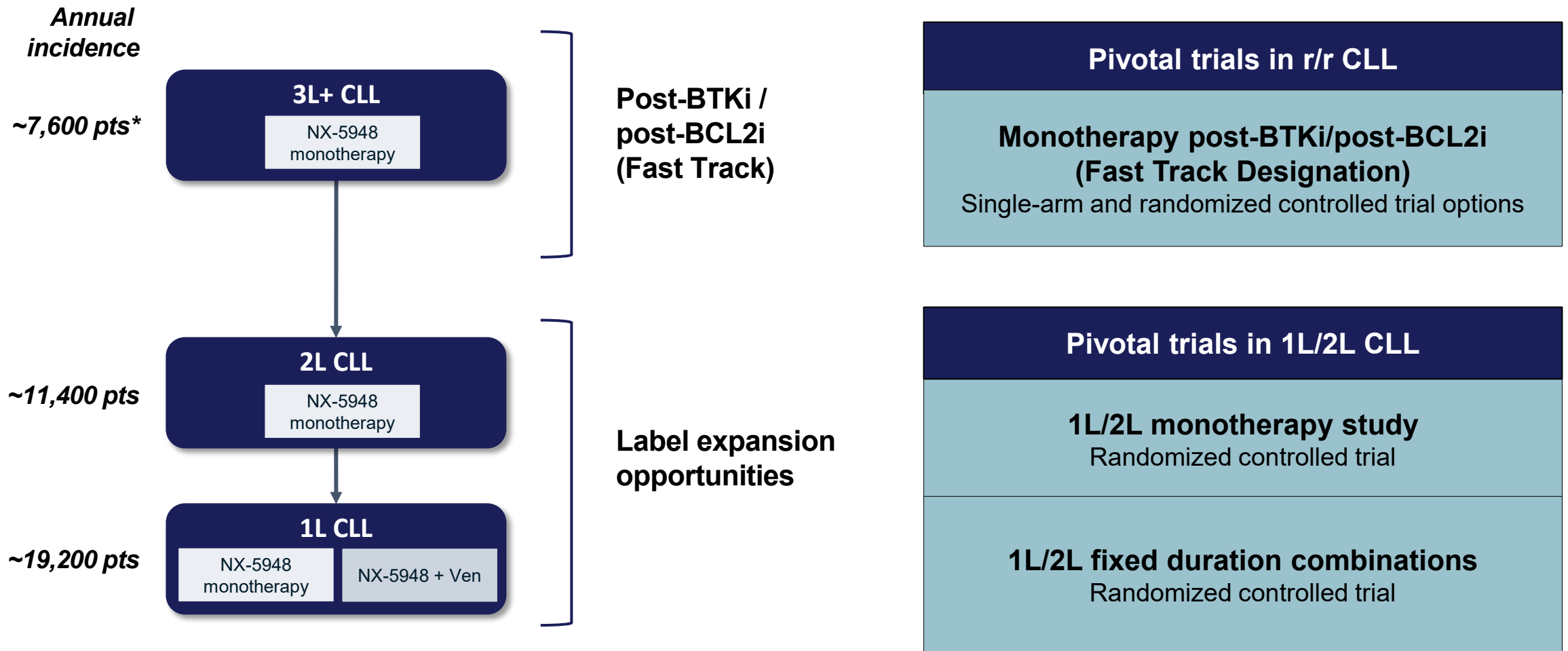
Data cutoff: 10 Oct 2024 20



# Nurix Is Accelerating Development of NX-5948 with First Pivotal Study To Be Initiated in 2025

- CLL: Clear demonstration of clinical activity in difficult to treat populations
  - Phase 1a enrollment complete with ~70% ORR as of April 17, 2024 data cutoff (announced at EHA 2024)
  - Enrolling Phase 1b in relapsed/refractory CLL patients post-BTKi/post-BCL2i
  - Preparing for initiation of pivotal trial(s) in 2025 in CLL patients post-BTKi/post-BCL2i where we have Fast Track Designation
  - Planning for a broad and parallel Phase 3 program across lines of therapy as monotherapy and in combination with other approved agents
  - Additional data in CLL patients will be presented at ASH in December 2024
- NHL: Broad activity with deep responses seen across NHL subtypes
  - Phase 1b expansion underway in selected NHL subtypes with initial focus on monotherapy in indolent indications (WM, MZL, FL)
  - Data presented at IWWM in October 2024 supports advancement of Phase 1b in WM

# Significant Opportunity in CLL Across Lines of Treatment

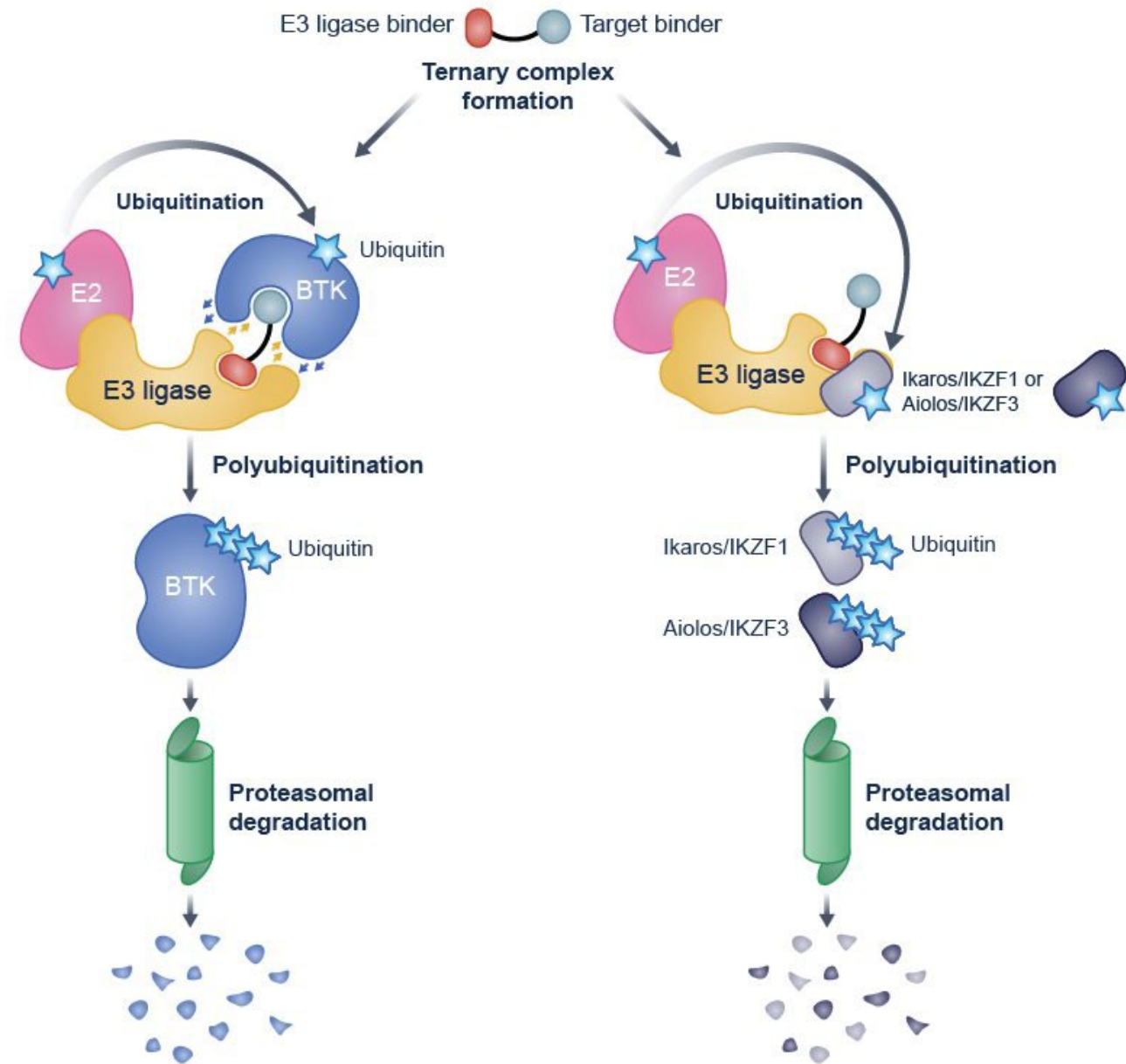


\* Based on data for 3L and 4L only

Source: Clarivate/DRG Landscape and Forecast Research Report NHL and CLL, April 2023

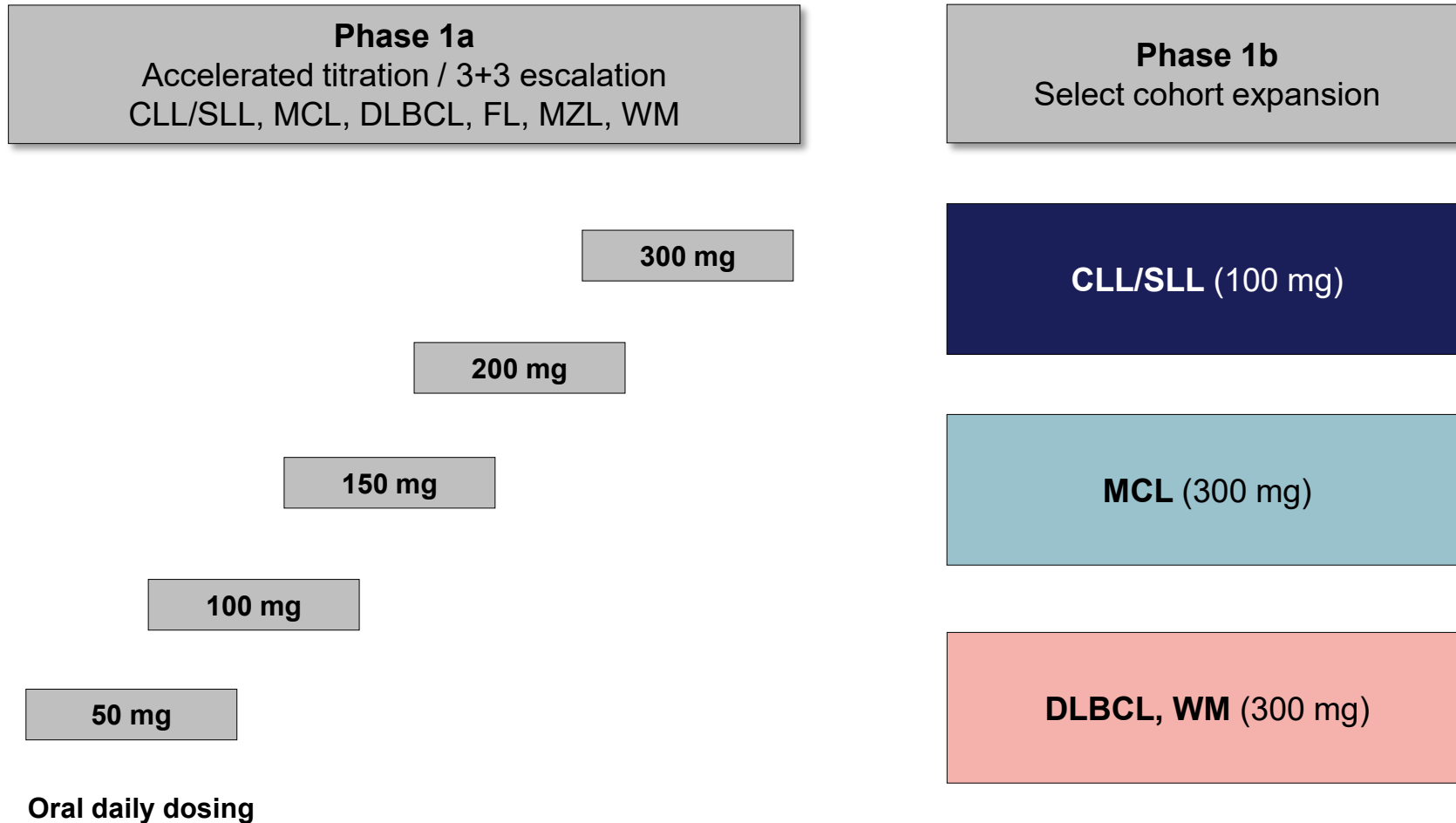
# NX-2127

Dual acting BTK/IKZF degrader with immunomodulatory activity



# NX-2127-001: Trial Design

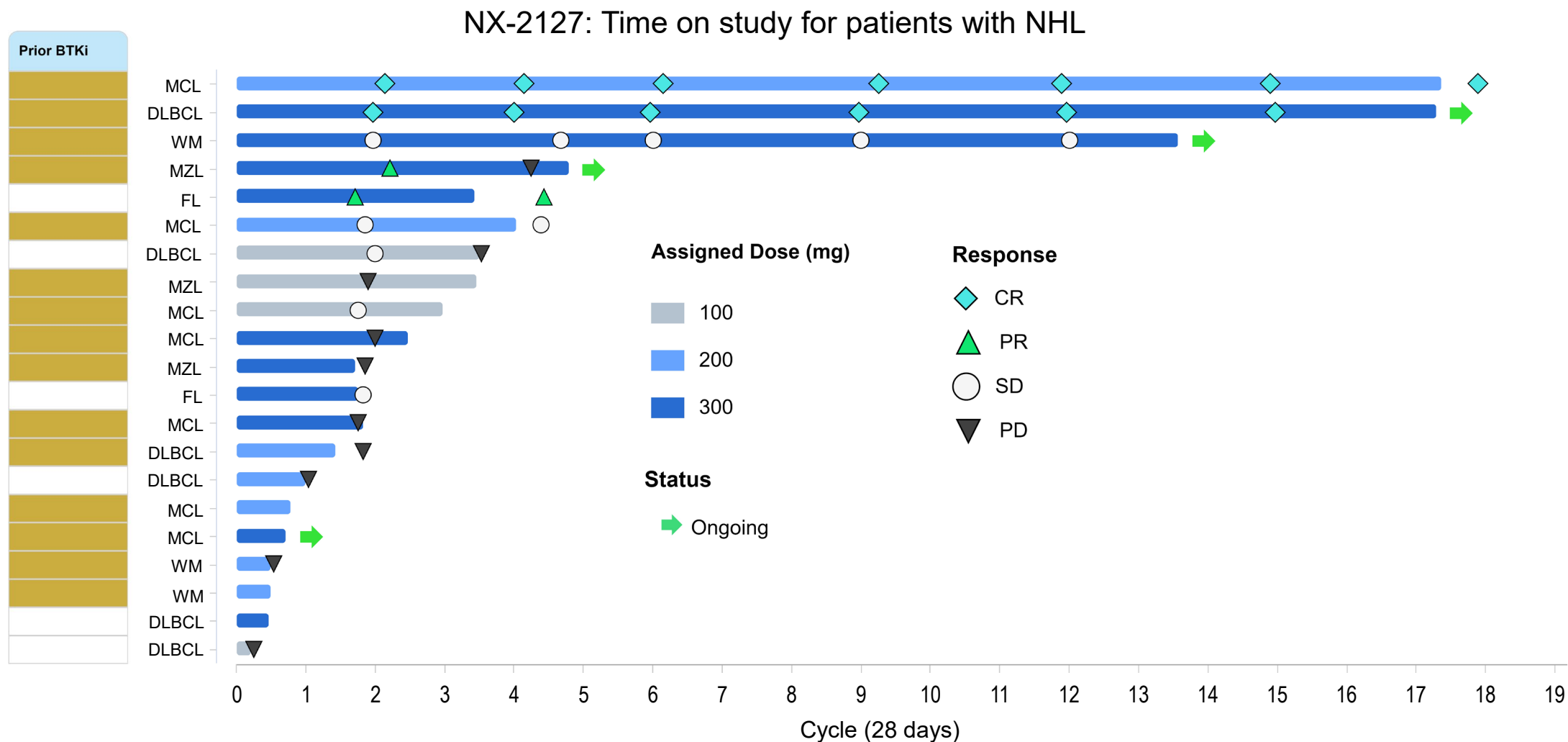
Phase 1a/b trial in adults with relapsed/refractory B-cell malignancies



- First-in-human, multicenter, open-label, Phase 1a/1b trial in adults with relapsed / refractory B-cell malignancies
- Enrollment ongoing with new chirally controlled drug substance in separate dose-escalation (previous data generated utilizing prior, chirally mixed drug substance)
- Other potential expansion cohorts include patients with FL, MZL and PCNSL



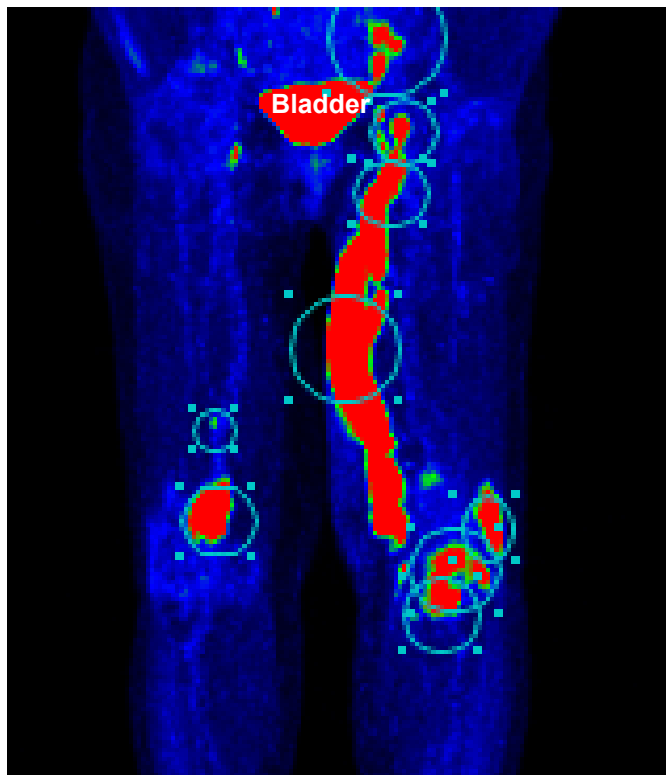
# Ongoing Durable Complete Responses With Over One Year of Follow Up Seen in DLBCL and MCL



# Rapid and Sustained Complete Response in Relapsed/Refractory DLBCL With NX-2127

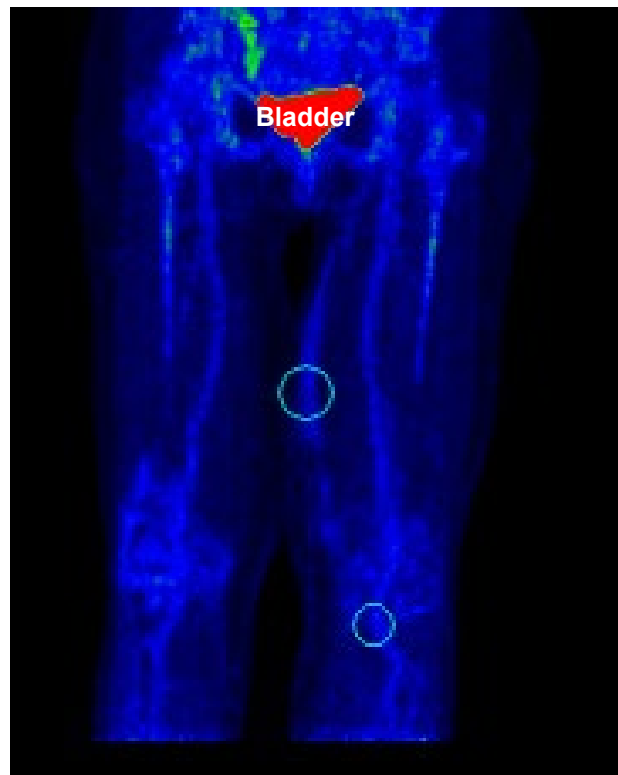
## FDG-PET CT Scan Disease Assessment

Baseline



Deauville score: 5

Confirmatory Week 16 Scan



Deauville score: 2

- 84-year-old woman with multiply relapsed ABC-DLBCL following 4 lines of aggressive therapy (including combination of rituximab, ibrutinib, and lenalidomide)
- Complete response on first assessment at week 8, confirmed at week 16
- As of September 15, 2023, this patient remains in complete response and on treatment with over 15 months of follow up

# Rapid and Sustained Complete Response in Relapsed/Refractory MCL With NX-2127

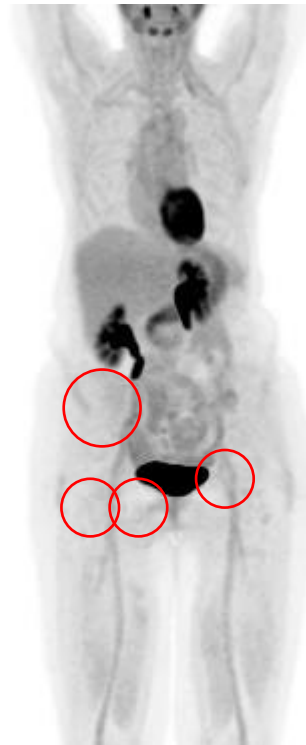
## FDG-PET CT Scan Disease Assessment

Baseline



Deauville score: 5

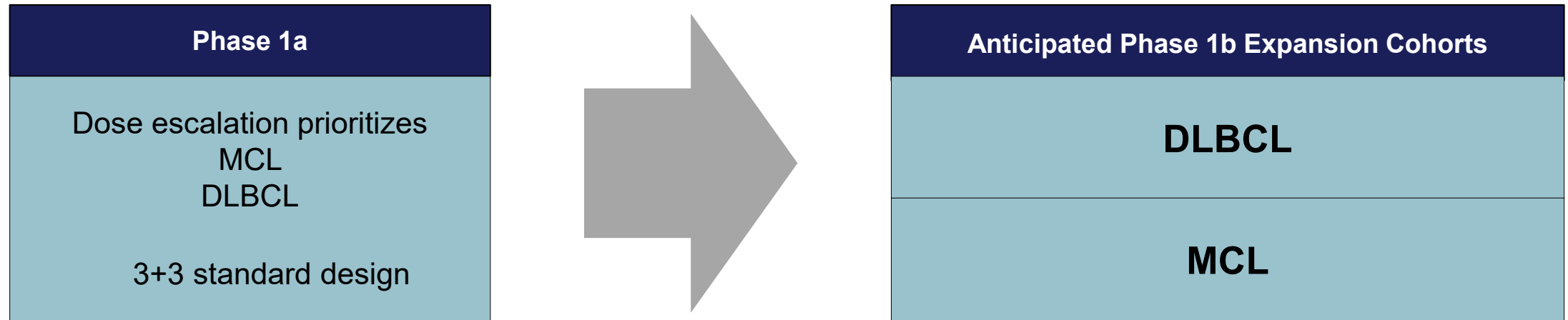
Week 8 Scan



Deauville score: 2

- 64-year-old woman with multiply relapsed MCL, following stem cell transplant, chemo-immunotherapy, and ibrutinib
- Complete response on first assessment at week 8, confirmed at week 16
- As of September 15, 2023, this patient remains in complete response having come off therapy by choice after 17 cycles of treatment

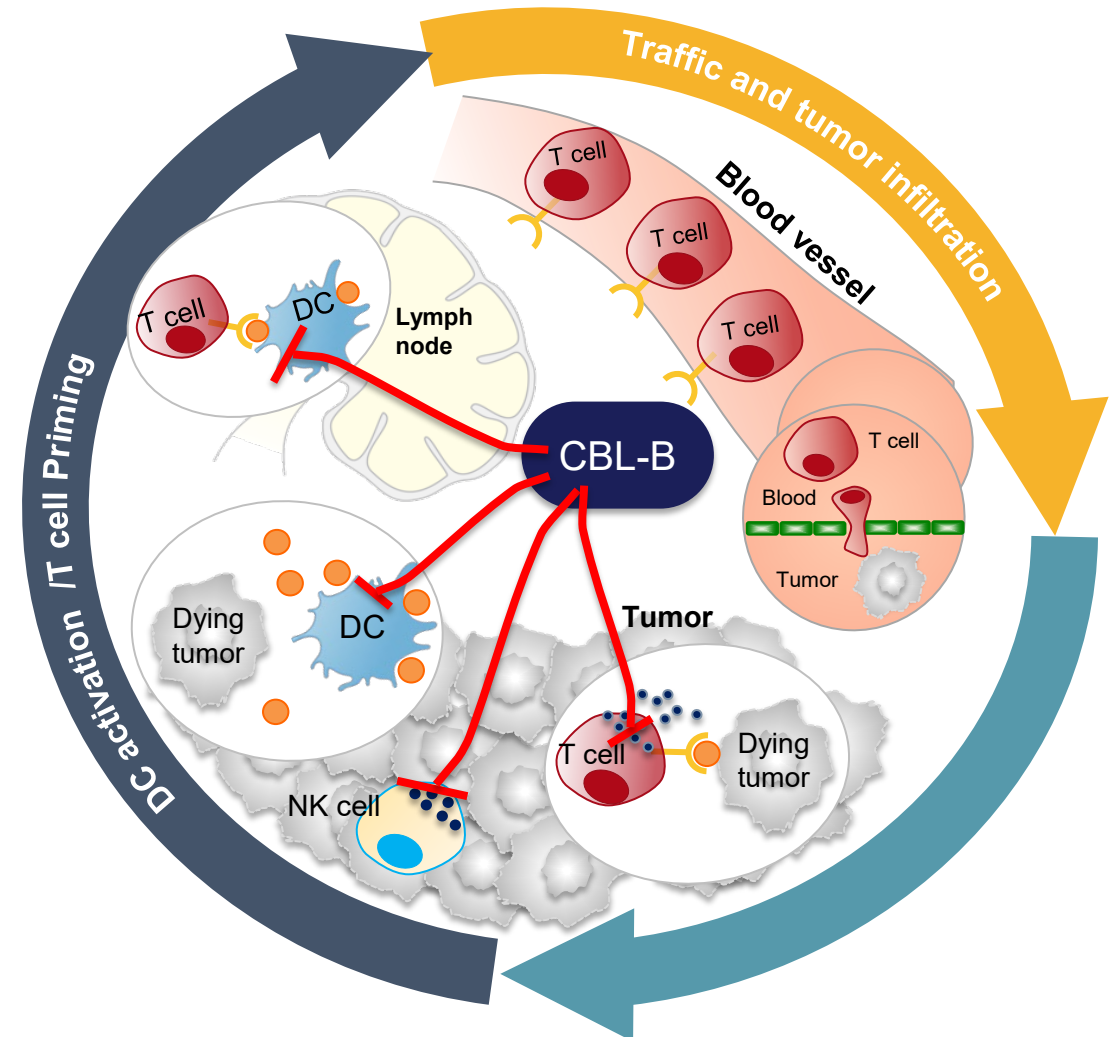
# Next Steps: Conduct Dose Escalation With New Commercial Form of NX-2127 and Reinitiate Phase 1b Enrollment for Aggressive NHL



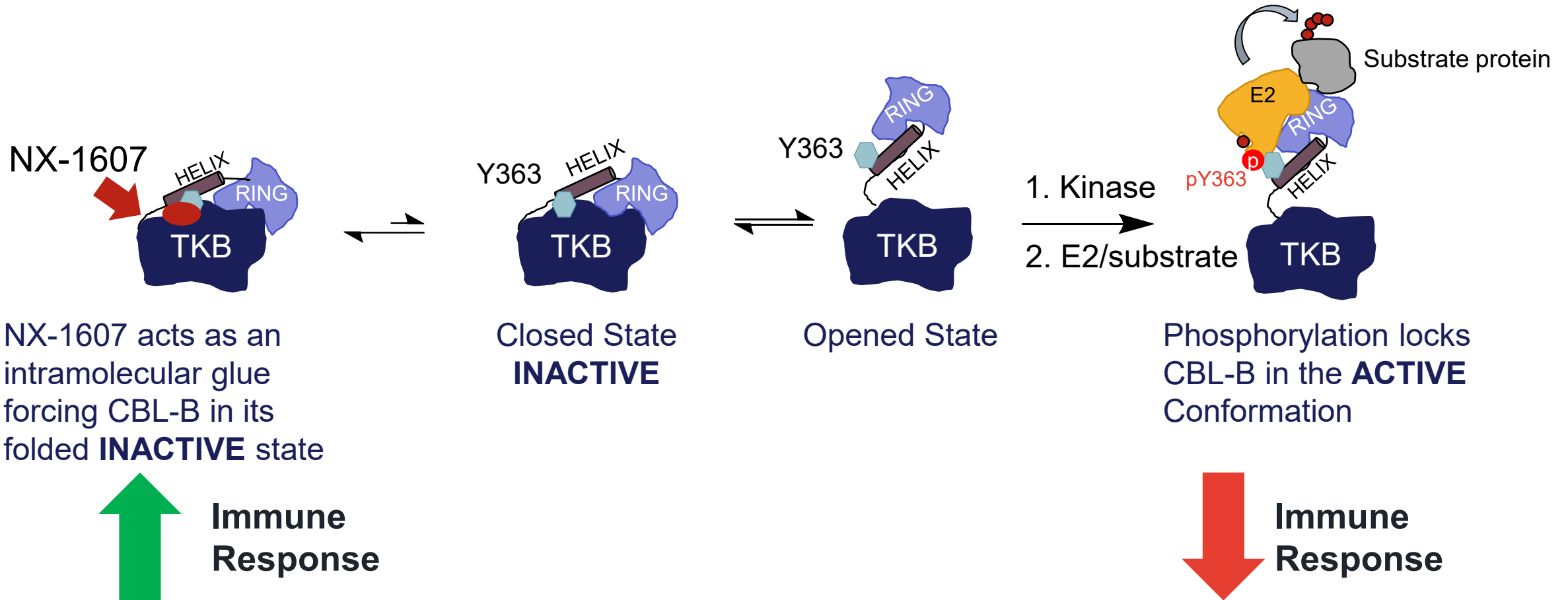
# NX-1607

Oral CBL-B Inhibitor for Immune Oncology Indications

CBL-B inhibition promotes the activation of T cells, NK cells, dendritic cells

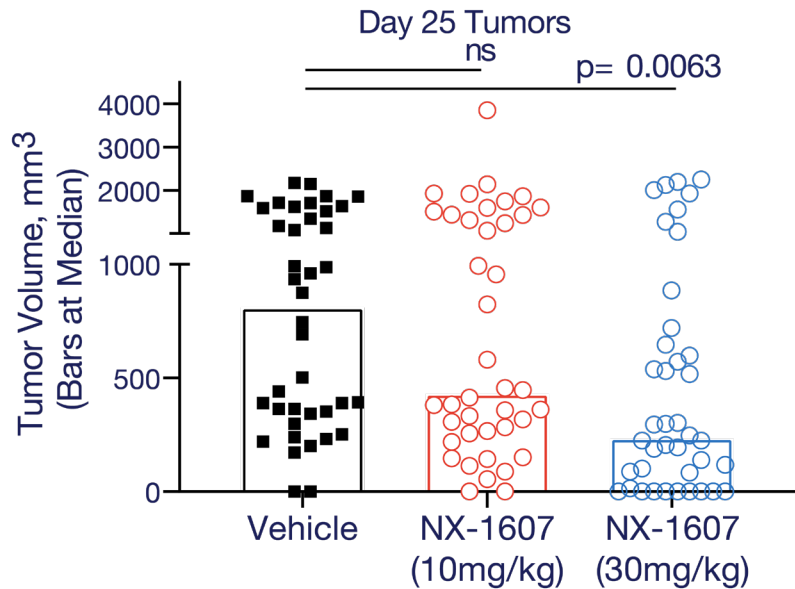


# NX-1607 Mechanism of Action: Intramolecular Glue

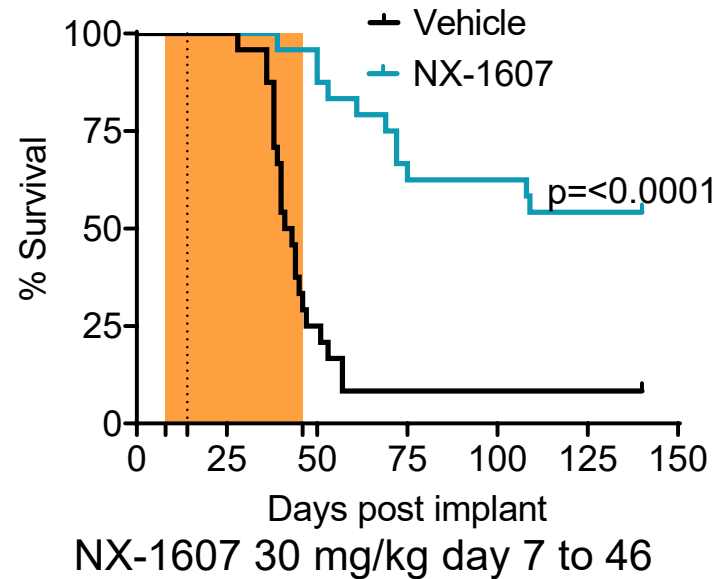


# Single-Agent NX-1607 Induces Antitumor Response in Multiple Models

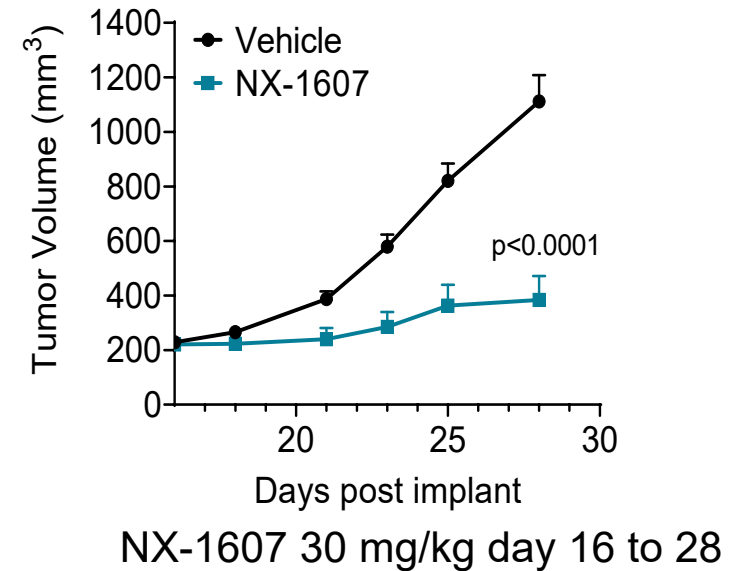
**NX-1607  
Reduced Tumor Volume  
Colorectal**



**NX-1607  
Prolonged Survival  
Triple-Negative Breast**



**NX-1607  
Reduced Tumor Volume  
B Cell Lymphoma**

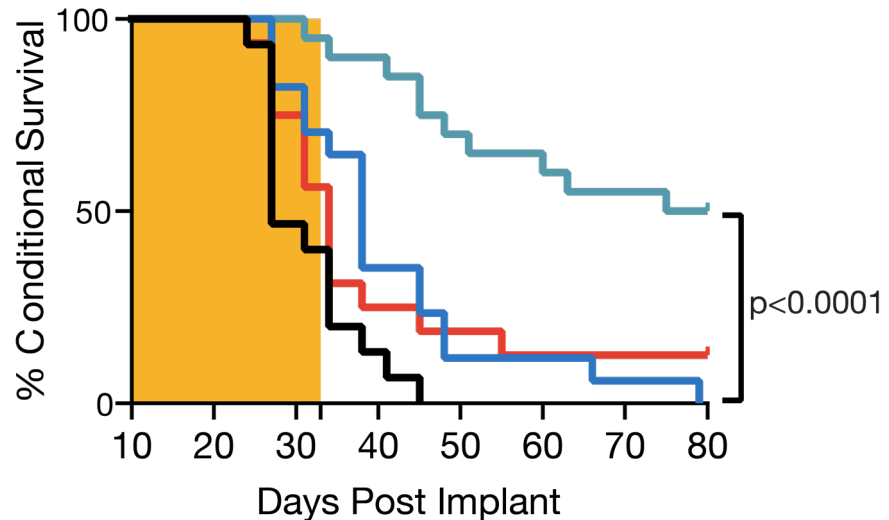


Shaded area indicates dosing period

# NX-1607 and Anti-PD-1 Synergize to Enhance Anti-Tumor Effects and Survival of Mice in Multiple Tumor Models

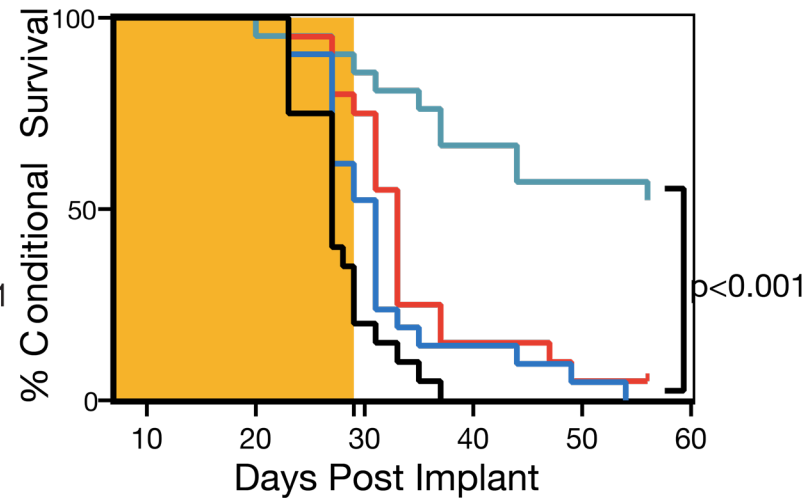
## Colorectal (CT26)

### Long-Term Survival



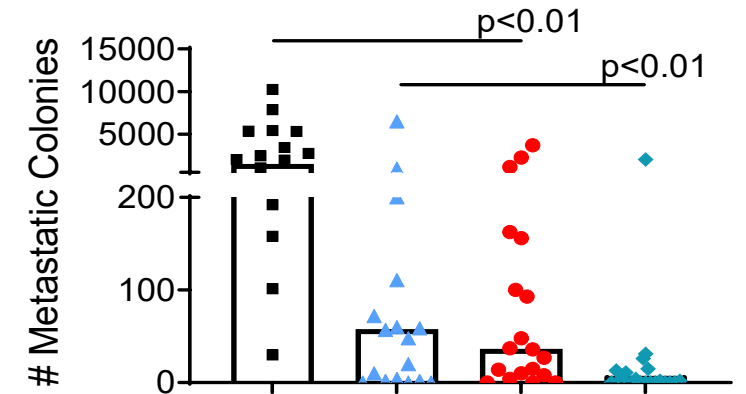
## Colorectal (MC38)

### Long-Term Survival



## Triple-Negative Breast (4T1)

### Day 28 4T1 Lung Metastases

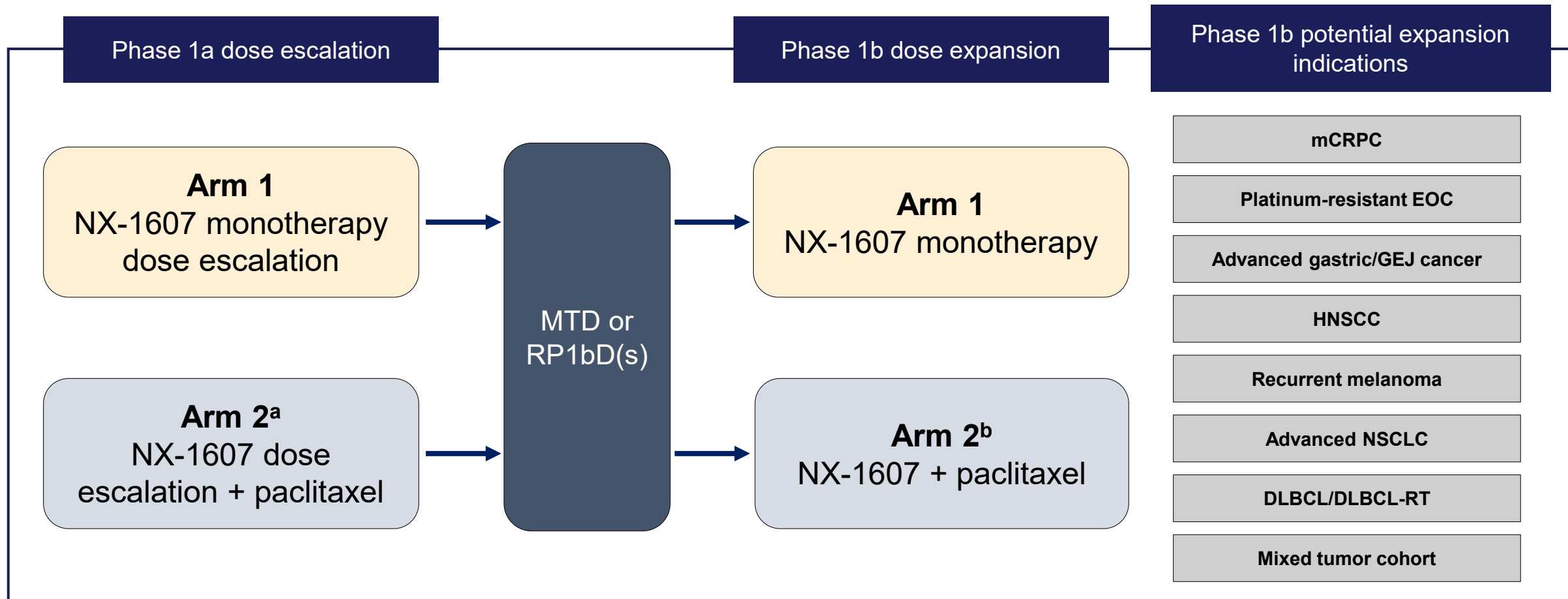


■ Vehicle ▲ NX-1607 ● anti-PD-1 ◆ NX-1607+anti-PD-1

Shaded area indicates dosing period: NX-1607 (30 mg/kg, PO daily) and anti-PD-1 twice a week at 10 mg/kg dosing period



# NX-1607-101: Phase 1 First-in-Human Clinical Trial Design



<sup>a</sup>Starting dose for NX-1607 in Arm 2 will be  $\geq 1$  dose level below the highest previously cleared monotherapy dose level and dosing regimen.

<sup>b</sup>Combination indications for Arm 2 may include platinum-resistant EOC, gastric cancer, HNSCC, NSCLC, TNBC, urothelial cancer, cervical cancer

# Defining Success in 2024

B-cell malignancies

Immune oncology

Platform & pipeline

**NX-5948**

- ✓ Present updated Phase 1a clinical data supporting Phase 1b dose expansion
- Accelerate Phase 1 enrollment to enable pivotal trials
- Complete IND-enabling studies for autoimmune indications

**NX-2127**

- ✓ Resolve partial clinical hold to enable the introduction of new drug product into the ongoing Phase 1 clinical trial

**NX-1607**

- Present Phase 1a monotherapy and paclitaxel combination data
- Define Phase 1b dose(s) for cohort expansion

**Research pipeline**

- Nominate new targeted protein degrader development candidate
- Achieve substantial research collaboration milestones throughout 2024

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

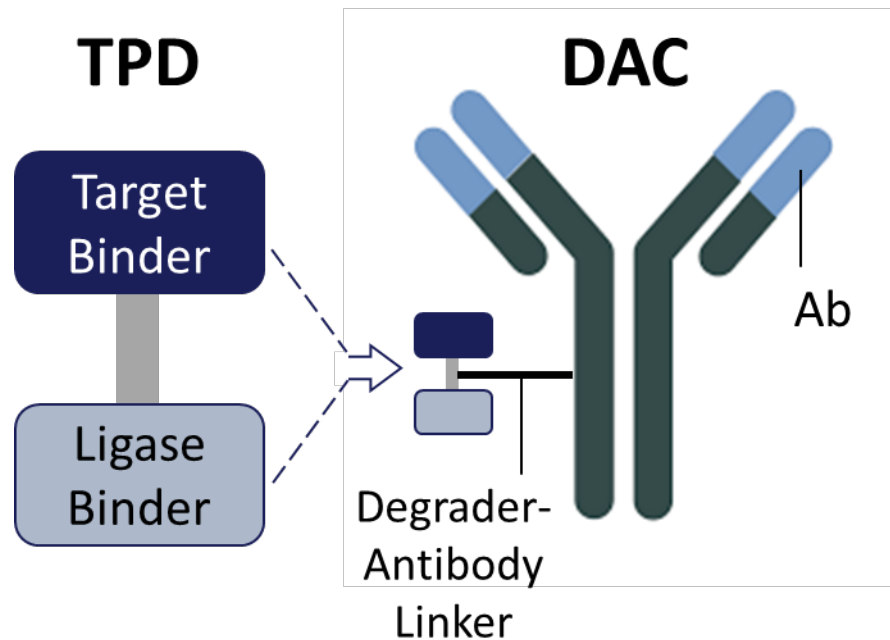
MOA	Oncology program	Target	Therapeutic area	Discovery – Lead Op	IND enabling	Phase 1a	Phase 1b
TPD	NX-5948	BTK	B-cell malignancies				
	NX-2127	BTK-IKZF	B-cell malignancies				
TPE	NX-1607	CBL-B	Immuno-Oncology				
TPD	Multiple	Undisclosed	Undisclosed				
	Multiple	Undisclosed	Undisclosed				
	Multiple	Undisclosed	Undisclosed				
DAC	Multiple	Undisclosed	Oncology				

MOA	I&I program	Target	Therapeutic area	Discovery – Lead Op	IND enabling	Phase 1a	Phase 1b
TPD	NX-5948	BTK	Inflammation / autoimmune				
	NX-0479 / GS-6791	IRAK4	Rheumatoid arthritis and other inflammatory diseases				
	STAT6 degrader	STAT6	Type 2 inflammatory diseases				
	Undisclosed	Undisclosed	Inflammation / autoimmune				

# Advancing a New Therapeutic Class

## Degrader-Antibody Conjugates (DACs)

- DACs combine the catalytic activity of a Targeted Protein Degrader (TPD) with the specificity of an antibody
- DACs represent the next generation of antibody drug conjugates (ADCs)



## Seagen\* Deal Terms

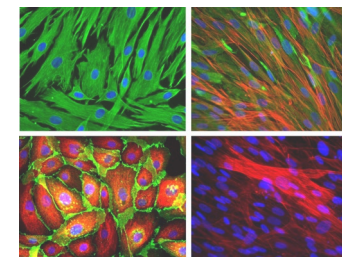
- \$60 million upfront cash payment
- \$3.4 billion in potential research, development, regulatory and commercial milestone payments
- Mid-single to low double-digit percentage tiered royalties on future product sales
- Option for U.S. profit sharing and co-promotion on up to two products arising from the collaboration



\* Seagen is now part of Pfizer

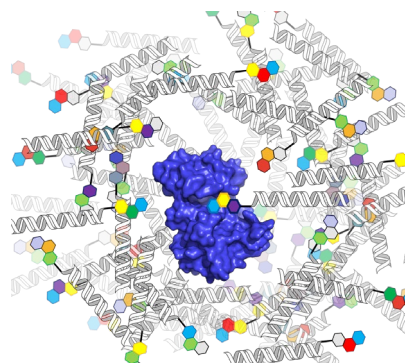
# Industry Leading DELigase Platform for TPD Drug Discovery

Chemistry Automation

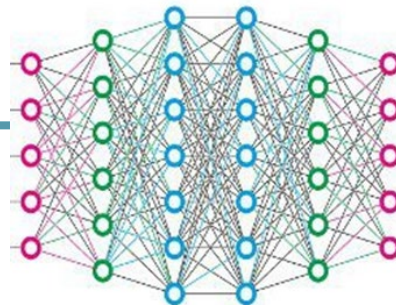


Direct-to-Cell Biology

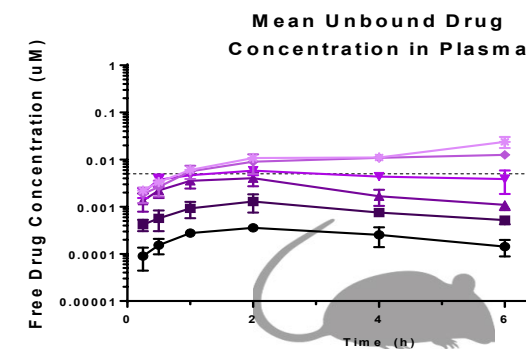
DEL Discovery



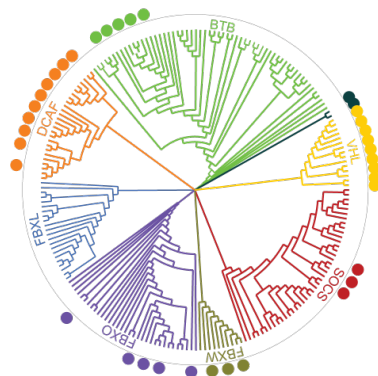
Machine Learning/  
Generative AI



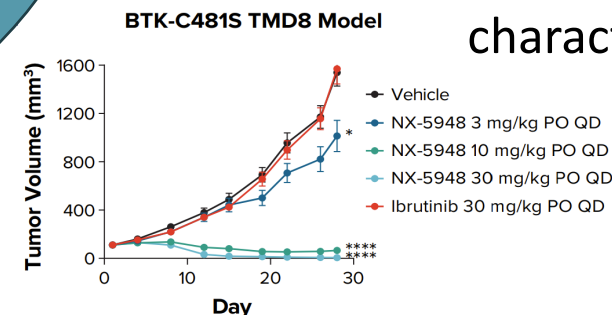
HT  
Screening  
for *in vivo*  
exposure



Ligase Enablement



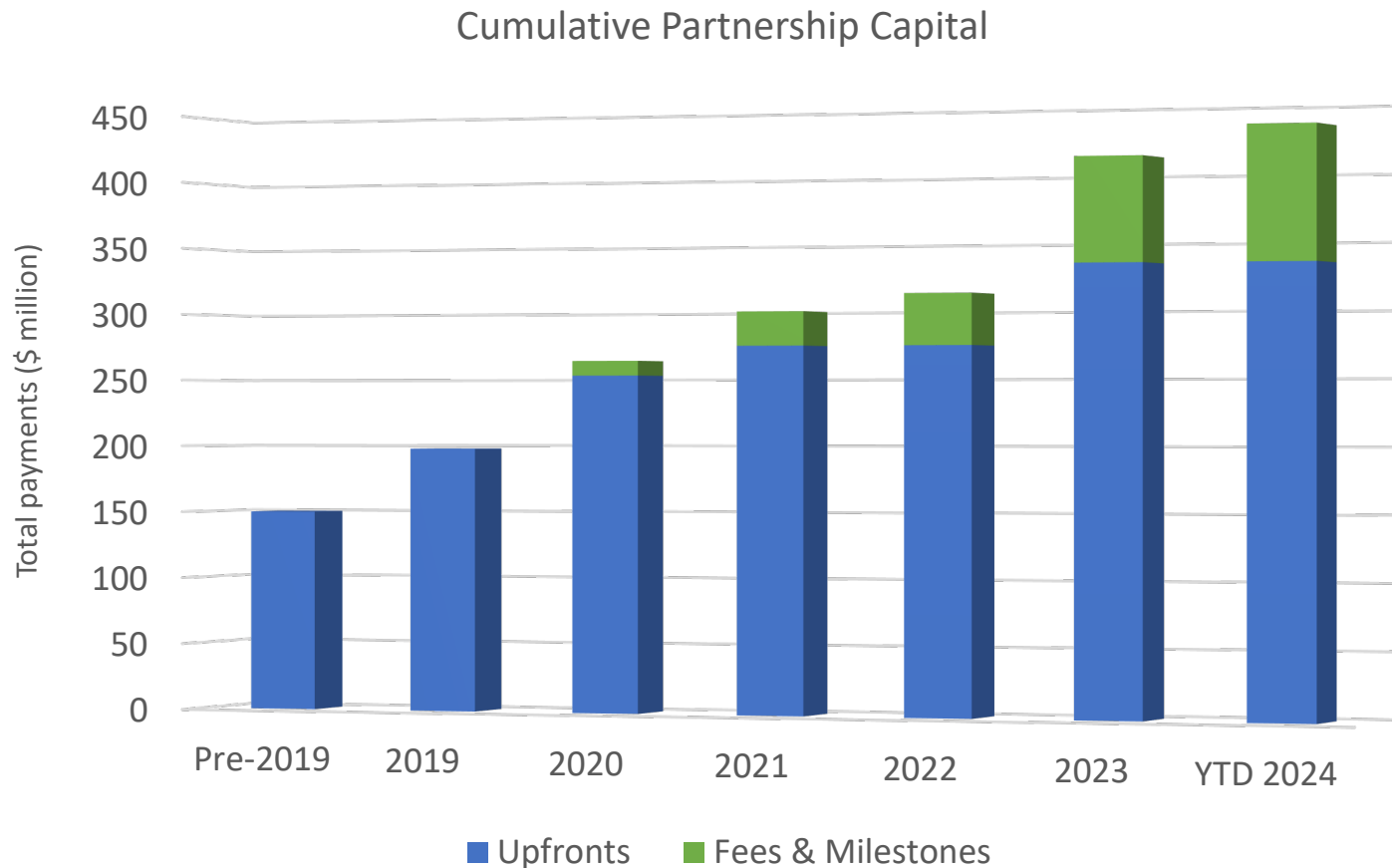
In depth *in vivo* biological characterization



# Strong Financial Position

**\$457.5M in cash and investments as of August 31, 2024**

- Cash runway to fund operations into H2 2026



## R&D collaboration cashflow:

- Gilead: \$45M upfront and \$85M in fees and milestone payments earned to date
- Sanofi: \$55M upfront, \$22M in expansion option exercise, and \$13M in milestone payments earned to date
- Seagen (now part of Pfizer): \$60M upfront and \$5M in milestone payments earned to date

Nurix retains option for U.S. profit share and co-promotion for six drug candidates across three partnerships

Thank you