

## Leader in Targeted Protein Modulation

# Nurix Therapeutics

Blazing a New Path in Medicine

Investor Presentation
April 2024

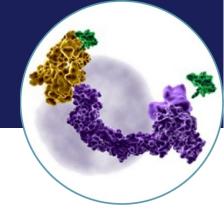
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## Nurix Therapeutics: Advancing a Robust, Innovative Pipeline Both small molecules and antibodies with blockbuster potential



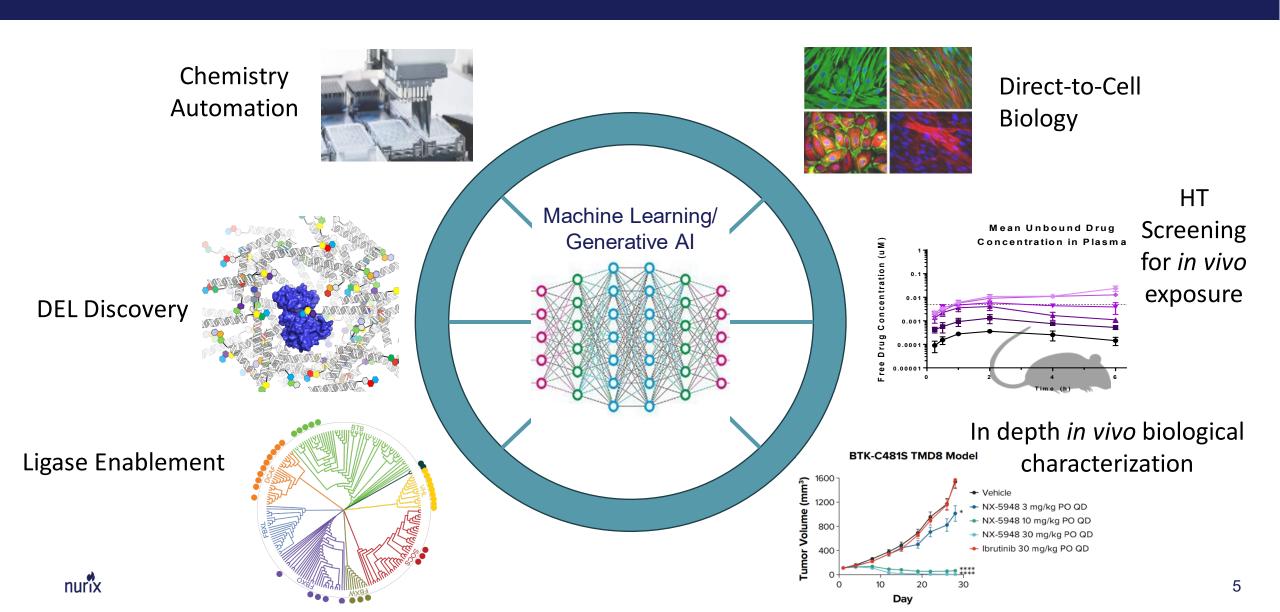
- First to introduce BTK degraders into the clinic and show efficacy across B-cell malignancies with the potential to displace BTK inhibitors by addressing drug resistance and scaffolding effects
- Expanded therapeutic focus into inflammation & immunology with IRAK4 degrader licensed by Gilead and plans to enable NX-5948 development in autoimmune disease
- Established strategic collaboration with Seagen (now part of Pfizer) to advance an innovative new class of cancer therapeutics called Degrader-Antibody Conjugates or DACs



# 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
TDD	NX-2127	BTK-IKZF	B-cell malignancies				
TPD	NX-5948	BTK	B-cell malignancies				
TPE	NX-1607	CBL-B	Immuno-Oncology				
	Multiple	Undisclosed	Undisclosed				
TPD	Multiple	Undisclosed	Undisclosed				<b>GILEAD</b>
	Multiple	Undisclosed	Undisclosed				sanofi
DAC	Multiple	Undisclosed	Oncology				<b>P</b> fizer
MOA	I&I program	Target	Therapeutic area	Discovery – Lead Op	IND enabling	Phase 1a	Phase 1b
	NX-5948	BTK	Inflammation / autoimmune				
TPD	NX-0479 / GS-6791	IRAK4	Rheumatoid arthritis and other inflammatory diseases				<b>GILEAD</b>
	STAT6 degrader	STAT6	Type 2 inflammatory diseases				sanofi
	Undisclosed	Undisclosed	Inflammation / autoimmune				sanofi

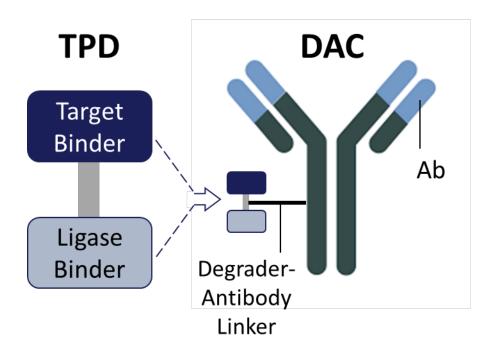
## Industry Leading DELigase Platform for TPD Drug Discovery



## **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

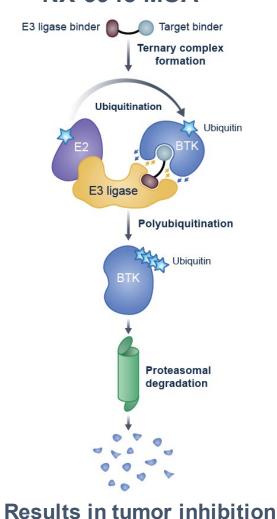
- \$60 million upfront cash payment
- \$3.4 billion in potential research, development, regulatory and commercial milestone payments
- Mid-single to low double-digit percentage tiered royalties on future product sales
- Option for U.S. profit sharing and copromotion on up to two products arising from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





## Why Do We Need BTK Degraders?

#### NX-5948 MOA



BTK degraders can overcome treatment emergent resistance mutations

BTK degraders address BTK scaffolding function

BTK degraders may be useful in other B-cell malignancies and autoimmune diseases

BTK degraders have the potential to displace inhibitors



## Blockbuster Opportunity in BTK Market

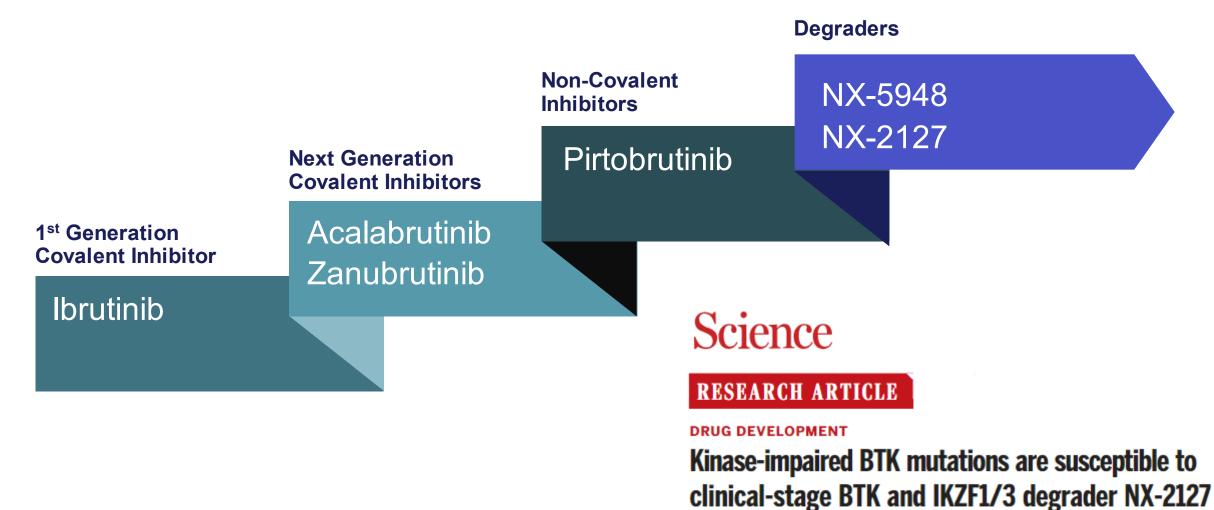
#### \$8.7 billion in annual sales of approved BTK inhibitors

- 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 noncovalent inhibitors and expand the market





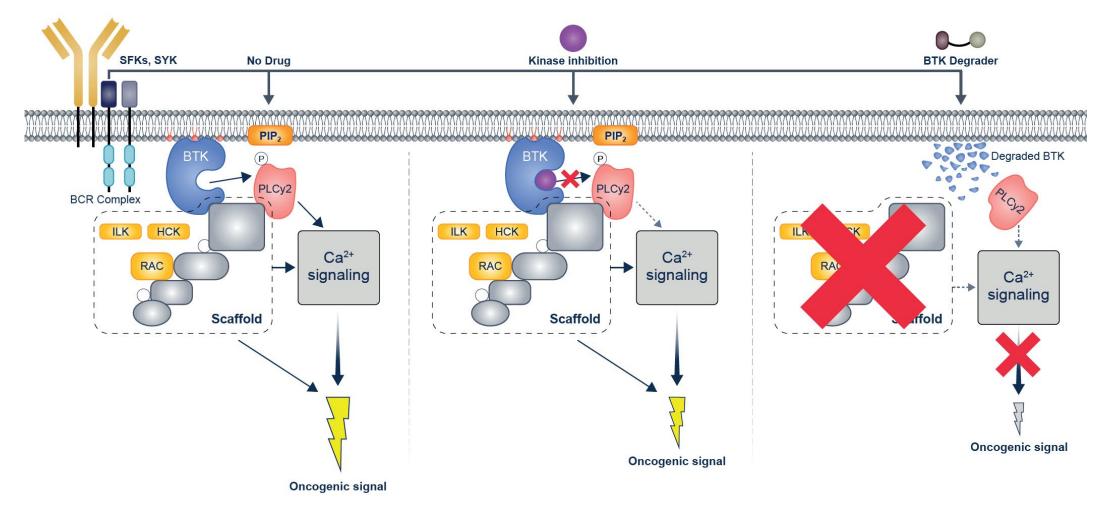
## **Evolution of BTK Targeted Therapies**



Montoya et al., Science 383, 496 (2024)



## BTK Degraders Disrupt BCR Signaling by Removing the Protein and All of Its Functions



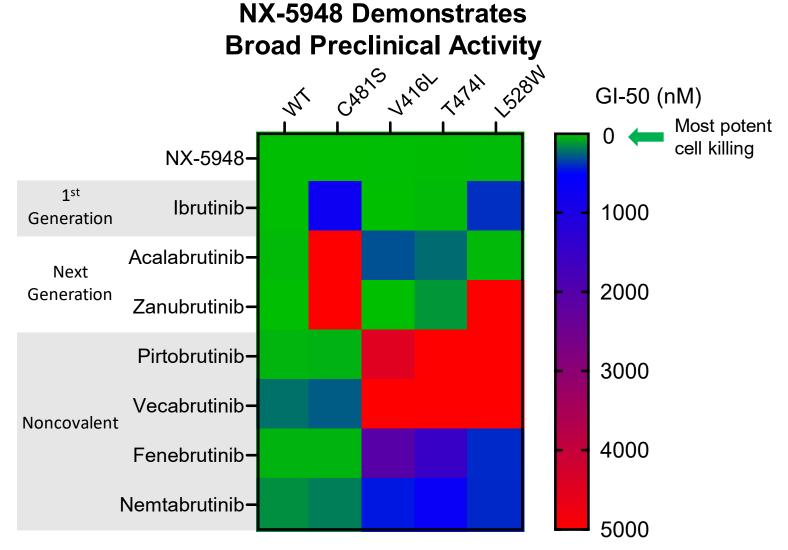
#### References

- 1. Montoya et al. Kinase-impaired BTK mutations are susceptible to clinical-stage BTK and IKZF1/3 degrader NX-2127. Science. 2024; 383
  - Eisen et al. Conditional Requirement for Dimerization of the Membrane-Binding Module of BTK. BioRxiv. January 17, 2024
- 3. Yuan et al. BTK kinase activity is dispensable for the survival of diffuse large B-cell lymphoma. J Biol Chem. 2022; 298 (11):102555



# 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



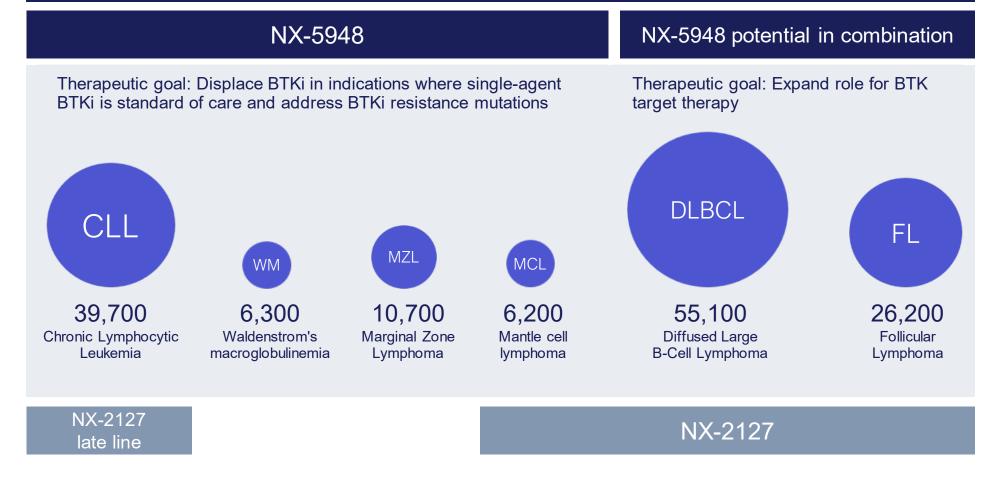


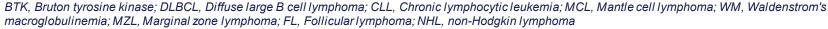
# Nurix BTK Degrader Franchise: Two BTK Degraders to Cover the Landscape of B-Cell Malignancies

#### **B-Cell Malignancies Annual Incidence (U.S. & EU)**

NX-5948
for all lines of
therapy in CLL and
potentially NHL
and WM as
monotherapy and
in combination

#### NX-2127 for aggressive NHL as monotherapy and in combination and potentially for late-line CLL

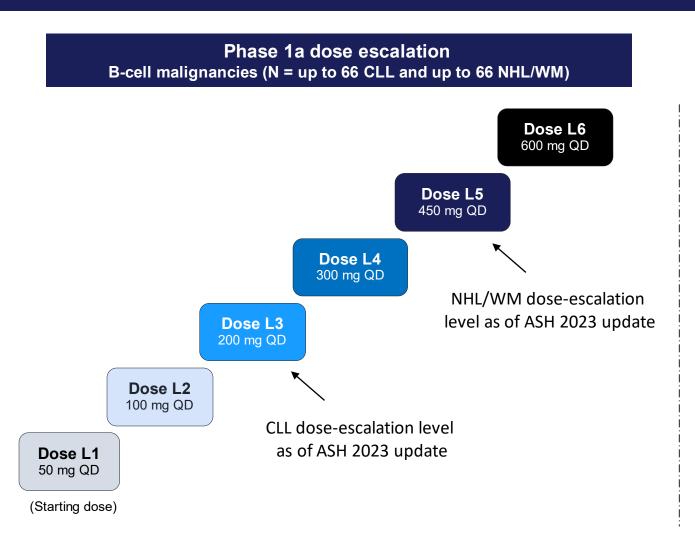






## NX-5948-301: Trial Design

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



## Potential Phase 1b dose expansion (N = up to 160 patients)

CLL/SLL dose level A
Prior BTKi and BCL-2i

CLL/SLL dose level B Prior BTKi and BCL-2i

#### **MCL**<sup>a</sup>

Prior BTKi and anti-CD20 CIT

#### **MZL**a

Prior anti-CD20 CIT and ≥2 prior LoT

#### **WM**a

Prior BTKi and ≥2 prior LoT

#### DLBCLa,b

Prior anthracycline, anti-CD20 CIT + 1 LoT<sup>c</sup>

#### FL

Prior anti-CD20 CIT + 1 LoTc

#### PCNSL/SCNSL

Who have progressed or had no response to ≥1 prior LoT



# Baseline Demographics and Disease Characteristics Heavily pretreated population

Characteristics	Patients with CLL (n=7)	Patients with NHL/WM (n=19)	Overall population (N=26)
Median age, years (range)	64.0 (53–75)	63.0 (42–79)	63.5 (42–79)
Male, n (%)	5 (71.4)	13 (68.4)	18 (69.2)
Female, n (%)	2 (28.6)	6 (31.6)	8 (30.8)
ECOG PS, n (%) 0 1	1 (14.3)	5 (26.3)	6 (23.1)
	6 (85.7)	14 (73.7)	20 (76.9)
Previous targeted treatments <sup>a</sup> , n (%) BTKi Pirtobrutinib BCL2i BTKi and BCL2i CAR-T therapy Bispecific antibody PI3Ki	7 (100.0)	10 (52.6)	17 (65.4)
	1 (14.3)	2 (10.5)	3 (11.5)
	6 (85.7)	3 (15.8)	9 (34.6)
	6 (85.7)	3 (15.8)	9 (34.6)
	0 (0.0)	7 (36.8)	7 (26.9)
	0 (0.0)	5 (26.3)	5 (19.2)
	2 (28.6)	2 (10.5)	4 (15.4)
Median prior lines of therapy (range)	3.0 (2–5)	5.0 (2–10)	4.0 (2–10)
Mutation status <sup>b</sup> , n (%)  BTK (T474)  PLCG1/2 <sup>c</sup> TP53  BCL2 (G101V and R107-R110dup)	n=6	n=15	n=21
	1 (16.7)	0 (0.0)	1 (4.8)
	2 (33.3)	2 (13.3)	4 (19.0)
	2 (33.3)	3 (20.0)	5 (23.8)
	2 (33.3)	0 (0.0)	2 (9.5)



#### NX-5948 Was Well Tolerated

Frequency of TEAEs in ≥15% of patients or grade ≥3 or SAEs in >1 patient, (n=26)

TEAEs, n (%)	Any grade	Grade ≥3	SAEs
Purpura/contusion <sup>a</sup>	12 (46.2)	_	_
Thrombocytopenia <sup>b</sup>	10 (38.5)	2 (7.7)	-
Neutropenia <sup>c</sup>	8 (30.8)	5 (19.2)	_
Anemia	6 (23.1)	1 (3.8)	_
Cough	5 (19.2)	_	-
Headache	5 (19.2)	_	_
Nausea	5 (19.2)	_	_
Rash	4 (15.4)	_	_
COVID-19	3 (11.5)	2 (7.7)	2 (7.7)
Pneumonia	2 (7.7)	2 (7.7)	2 (7.7)

<sup>&</sup>lt;sup>a</sup>Purpura/contusion includes episodes of contusion or purpura; <sup>b</sup>Aggregate of 'thrombocytopenia' and 'platelet count decreased'; <sup>c</sup>Aggregate of neutrophil count decreased or neutropenia

- No atrial fibrillation/flutter or hypertension
- No DLTs and no TEAEs resulting in drug discontinuation
- Four NX-5948-related grade ≥3 TEAEs (3 neutropenia, 1 thrombocytopenia); no related serious adverse events



#### NX-5948 Was Well Tolerated Across Doses Tested

Frequency of any grade TEAEs in ≥15% of patients

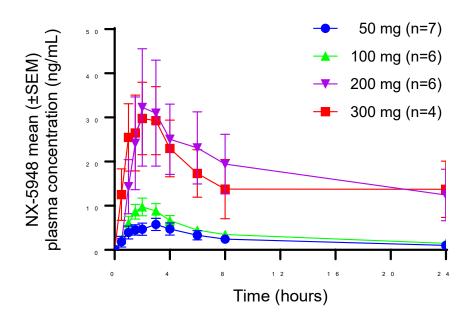
TEAEs, n (%)	<b>50 mg</b> (n=7)	<b>100 mg</b> (n=6)	<b>200 mg</b> (n=6)	<b>300 mg</b> (n=4)	<b>450 mg</b> (n=3)	All doses (N=26)
Purpura/contusion <sup>a</sup>	5 (71.4)	2 (33.3)	1 (16.7)	2 (50.0)	2 (66.7)	12 (46.2)
Thrombocytopeniab	2 (28.6)	3 (33.3)	2 (33.3)	3 (75.0)	1 (33.3)	10 (38.5)
Neutropenia <sup>c</sup>	1 (14.3)	3 (50.0)	0 (0.0)	4 (100.0)	0 (0.0)	8 (30.8)
Anemia	2 (28.6)	2 (33.3)	0 (0.0)	1 (25.0)	1 (33.3)	6 (23.1)
Cough	0 (0.0)	2 (33.3)	1 (16.7)	2 (50.0)	0 (0.0)	5 (19.2)
Headache	2 (28.6)	0 (0.0)	2 (33.0)	1 (25.0)	0 (0.0)	5 (19.2)
Nausea	3 (42.9)	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)	5 (19.2)
Rash	2 (28.6)	2 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	4 (15.4)

<sup>&</sup>lt;sup>a</sup>Purpura/contusion includes episodes of contusion or purpura; <sup>b</sup>Aggregate of 'thrombocytopenia' and 'platelet count decreased'; <sup>c</sup>Aggregate of neutrophil count decreased or neutropenia

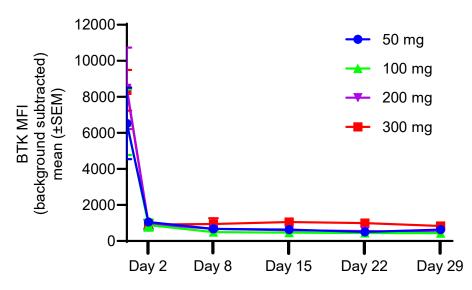


# NX-5948 Treatment Results in Rapid, Robust and Sustained BTK Degradation

#### A) NX-5948 C1D1 pharmacokinetics



#### B) BTK<sup>a</sup> degradation in patients receiving NX-5948



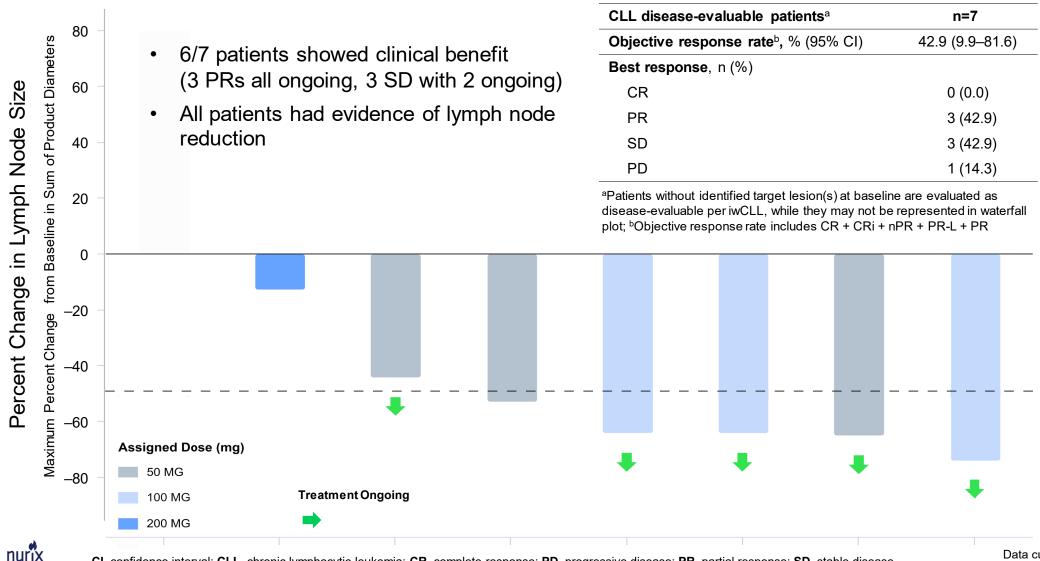
Dose	Number of patients per day						
(mg)	Day 1	Day 2	Day 8	Day 15	Day 22	Day 29	
50	7	7	7	6	5	6	
100	6	6	5	6	6	5	
200	6	6	6	6	4	3	
300	4	4	4	4	4	2	

<sup>&</sup>lt;sup>a</sup>BTK measured in patient B-cells whole blood using flow cytometry assay

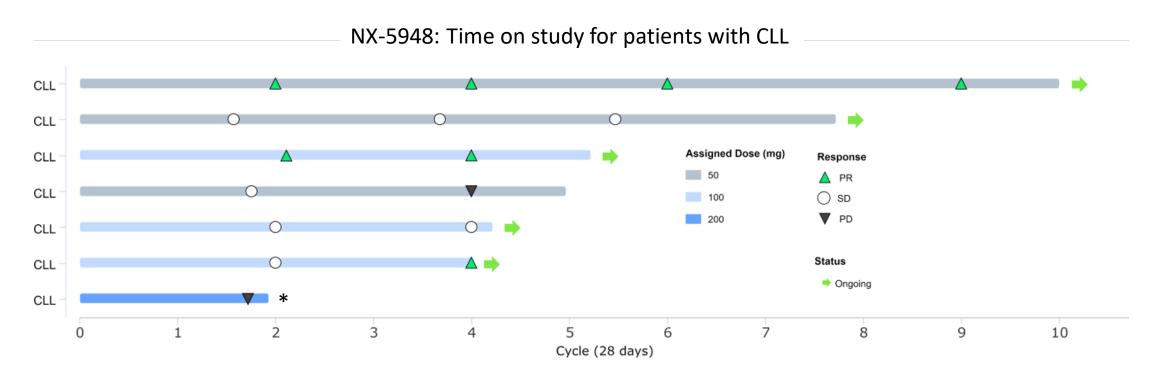
BTK, Bruton's tyrosine kinase; MFI, mean fluorescence intensity; SEM, standard error of the mean



## NX-5948 Shows Broad Antitumor Activity in CLL as Demonstrated by Significant Lymph Node Reduction and Objective Response Rate



## Responses Are Durable and Treatment Ongoing in Patients with CLL



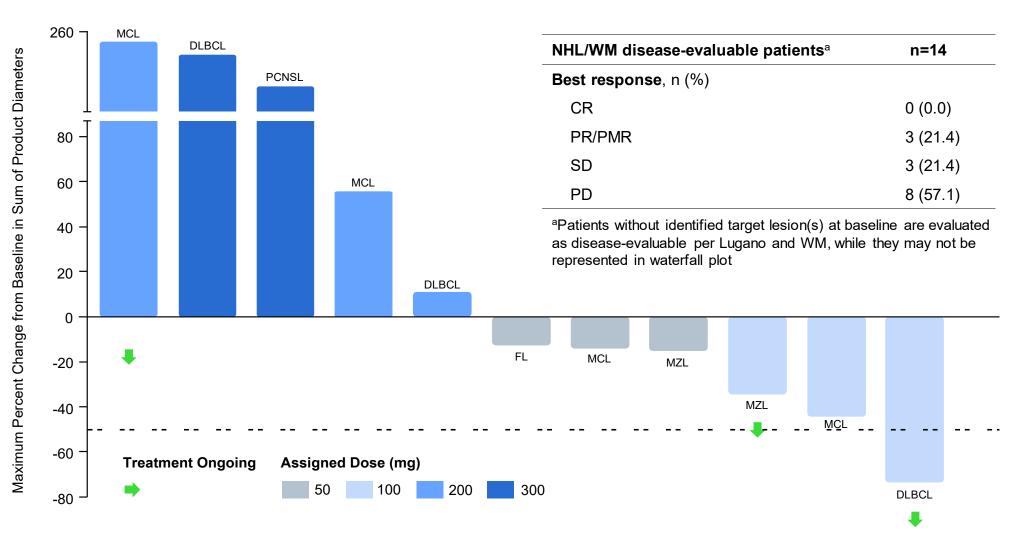
CLL, chronic lymphocytic leukemia



<sup>\*</sup> Patient enrolled with CLL subsequently confirmed to have Richter's transformation to Hodgkin's disease

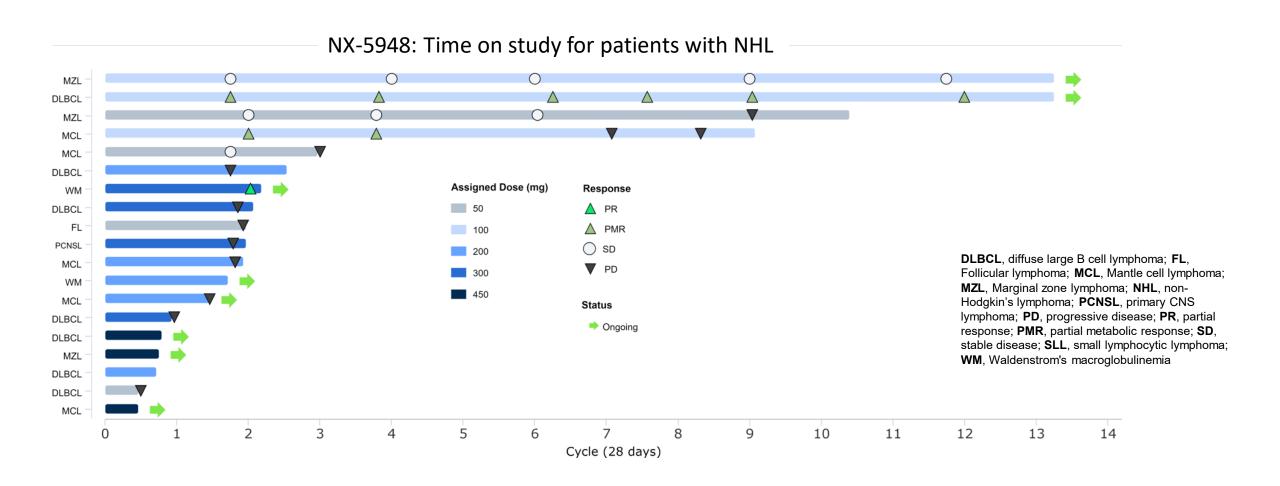
## Responses to NX-5948 Observed Across NHL Subtypes

Activity observed across NHL subtypes





## Durable Responses in Patients with NHL





21

## NX-5948 Update From AACR 2024

Evidence of CNS penetration and activity in the brain



## CLL and NHL with CNS Involvement Remain an Area of High Unmet Need

• CNS involvement of B cell malignancies span various conditions including:

#### **Primary CNS Lymphoma (PCNSL)**

Comprises ~4% of all primary CNS tumors and 4-6% of all extranodal lymphomas<sup>1</sup>

## Secondary CNS Lymphoma (SCNSL)

Affects ~5% of patients with DLBCL<sup>2</sup>

#### **CNS involvement with CLL**

Rare complication of CLL with dismal prognosis in patients with clinically significant disease<sup>3</sup>

- First-line standard of care typically involves high-dose methotrexate-based chemotherapy regimens with limited option in the relapse / refractory setting
- Investigational drugs (BTKi, CAR-T, immune check point inhibitors) have been used in the relapse/refractory setting with some limitation including short duration of response and challenging safety profile



<sup>&</sup>lt;sup>1</sup> Ferreri et al. Nat Rev Dis Primers. 2023 Jun 15;9(1):29.

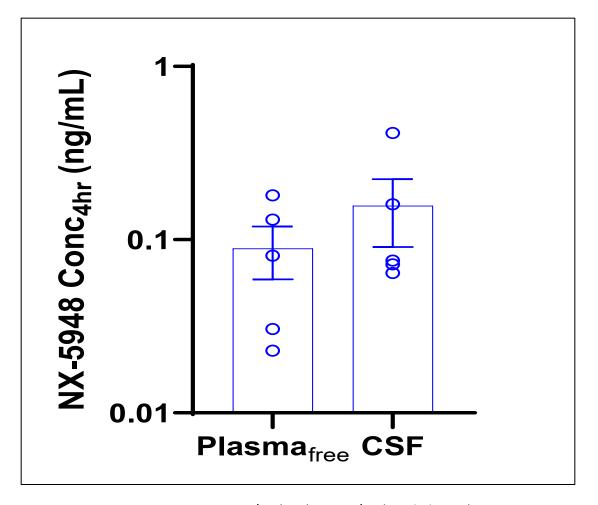
<sup>&</sup>lt;sup>2</sup> Bobillo et al. Haematologica. 2023 Mar 1;108(3)

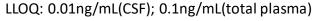
<sup>&</sup>lt;sup>3</sup> Strati P. et al. Haematologica. 2016 Apr; 101(4)

#### Detectable Levels of NX-5948 in CSF of Patients With CNS Involvement

As of Jan 16, 2024:

- Six patients with CNS involvement (1 CLL, 5 NHL) were enrolled
- 5 patients with available PK data







# NX-5948 in Patients with NHL and CLL With CNS Involvement Two Case Reports

	Patient #1	Patient #2	
Disease	PCNSL	CLL with CNS involvement	
Age, M/F	65, F	58, M	
Dose	450 mg QD	100 mg QD	
Time on Study*	Off Treatment, @ 16wk assesment	Ongoing, Cycle #10 (>36wks)	
Prior lines of tx	2	3	
Prior BTKi?	Yes (ibrutinib)	Yes (acalabrutinib)	
CSF PK (Y/N)	Υ	Υ	



## First Case Study: PCNSL

Multiple lines of prior therapies including cytotoxic chemotherapy and BTK inhibitor

#### Patient demographics and disease characteristics

- 65-year-old female with PCNSL
- Initial Diagnosis: Oct 2021

#### **Prior treatments**

- 1. Cytotoxic chemotherapy: Oct 2021 Feb 2022 (CR)
  - Induction: Methotrexate, TMZ + R
  - Consolidation: High dose Ara-C
- 2. Ibrutinib: June 2022 Sept 2023 (SD)

#### Relevant medical history

- Hypertension, Feb 2023
- Purpura, 2021

#### Molecular and cytogenetic features (from history)

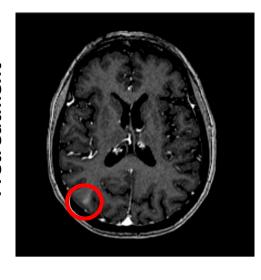
- MYC rearrangement
- MYC and BCL2 ICH +

Safety				
Exposure	No dose interruptions or dose modifications			
DLT's	None			
SAE's	None			
Grade 3 or > AE	Gr3 HTN All other TEAEs Gr 1 or 2			



## First Case Study: PCNSL









**Pretreatment:** 

3 contrast enhancing lesions in the right temporal lobe



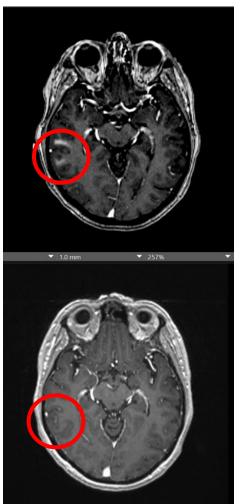
# Pretreatment

## First Case Study: PCNSL

Complete Response observed at 8 weeks







#### **Pretreatment:**

3 contrast enhancing lesions in the right temporal lobe



8 weeks: Complete Response
Complete resolution of all temporal lobe lesions



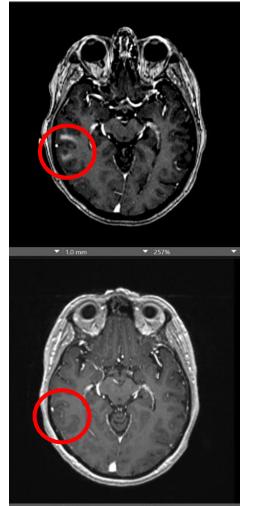
# **Pretreatment**

## First Case Study: PCNSL

Complete Response observed at 8 weeks

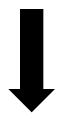




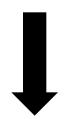


#### **Pretreatment:**

3 contrast enhancing lesions in the right temporal lobe



8 weeks: Complete Response
Complete resolution of all temporal lobe lesions



**16 weeks: Progressive Disease**New lesions



## Second Case Study: CLL With CNS Involvement

#### Multiple lines of prior therapies including BTK inhibitor

## Patient demographics and disease characteristics

- 58-year-old male with CLL
- Initial CLL diagnosis: 2015
- CNS disease diagnosis: May 2023

#### **Prior treatments**

- 1. Idelalisib: 2015 2018
- 2. Venetoclax-Rituximab: 2018 2022
- 3. Acalabrutinib: 2022 June 2023

#### Relevant medical history

- Facial numbness
- Shingles

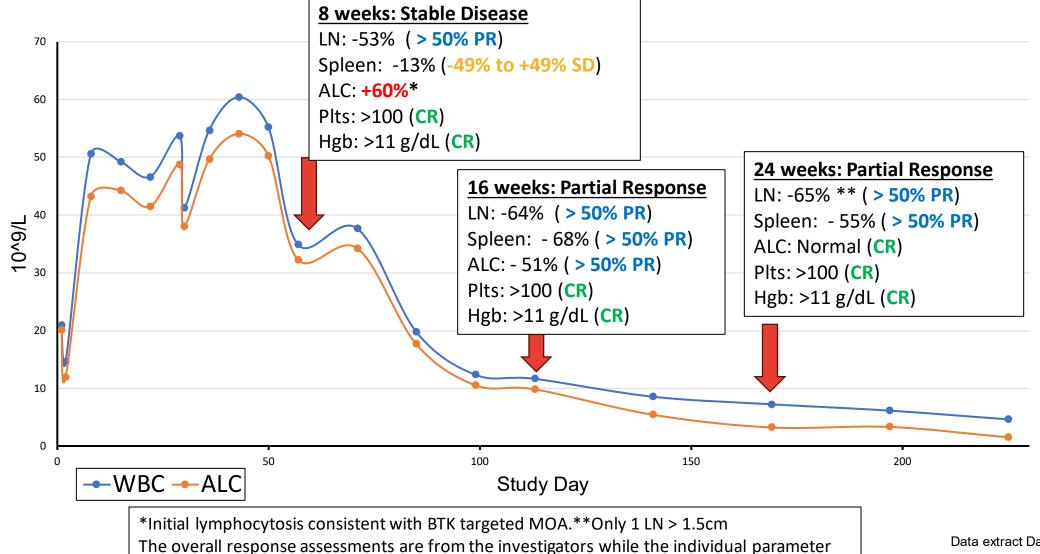
## Molecular and cytogenetic features (from history)

• Del (17p)

Safety	
Exposure	Dose interruptions (infections)
DLT's	None
SAE's	None
Grade 3 or > AE	<ul> <li>Baseline Gr4 Neutropenia</li> <li>Managed with intermittent GCSF which required increased frequency during cycle 1</li> <li>ANC normalized beginning C6D1 *</li> <li>Two unrelated Gr 3 infections: PICC line infection and RSV</li> <li>All other related AEs Gr 1 or 2</li> </ul>

## Second Case Study: CLL With CNS Involvement

Early clinical activity deepening over time



response assessment criteria are calculated per iwCLL from the data entered.



# Second Case Study: CLL with CNS Involvement Timing of CSF clearance correlates with overall clinical response

	Screening	Week 8	Week 16	Week 24
Extra-CNS response	-	Stable Disease	Partial Response	Partial Response
CSF RBC (cells/mm³)	63	522	65	82
CSF WBC (cells/mm³)	173	63	28	18
Presence of malignant cells in the CSF	Yes	Yes	Yes	No



#### Vision: Prioritizing NX-5948 in CLL and Enabling Broad Strategy in NHL

 Accelerating enrollment in dose escalation to identify Phase 1b expansion dose levels for CLL and NHL with expansion planned for 2024

B-cell malignancies
Phase 1 & 2

Enable potential accelerated approval(s) in r/r CLL, MCL, MZL, WM, PCNSL

Enable combinations for earlier line trials

CLL Phase 3

2L+ CLL
Superiority post
BTKi +/- BCL-2i failure

1L CLL Displace BTKi MCL, MZL, WM Phase 3

r/r MCL, MZL, WM Superiority to BTKi

1L MCL, MZL, WM
Displace or improve
standard of care

DLBCL, PCNSL Phase 3

1L DLBCL, PCNSL
Improve standard of care with combination regimens



# Beyond Hem/Onc: NX-5948 Is Highly Effective in Models of Major Inflammation & Immunology Indications

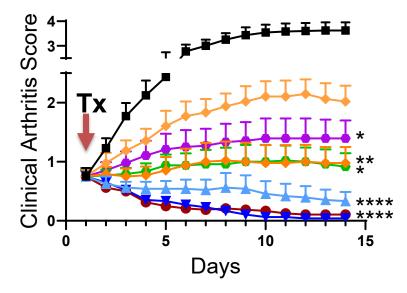
NX-5948 in Inflammation & Immunology

Plans to enable initiation of I&I development

Extended preclinical toxicology

Healthy volunteer study

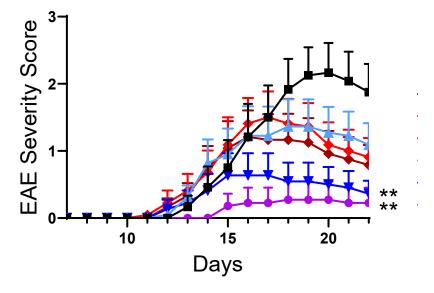
#### Rheumatoid Arthritis Model





- Rilzabrutinib 10 mg/kg
- Rilzabrutinib 30 mg/kg
- Enbrel 10 mg/kg
- Tofacitinib 30 mg/kg BID
- Ibrutinib 30 mg/kg
- → NX-5948 10 mg/kg
- NX-5948 30 mg/kg

#### Multiple Sclerosis Model



- Vehicle
- → Ibrutinib 10 mg/kg
- Ibrutinib 30 mg/kg
- → NX-5948 10 mg/kg
- NX-5948 30 mg/kg
- → FTY720 3 mg/kg

\*p<0.05, \*\*p<0.01, \*\*\*, p<0.001, \*\*\*\*p<0.0001 compared to vehicle control

Source: Rountree et al., 3rd B&T-cell Summit 2022



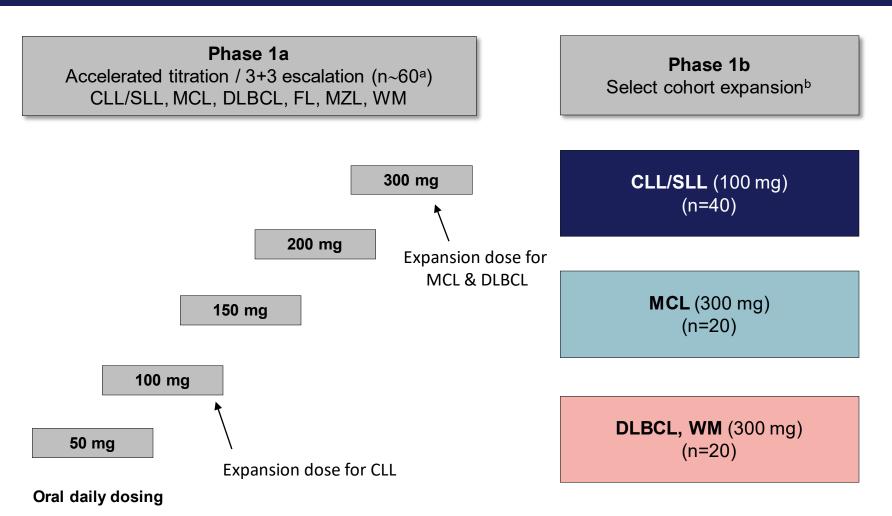
## NX-2127

Dual acting BTK 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
- Plan to reinitiate enrollment 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

<sup>a</sup>Planned number of evaluable patients (i.e., meeting DLT evaluability criteria); <sup>b</sup>Planned number of evaluable patients (i.e., meeting efficacy evaluability criteria)



### Baseline Demographics and Disease Characteristics

Heavily pretreated population with significant acquired resistance mutations

Characteristic	CLL/SLL (n=33)	NHL/WM (n=21)	Overall population (N=54)
Median age, years (range)	74.0 (58.0–90.0)	70.0 (50.0–92.0)	72.5 (50.0–92.0)
Female, n (%)	11 (33.3)	6 (28.6)	17 (31.5)
<b>Male</b> , n (%)	22 (66.7)	15 (71.4)	37 (68.5)
ECOG PS, n (%)			
0	18 (54.5)	10 (47.6)	28 (51.9)
1	15 (45.5)	11 (52.4)	26 (48.1)
No. of lines of prior therapy <sup>a</sup> , median (range)	5 (2–11)	4 (2–10)	4 (2–11)
BTKi, n (%)	33 (100.0)	15 (71.4)	48 (88.9)
Pirtobrutinib, n (%)	9 (27.3)	5 (23.8)	14 (25.9)
BTKi and BCL2i, n (%)	26 (78.8)	1 (4.8)	27 (50.0)
cBTKi, ncBTKi, and BCL2i, n (%)	8 (24.2)	0 (0.0)	8 (14.8)
CAR-T/-NK therapy, n (%)	1 (3.0)	3 (14.3)	4 (7.4)
Bispecific antibody, n (%)	0 (0.0)	2 (9.5)	2 (3.7)
Immunomodulatory therapy (lenalidomide), n (%)	4 (12.1)	4 (19.0)	8 (14.8)



## Baseline Demographics and Disease Characteristics (Cont'd)

Heavily pretreated population with significant acquired resistance mutations

Mutation <sup>a</sup>	CLL/SLL (n=33)	NHL/WM (n=21)	Overall population (N=54)
<i>BTK</i> , n (%)	12 (36.4)	3 (14.3)	15 (27.8)
C481S or C481R	7 (21.2)	1 (4.8)	8 (14.8)
L528W	4 (12.1)	1 (4.8)	5 (9.3)
T474F or T474I	4 (12.1)	1 (4.8)	5 (9.3)
V416L	1 (3.0)	0 (0.0)	1 (1.9)
L512V	0 (0.0)	1 (4.8)	1 (1.9)
PLCG2b	1 (3.0)	2 (9.5)	3 (5.6)
BCL2 (G101V)	4 (12.1)	0 (0.0)	4 (7.4)

<sup>&</sup>lt;sup>a</sup>Patients could have multiple prior treatments and multiple BTK mutations; mutations were tested centrally at baseline by next-generation sequencing (allelic frequency ≥5% is reported) <sup>b</sup>L845F, D334H, D1140N, T961M, S707F



## Safety Profile Manageable With Decreasing Incidence of Atrial Fibrillation Frequency of TEAEs in ≥20% of patients or grade ≥3 or SAEs in >1 patient (n=54)

Treatment emergent adverse events (TEAEs), n (%)	Any grade	Grade ≥3	SAEs
Fatigue	25 (46.3)	-	_
Neutropenia <sup>a</sup>	25 (46.3)	23 (42.6)	-
Hypertension	18 (33.3)	8 (14.8)	_
Bruising/contusion <sup>b</sup>	16 (29.6)	-	1 (1.9)
Diarrhea	16 (29.6)	-	-
Anemia	13 (24.1)	8 (14.8)	1 (1.9)
Dizziness	13 (24.1)	-	-
Dyspnea	13 (24.1)	1 (1.9)	_
Thrombocytopeniac	13 (24.1)	4 (7.4)	-
Constipation	12 (22.2)	-	-
Headache	11 (20.4)	-	-
Upper GI hemorrhaged	2 (3.7)	2 (3.7)	2 (3.7)
Pruritus	11 (20.4)	1 (1.9)	_
COVID-19	7 (13.0)	4 (7.4)	3 (5.6)
Atrial fibrillatione	6 (11.1)	3 (5.6)	3 (5.6)
Pneumonia	6 (11.1)	3 (5.6)	3 (5.6)
Pain in extremity	5 (9.3)	2 (3.7)	1 (1.9)
Leukocytosis	3 (5.6)	3 (5.6)	-
Lymphocyte count increased	2 (3.7)	2 (3.7)	-
Sepsis <sup>f</sup>	2 (3.7)	2 (3.7)	2 (3.7)

No new cases of atrial fibrillation since 9/21/22 data cutoff used for ASH 2022 presentation

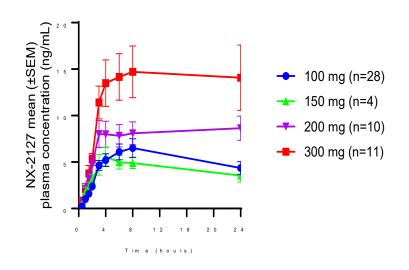


Incidence decreased from previously reported 17% to 11%

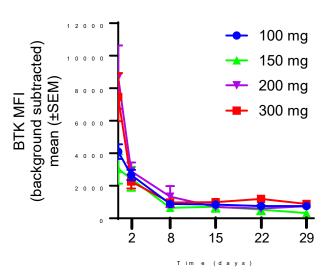
<sup>&</sup>lt;sup>a</sup>Aggregate of 'neutropenia' and 'neutrophil count decreased'; <sup>b</sup>Bruising/contusion includes episodes coded as contusion; <sup>c</sup>Aggregate of 'thrombocytopenia' and 'platelet count decreased'; <sup>d</sup>Includes one Grade 5 event; <sup>e</sup>Aggregate of 'atrial fibrillation' and 'atrial flutter'; <sup>f</sup>Includes two Grade 5 events

## NX-2127 Treatment Results in Rapid, Robust and Sustained BTK Degradation With Clinically Relevant Ikaros Degradation

#### A) NX-2127 C1D1 plasma pharmacokinetics

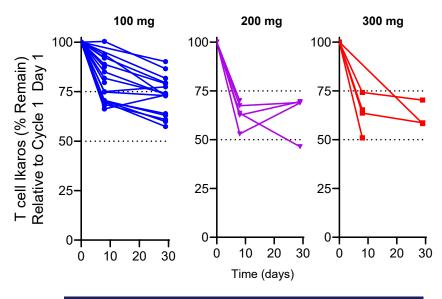


#### B) BTKa degradation in patients receiving NX-2127



	Number of patients per day					
Dose (mg)	Day 0	Day 2	Day 8	Day 15	Day 22	Day 29
100	28	27	24	23	22	20
150	4	4	4	3	2	2
200	9	9	8	9	7	6
300	10	10	8	9	6	4

#### C) Ikaros<sup>b</sup> degradation in patients receiving NX-2127



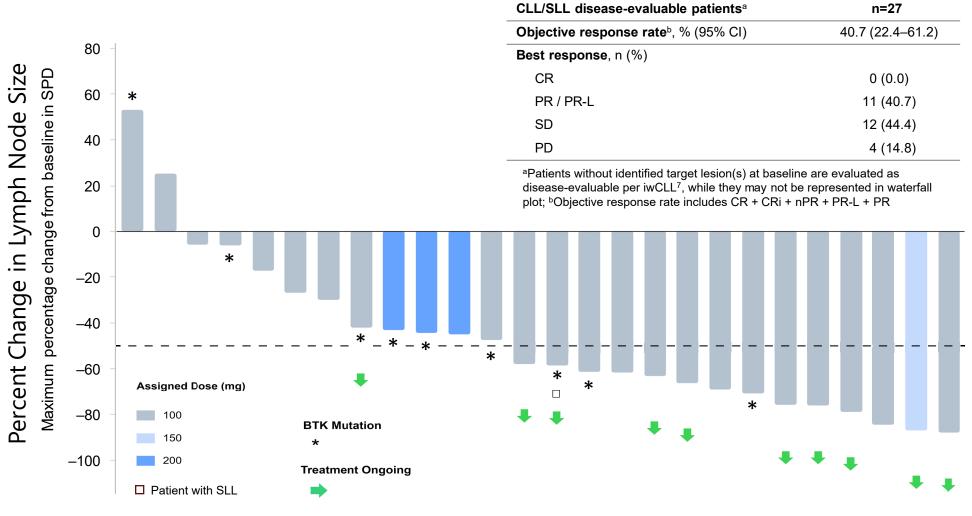
	Number of patients per day			
Dose (mg)	Day 0	Day 8	Day 29	
100	23	19	16	
200	5	5	4	
300	5	4	3¢	



40

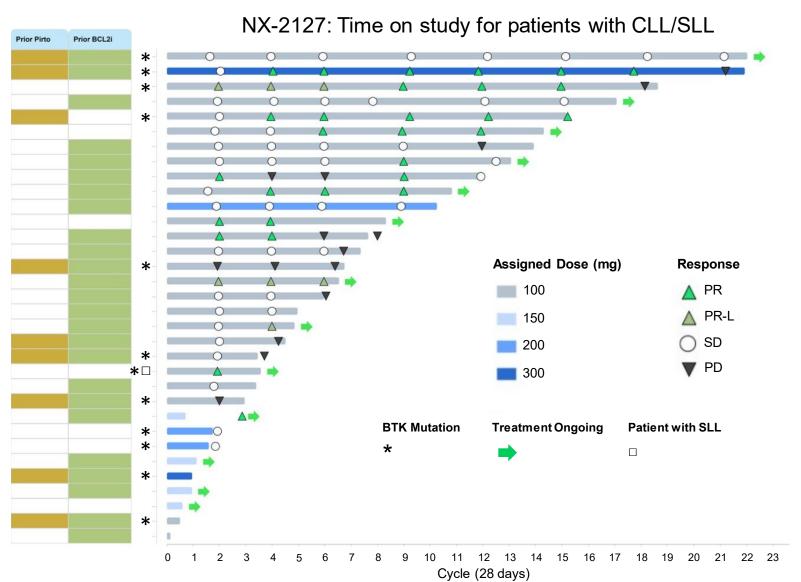
# Broad Antitumor Activity in CLL/SLL as Demonstrated by Significant Lymph Node Reduction and Objective Response Rate

Objective response rate in heavily pretreated population was 41% with treatment ongoing in 13 patients, up from 33% reported at ASH 2022





## Durable Responses Seen in Heavily Pretreated CLL/SLL Patients



All patients had prior cBTKi

Double exposed:

Prior cBTKi and BCL2i

Triple exposed:

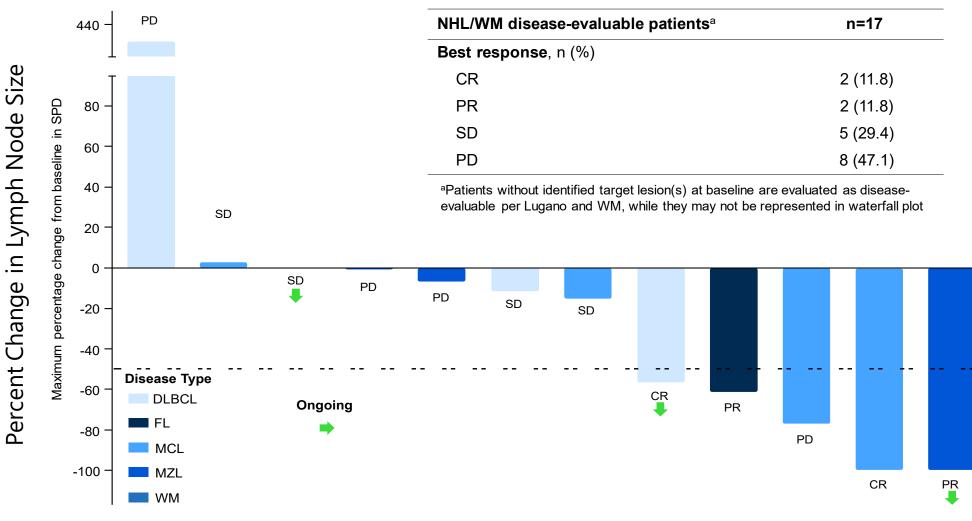
Prior cBTKi, ncBTKi, and BCL2i

BCL2i, B-cell lymphoma-2 inhibitor; BTK, Bruton's tyrosine kinase; cBTKi, covalent BTK inhibitor; ncBTKi, noncovalent BTK inhibitor; PD, progressive disease; Pirto, pirtobrunib; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease

Mutations were tested at baseline by NGS centrally

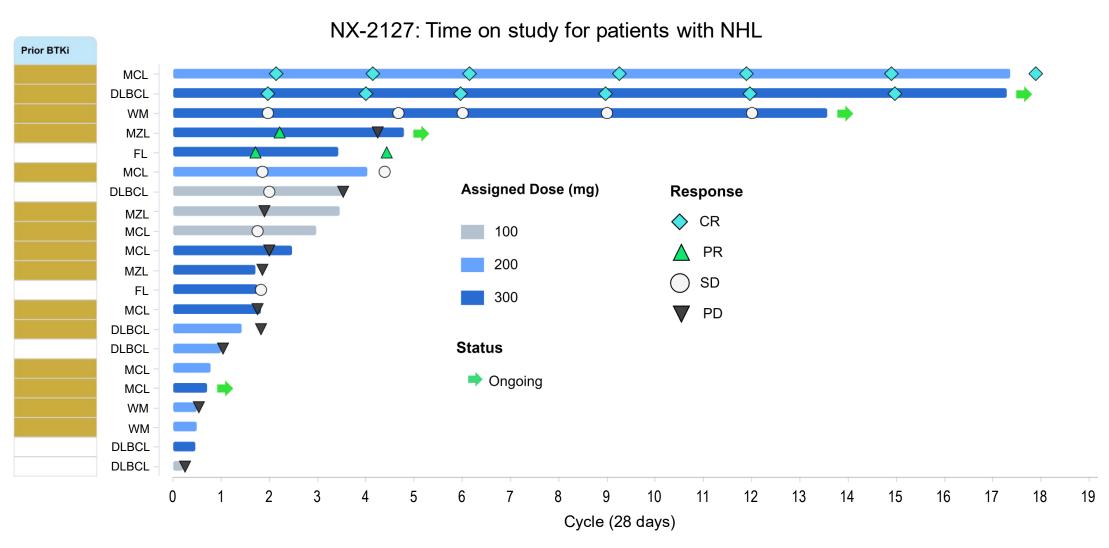
## Responses Observed Across NHL Subtypes Including Rapid and Sustained Complete Responses

- Rapid CR at 8
   weeks observed
   in 2 patients
   (DLBCL, MCL)
   with 15+ months
   durability
- Rapid PRs at 8
   weeks were
   observed in
   2 patients (FL,
   MZL)





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

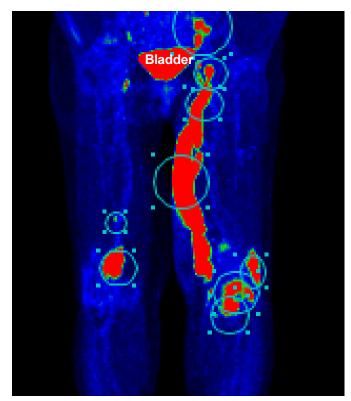




# Rapid and Sustained Complete Response in Relapsed/Refractory DLBCL With NX-2127

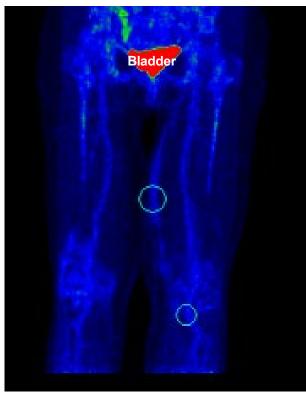
#### FDG-PET CT Scan Disease Assessment

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



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





## Vision: Focused Strategy With NX-2127 in NHL

B-cell malignancies
Phase 1 & 2

Establish single-agent response rate in DLBCL and MCL

Enable combinations for earlier line trials

DLBCL Phase 3

r/r DLBCL
Potential monotherapy

1L DLBCL
Improve standard of care

MCL Phase 3

r/r MCL
Potential monotherapy

Initiation of advanced development activities are dependent on threshold activity in Phase 1b and emerging data for NX-5948



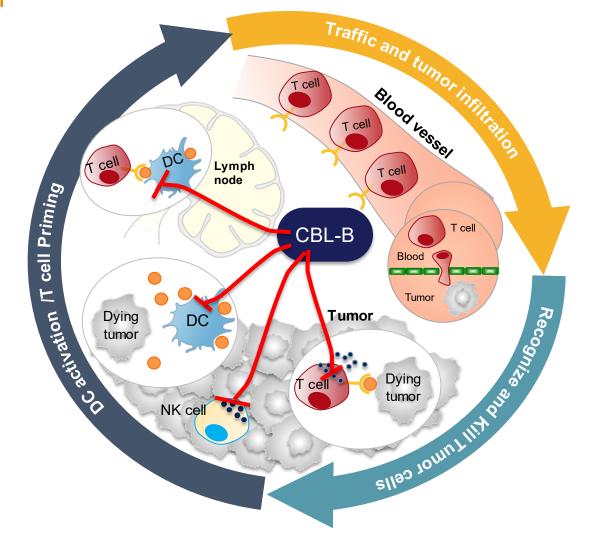
### Targeting CBL-B Enhances Antitumor Response

A Master Orchestrator of the Immune System

CBL-B mediated mechanisms strongly restrain a productive anti-tumor response

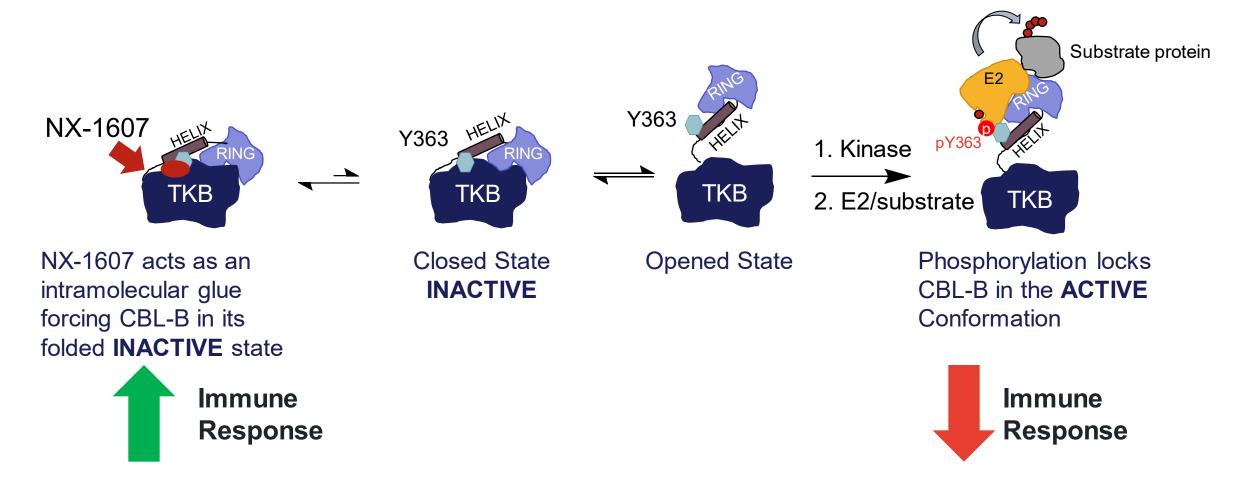
#### CBL-B inhibition increases:

- DC and NK infiltration and function
- T cell priming
- Cytotoxic T cells function
- Ability of T cells to resist tumor immunosuppressive mechanisms: Treg, MDSC, and TGF-β



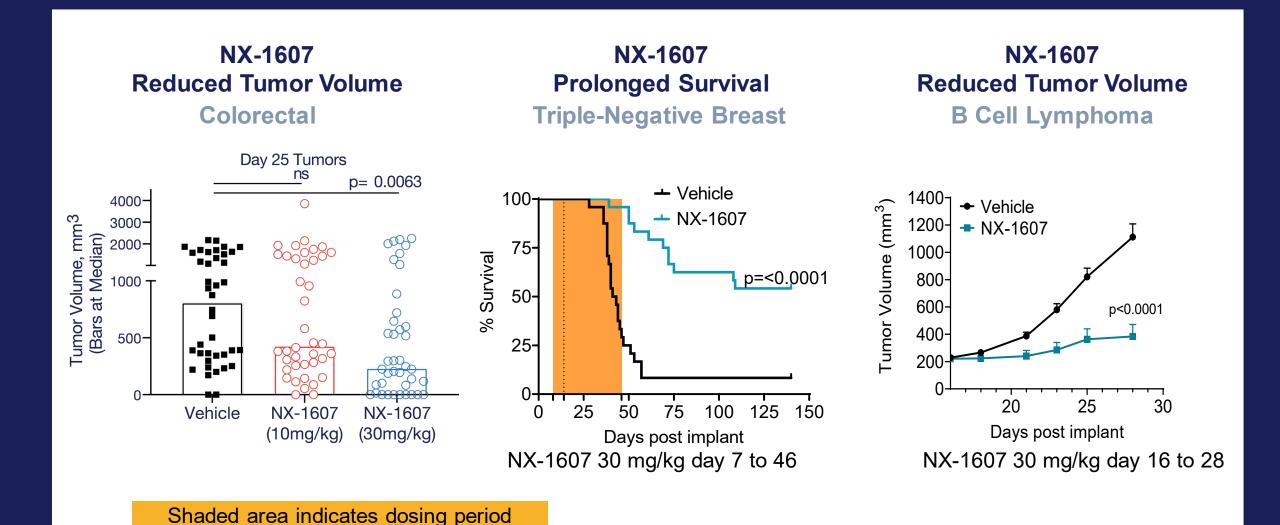


#### NX-1607 Mechanism of Action: Intramolecular Glue



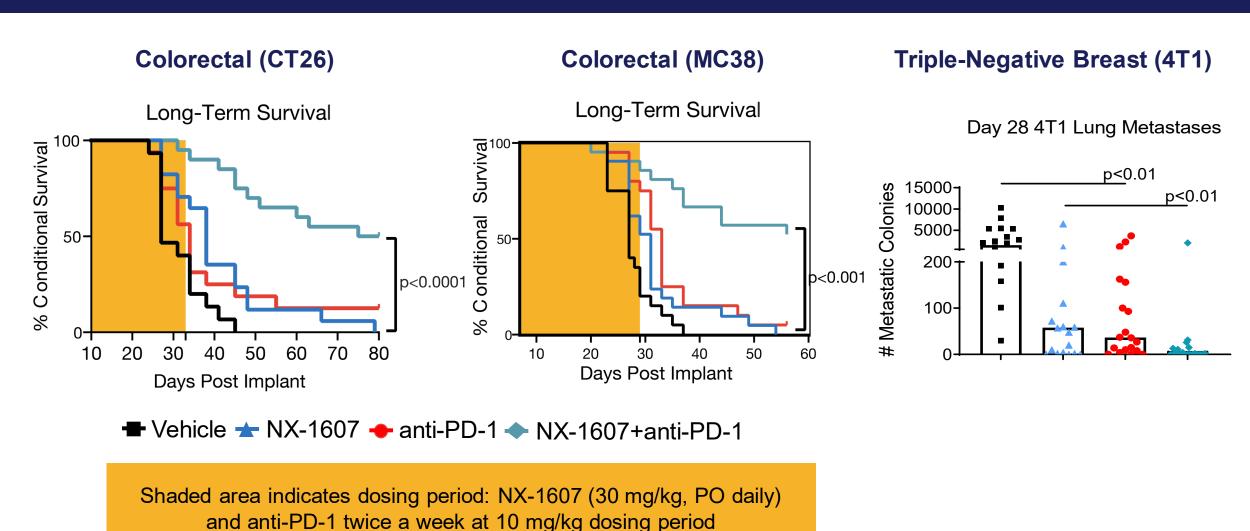


### Single-Agent NX-1607 Induces Antitumor Response in Multiple Models



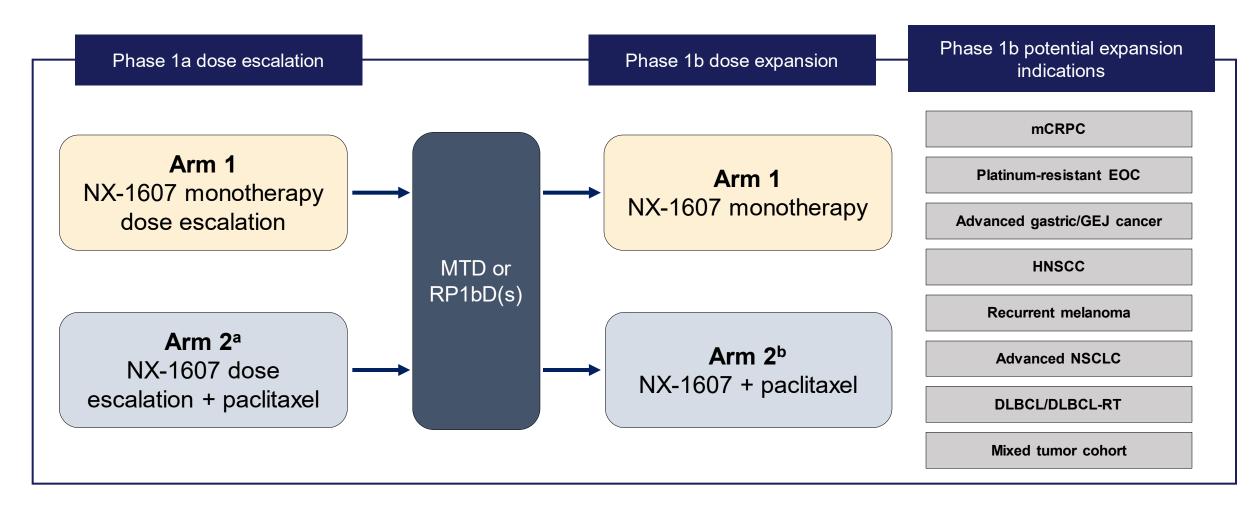


## NX-1607 and Anti-PD-1 Synergize to Enhance Anti-Tumor Effects and Survival of Mice in Multiple Tumor Models





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



<sup>&</sup>lt;sup>a</sup>Starting dose for NX-1607 in Arm 2 will be ≥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

**NX-2127** 

✓ Resolve partial clinical

hold to enable the

introduction of new

ongoing Phase 1

clinical trial

drug product into the

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

Immune oncology

NX-1607

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

Platform & pipeline

Research pipeline

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

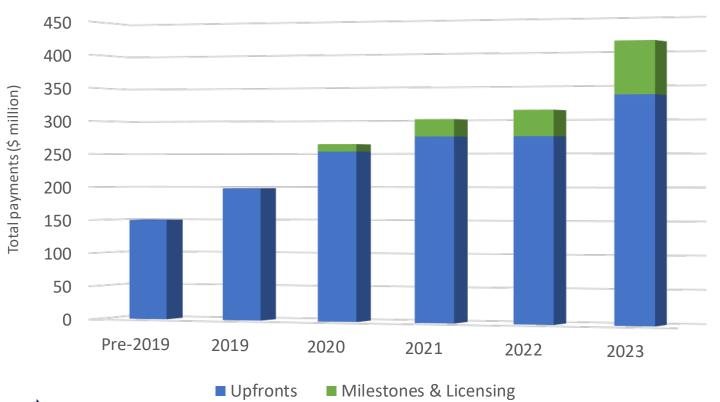


## **Strong Financial Position**

#### \$442.9M in proforma cash and investments

- Includes \$254.3M as of February 29, 2024, plus an estimated \$188.6M in net proceeds from recent follow-on offering
- Cash runway to fund operations into H2 2026

#### Cumulative Partnership Capital



#### R&D collaboration cashflow:

- Gilead: \$45M upfront and \$67M in licensing fee and milestone payments earned to date
- Sanofi: \$55M upfront, \$22M in expansion option exercise, and \$11M in milestone payments earned to date
- Seagen (now part of Pfizer):
   \$60M upfront payment
- \$413 million generated through discovery partnership payments

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



## Thank you

