Leader in Targeted Protein Modulation

Nurix Therapeutics

Blazing a New Path in Medicine

Investor Presentation

January 2023

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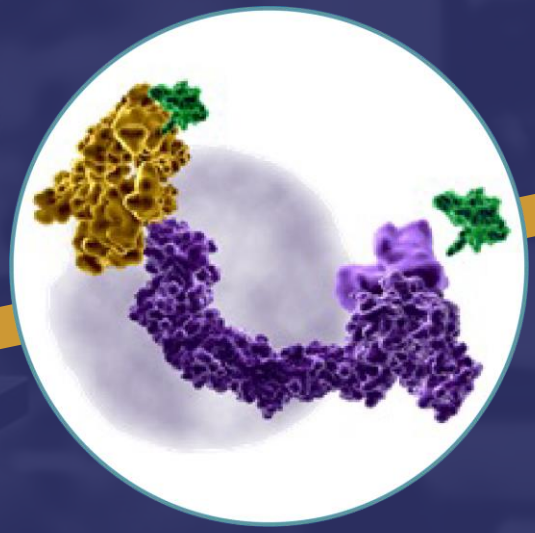
Nurix Drugs Engage Ligases for the Treatment of Cancer

Targeted Protein Modulation: TPM = TPD + TPE

A Powerful Cellular System

Harness ligases to decrease specific protein levels

Targeted Protein Degradation (TPD)



Ubiquitin is ligated to target proteins to tag them for degradation by the proteasome

Targeted Protein Elevation (TPE)

Inhibit ligases to increase specific protein levels

Three Major Medical and Scientific Advances by Nurix in 2022

NX-2127 data highlighted in two oral presentations at ASH

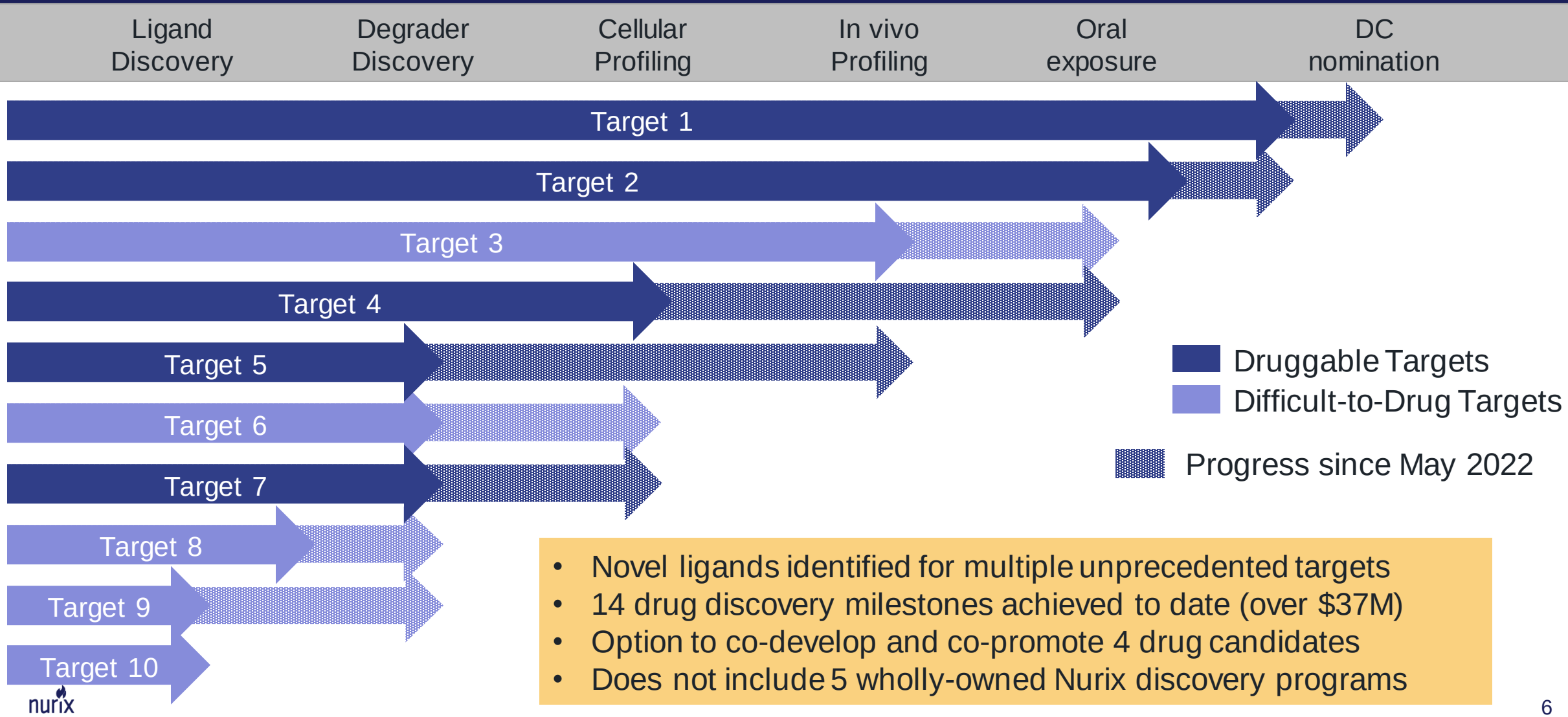
- First evidence of clinical benefit for patients with advanced B cell malignancies treated with a targeted protein degrader
- Target degradation can overcome treatment-emergent inhibitor resistance mutations
- First evidence that degraders uniquely address non-catalytic functions of proteins (e.g., scaffolding functions)

Nurix Is Advancing Four Wholly Owned Clinical Programs with a Deep Pipeline of Proprietary and Partnered Novel Targets

MOA	Drug program	Target/delivery	Therapeutic area	Preclinical	Phase 1	Phase 2	Phase 3
TPD	**NX-2127** Degrader	BTK-IKZF *Oral*	B-cell malignancies			✓ Advanced to Ph 1b in CLL ✓ Efficacy established in CLL ✓ Single agent CR in DLBCL	
TPD	**NX-5948** Degrader	BTK *Oral*	B-cell malignancies			✓ Dosed first patient in U.K. ✓ Demonstrated BTK degradation ✓ IND cleared for U.S. enrollment	
TPE	**NX-1607** Inhibitor	CBL-B *Oral*	Immuno-Oncology			✓ Demonstration of CBL-B inhibition with novel biomarker ✓ IND cleared for U.S. enrollment	
TPE	**DeTIL-0255** Cell therapy	*Ex vivo CBL-B inhibition*	Gynecologic malignancies			✓ Dosed first patient ✓ Completed safety run-in	
TPM	Wholly owned & partnered	15 targets	Multiple				

Progress since January 2022

Significant Advancement of the Collaboration Pipeline during 2022, Including Targets Considered Undruggable



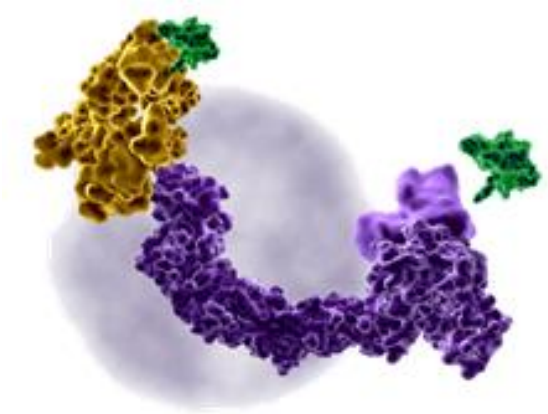
- Novel ligands identified for multiple unprecedented targets
- 14 drug discovery milestones achieved to date (over $37M)
- Option to co-develop and co-promote 4 drug candidates
- Does not include 5 wholly-owned Nurix discovery programs

A First-In-Class Franchise of BTK Degraders:
NX-2127 & NX-5948

NX-2127

BTK DEGRADATION
& IMMUNOMODULATION

- Positive clinical activity in CLL patients, including responses in patients with BTK or BCL2 mutations
- Active in the clinic against multiple BTK inhibitor-resistant mutations
- Complete response observed in a patient with DLBCL
- Phase 1b cohort expansion for CLL patients is ongoing
- Dose exploration is ongoing for patients with NHL



NX-5948

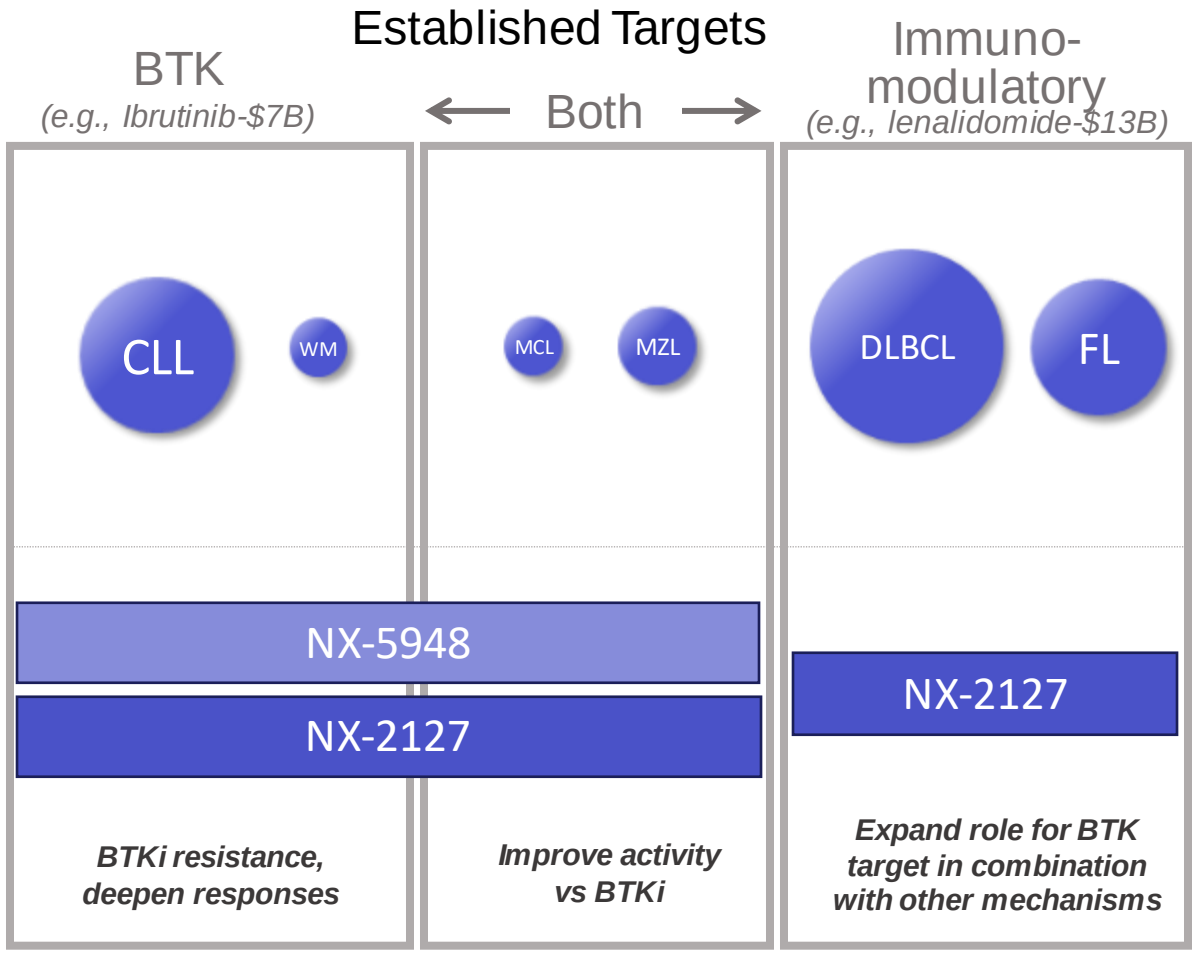
BTK DEGRADATION

- Clinical evidence of potent BTK degradation in all patients tested
- Active in vitro against multiple BTK inhibitor-resistant mutations
- Crosses blood brain barrier and degrades BTK in brain-resident lymphoma cells and microglia in animal models
- Activity in multiple models of autoimmune disease
- Phase 1a dose escalation trial ongoing in U.K. and IND accepted in the U.S.

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

NX-2127 for BTK inhibitor resistance in CLL and for aggressive NHL

NX-5948 may be the degrader of choice for single-target therapy with potential in autoimmunity



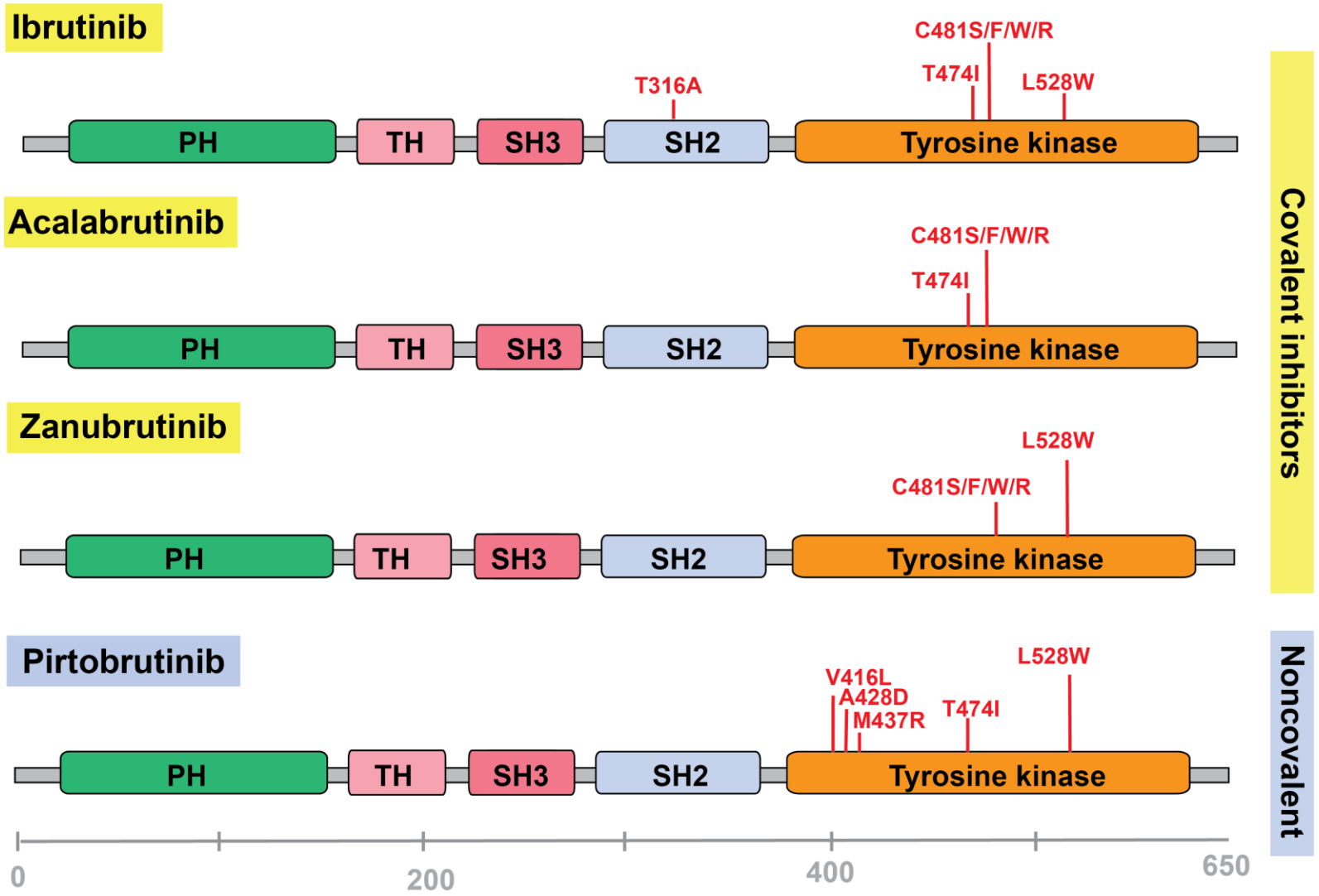
Size of bubble=annual incidence in US and EU

B-CELL MALIGNANCIES ANNUAL INCIDENCE (US & EU)	
Chronic Lymphocytic Leukemia (CLL)	39,700
Diffused Large B-Cell Lymphoma (DLBCL)	55,100
Follicular Lymphoma (FL)	26,200
Mantle cell lymphoma (MCL)	6,200
Marginal Zone Lymphoma (MZL)	10,700
Waldenstrom's macroglobulinemia (WM)	6,300

Estimates based on 2020 incidence from DRG, GlobalData and secondary research; EU comprised of France, Germany, Italy, Spain and UK

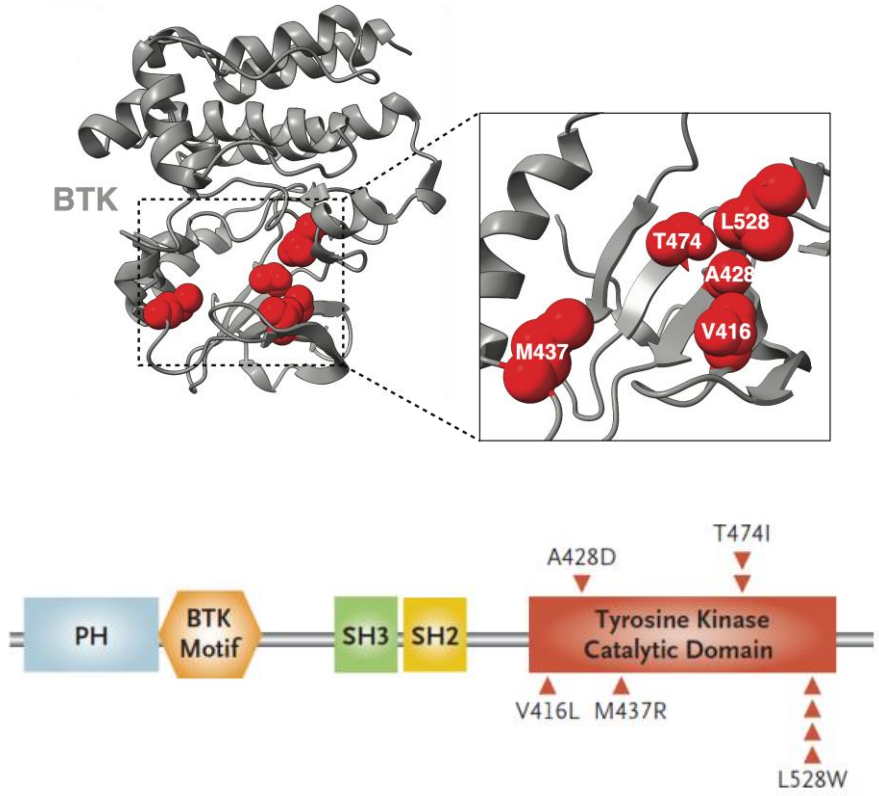
BTK, Bruton tyrosine kinase; DLBCL, Diffuse large B cell lymphoma; CLL, Chronic lymphocytic leukemia, SLL, small lymphocytic lymphoma; MCL, Mantle cell lymphoma; WM, Waldenstrom's macroglobulinemia; MZL, Marginal zone lymphoma; FL, Follicular lymphoma; NHL, non-Hodgkin lymphoma

Diverse BTK Mutations Cause Resistance to Covalent & Non-Covalent BTK Inhibitors



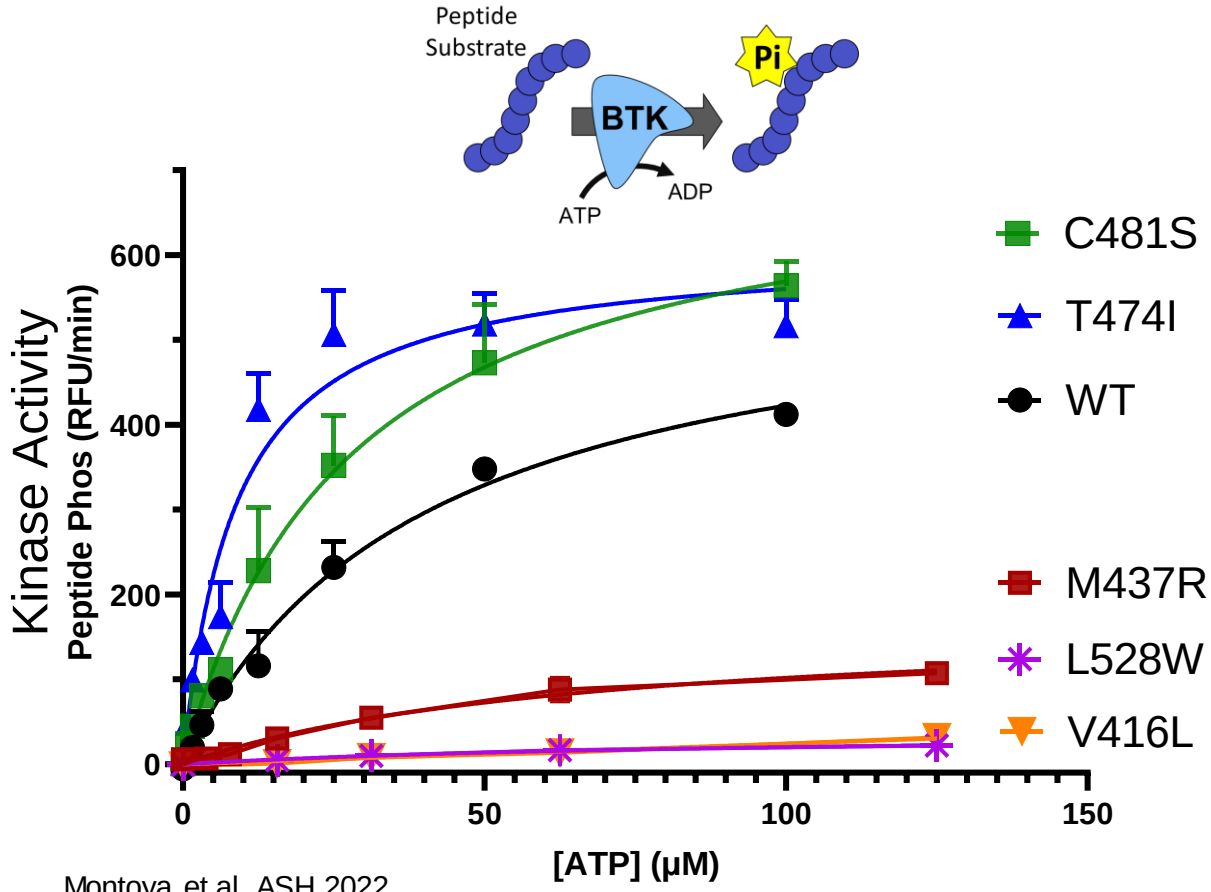
Nurix Degraders Directly Address Emerging Resistance Mutations and BTK Scaffolding Activity

Treatment with BTK inhibitors is changing the resistance landscape



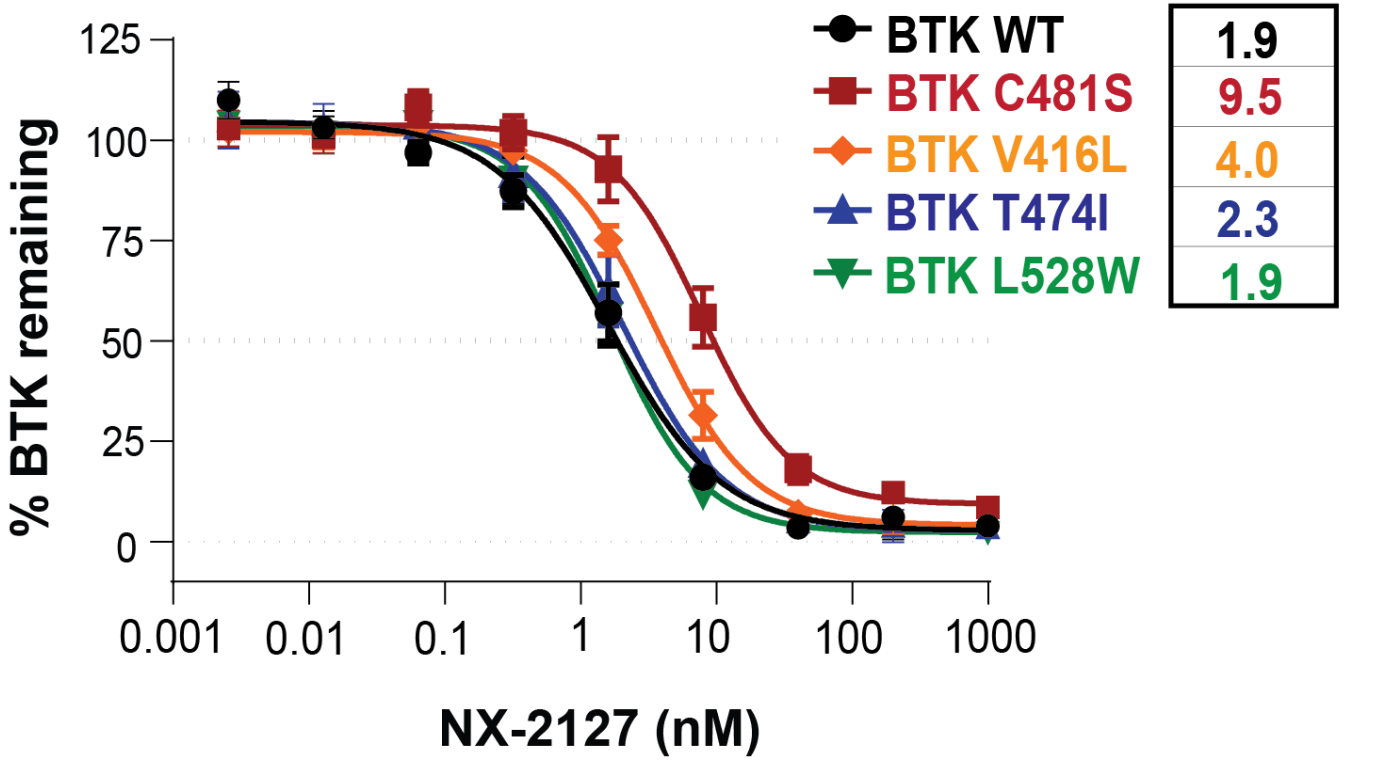
Wang E, et al. NEJM 2022

Many of the mutations that confer resistance to BTK inhibitors lack kinase activity

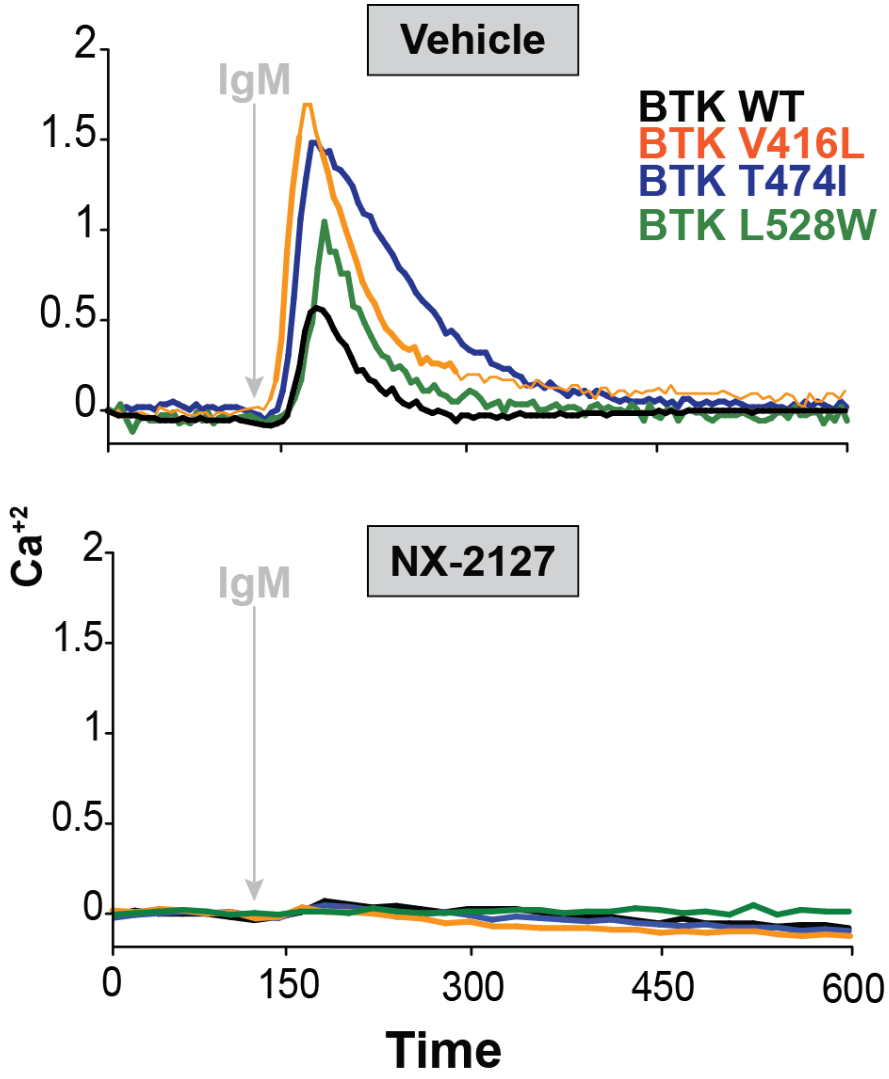


Montoya et al, ASH 2022

NX-2127 Degrades Both Wild-Type and Kinase Dead Mutant BTK and Suppresses Ca2+ Signaling



DC_{50} (nM)
1.9
9.5
4.0
2.3
1.9



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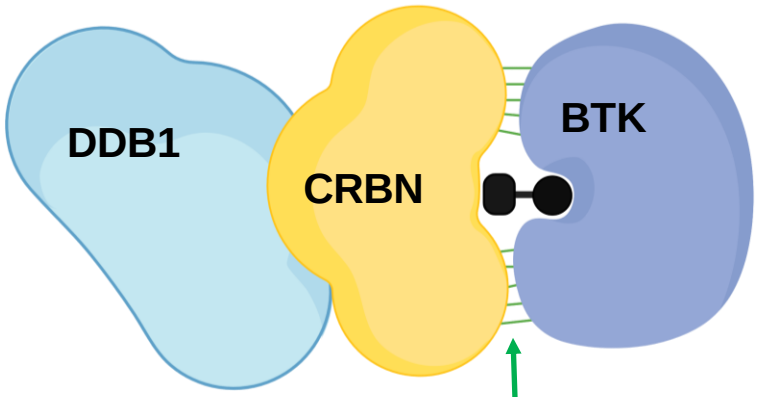
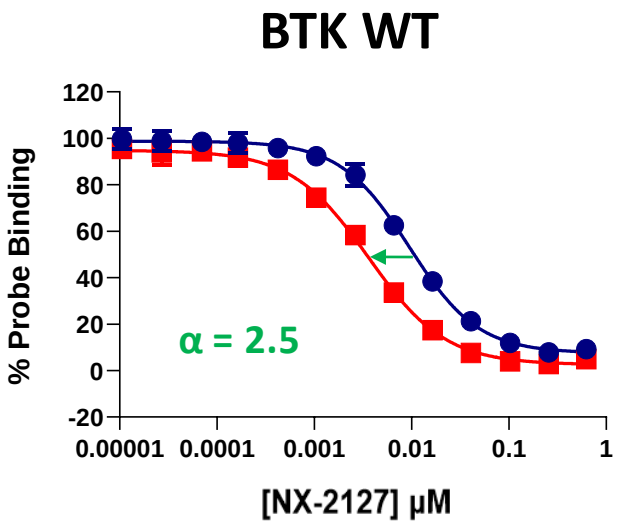
NX-2127 Induces Positive Cooperativity Between BTK and Cereblon



NX-2127

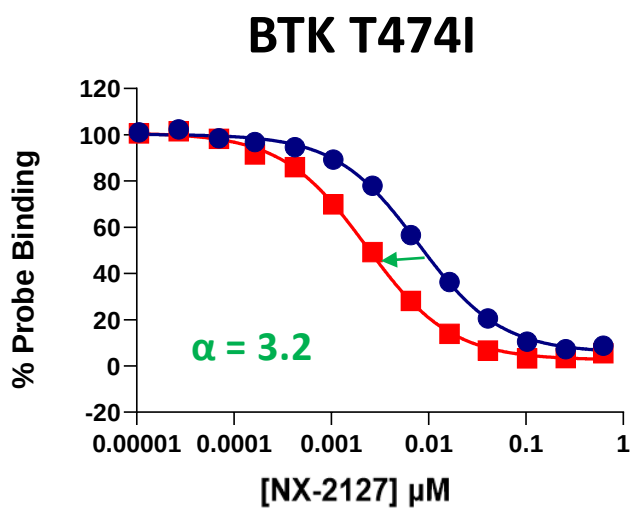
- Positive Cooperativity (α>1)
- Stable ternary complex
- Induced protein-protein interactions
- Greater tolerance for reduced binary affinity

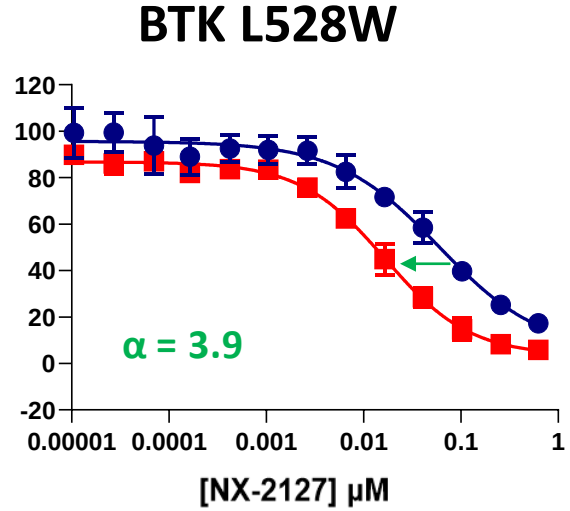


No CRBN

⊕ CRBN (1 µM)

$$\alpha = \frac{IC_{50}\ \text{No CRBN}}{IC_{50}\ \text{with CRBN (1 µM)}}$$





CRBN, cereblon; **DDB1**, DNA damage binding protein 1.

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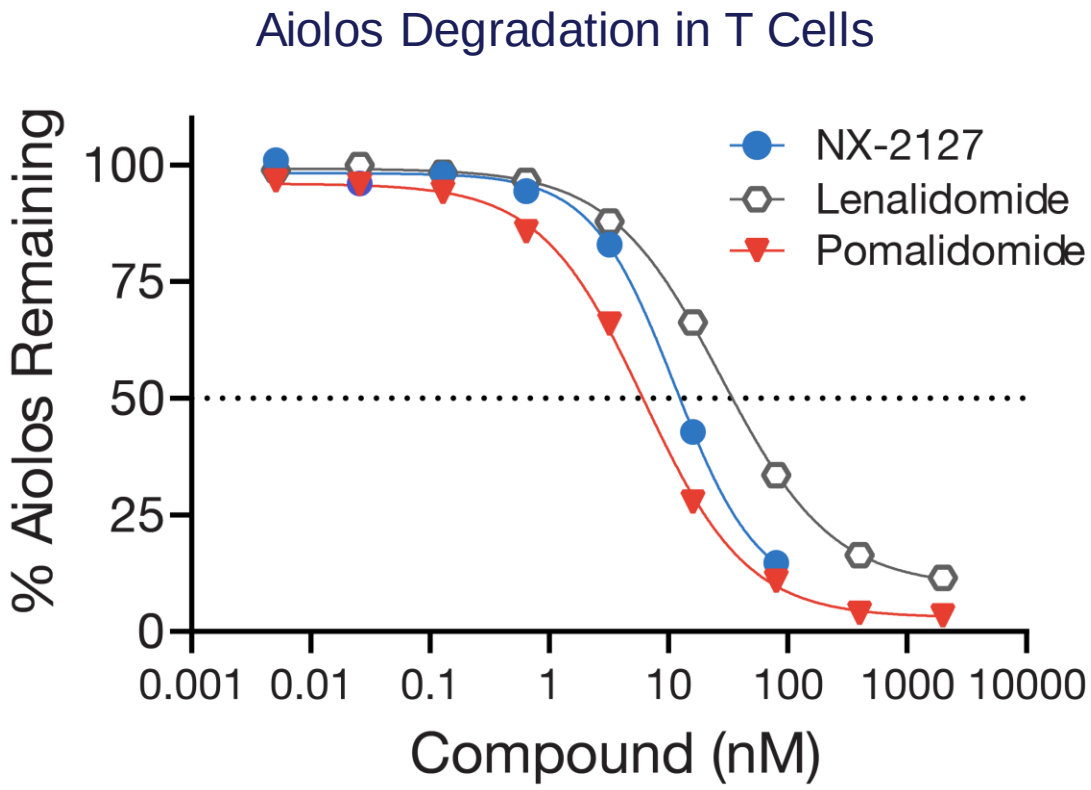
NX-2127 is a Dual Acting Agent That Also Degrades Immunomodulatory Cereblon Neosubstrate Aiolos

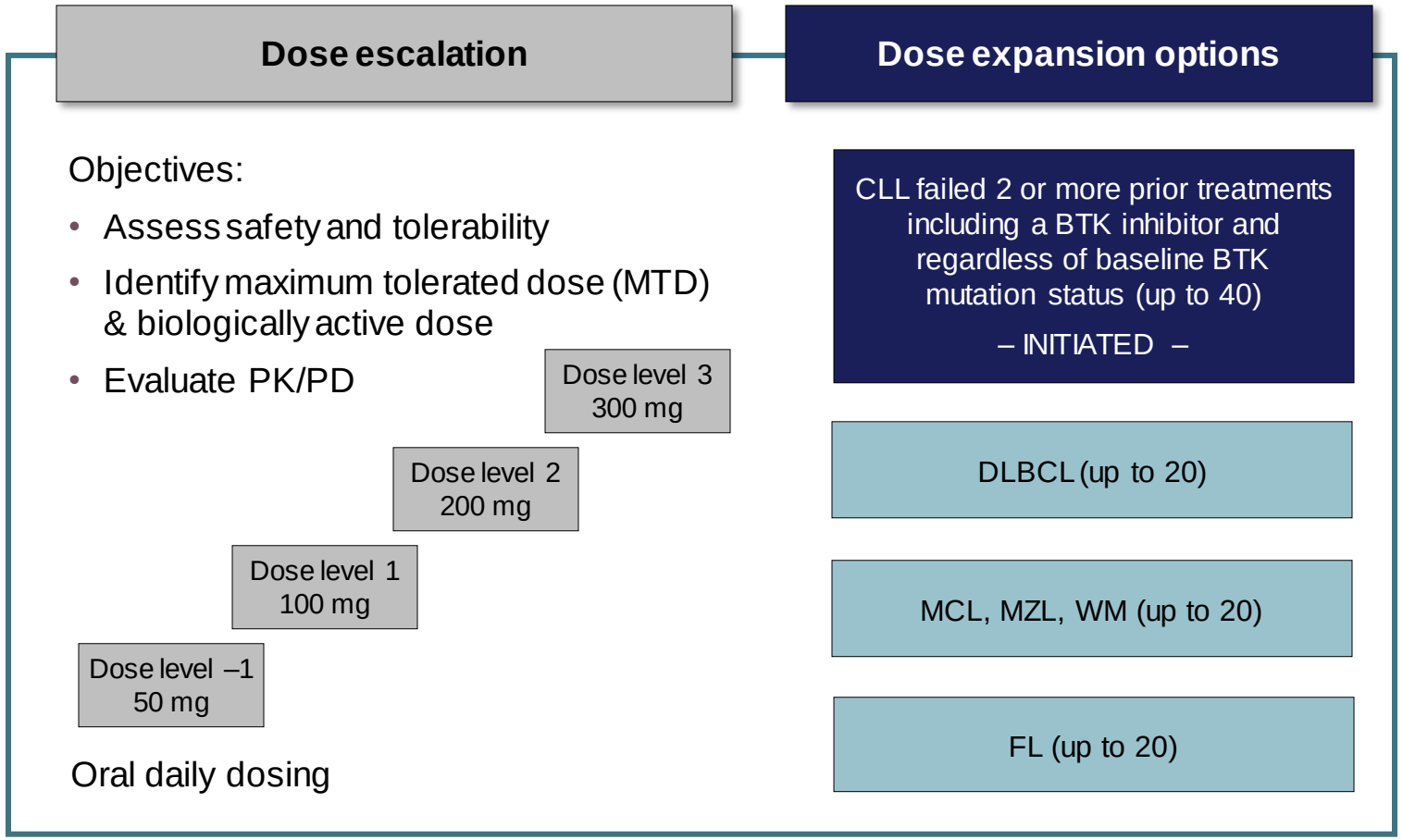


NX-2127 degradation of Aiolos in human T cells occurs at a similar potency to lenalidomide and pomalidomide

- Activity of NX-2127 is pegged to approved agents with well-established efficacy and safety
- Dual activity potentially addresses alternative resistance mechanism in CLL
- Emerging clinical data supports pathway combination approach in ABC-subtype DLBCL
- Dual mechanism shows strong benefit in MCL where both classes of agents are approved single agents

NX-2127-001: Trial Design

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



- CLL Phase 1b expansion cohort ongoing at 100 mg dose
  - MTD not established
  - 100 mg dose chosen as expansion dose based on PD, clinical activity and safety profile
- Phase 1a dose escalation is ongoing at 200 mg and 300 mg doses for patients with NHL (e.g., DLBCL, MCL, MZL, WM, FL)

BTK, Bruton tyrosine kinase; **CLL**, chronic lymphocytic leukemia; **DLBCL**, diffuse large B-cell lymphoma; **FL**, follicular lymphoma; **MCL**, mantle cell lymphoma; **MZL**, marginal zone lymphoma; **PD,** pharmacodynamics; **PK,** pharmacokinetics; **WM**, Waldenstrom's macroglobulinemia

Baseline Characteristics

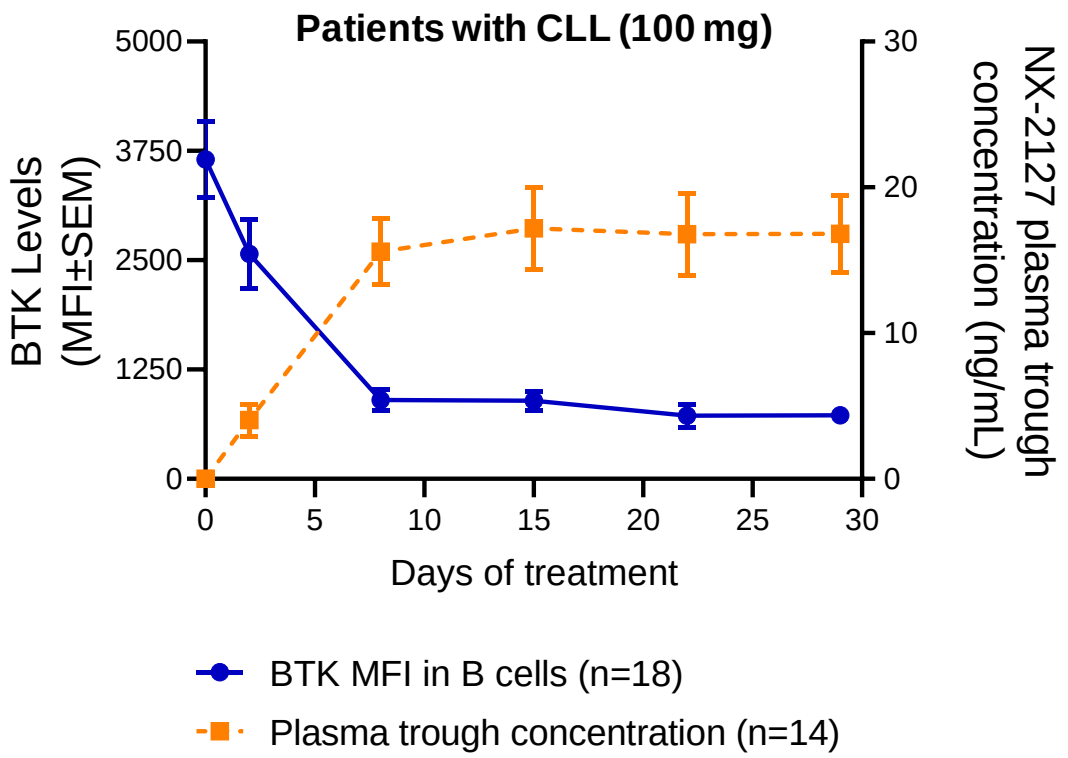
Elderly population with multiple prior lines of targeted therapies and acquired mutations

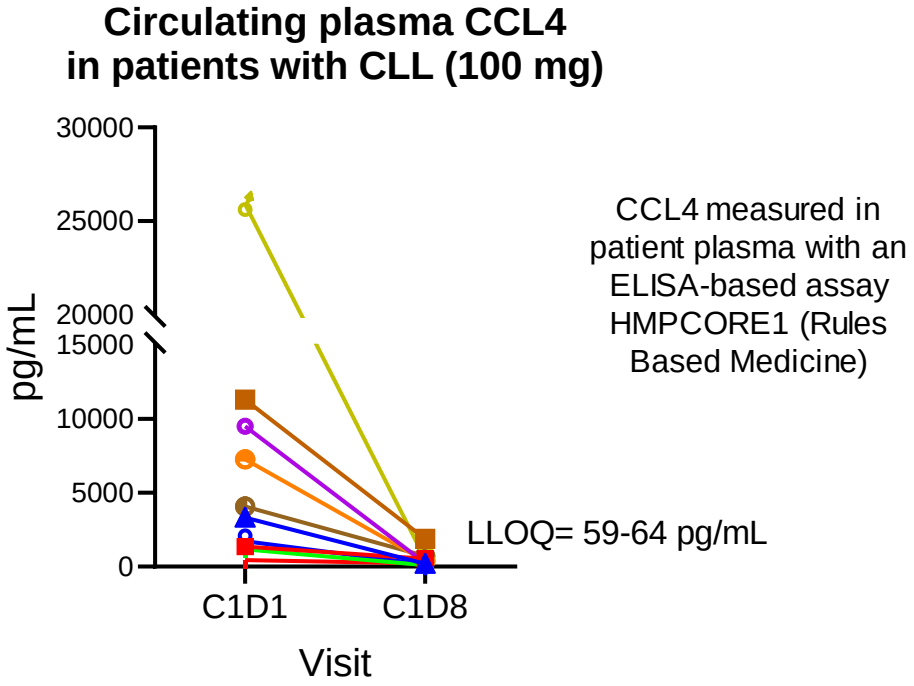
Characteristics	CLL (n=23)	Overall population (N=36)
Median age, years (range)	75 (61–90)	75 (50–92)
Female, n (%)	9 (39.1)	13 (36.1)
Male, n (%)	14 (60.9)	23 (63.9)
Lines of prior therapy, median (range)	5 (2–11)	4 (2–11)
BTKi, n (%)	23 (100)	31 (86.1)
Pirtobrutinib, n (%)	8 (34.8)	11 (30.6)
BTKi and BCL2i, n (%)	18 (78.3)	19 (52.8)
cBTKi, ncBTKi, and BCL2i, n (%)	7 (30.4)	7 (19.4)
***BTK* mutation present**[a], n (%)	10 (48)	11 (35)
C481	5 (24)	5 (16)
L528W	4 (19)	4 (13)
T474	3 (14)	4 (13)
V416L	1 (5)	1 (3)
***BCL2* mutation present**[a], n (%)	4 (19)	4 (13)
***PLCG2* mutation present**[a], n (%)	0 (0)	1 (3.2)

[a]Specific mutations are not additive as some patients have multiple *BTK* mutations
Mutations were tested by NGS centrally in those patients with available samples (n=31 in total population; n=21 in CLL population)

Data cutoff: September 21, 2022

NX-2127 Leads to Robust BTK Degradation and Decrease in B-cell Activation





- Daily treatment with NX-2127 resulted in a rapid and sustained suppression of BTK (CD19+) as measured in patient whole blood using a flow cytometry assay. BTK suppression target of 80% reached consistently (data not shown here)
- Robust decrease of plasma CCL4 by Cycle 1 Day 8 and suppression was maintained through Cycle 2 Day 1, consistent with clinically observed lymphocytosis occurring in majority of patients with nodal disease by Cycle 1 Day 8
- NX-2127 treatment also resulted in degradation of cereblon neo-substrate Ikaros

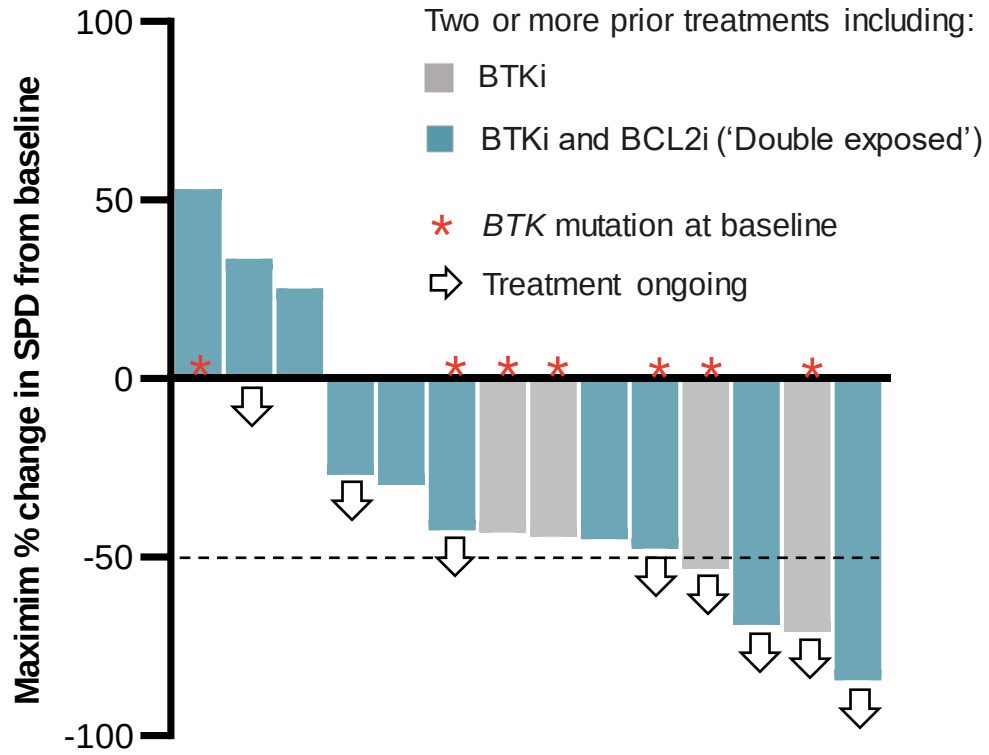
BTK, Bruton's tyrosine kinase; **CCL4**, C–C motif ligand 4; **LLOQ**, lower limit of quantification

Data cutoff: September 21, 2022

NX-2127 Preliminary Efficacy
Positive Initial Findings in CLL

Disease-evaluable patients	n=15
Objective response rate,[a] % (95% CI)	33 (12–62)
Best response, n (%)	
CR	0 (0)
PR	5 (33.3)
SD	5 (33.3)
PD	2 (13.3)
NE[b]	3 (20)

[a]Objective response rate includes CR + CRi + nPR + PR-L + PR
[b]Patients who discontinued after a single assessment of SD are considered as NE



***One patient, not shown above, with prior BTKi and BCL2i treatment and with a *BTK* mutation detected at baseline, had no nodal disease at baseline. Their treatment is ongoing with a PR**

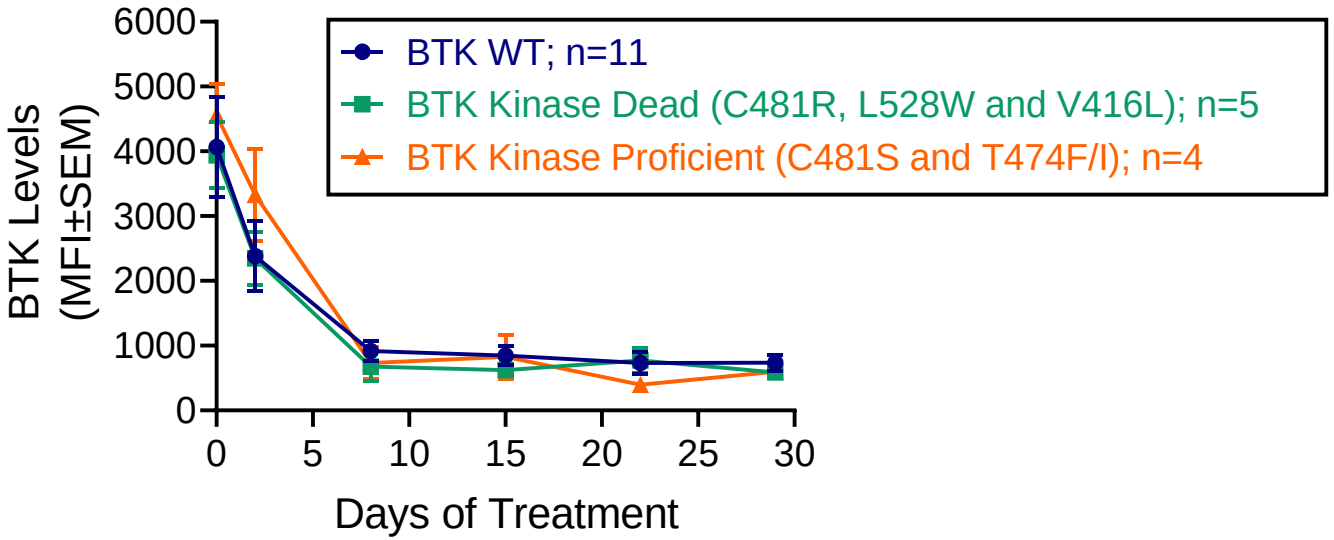
BCL2i, B-cell lymphoma-2 inhibitor; **BTK**, Bruton's tyrosine kinase; **BTKi**, BTK inhibitor; **CR**, complete response; **CRi**, complete response with incomplete count recovery; **NE**, not evaluable; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease

Data cutoff: September 21, 2022

First Demonstration of Clinical Activity of a Degrader Against a Range of BTK Mutations

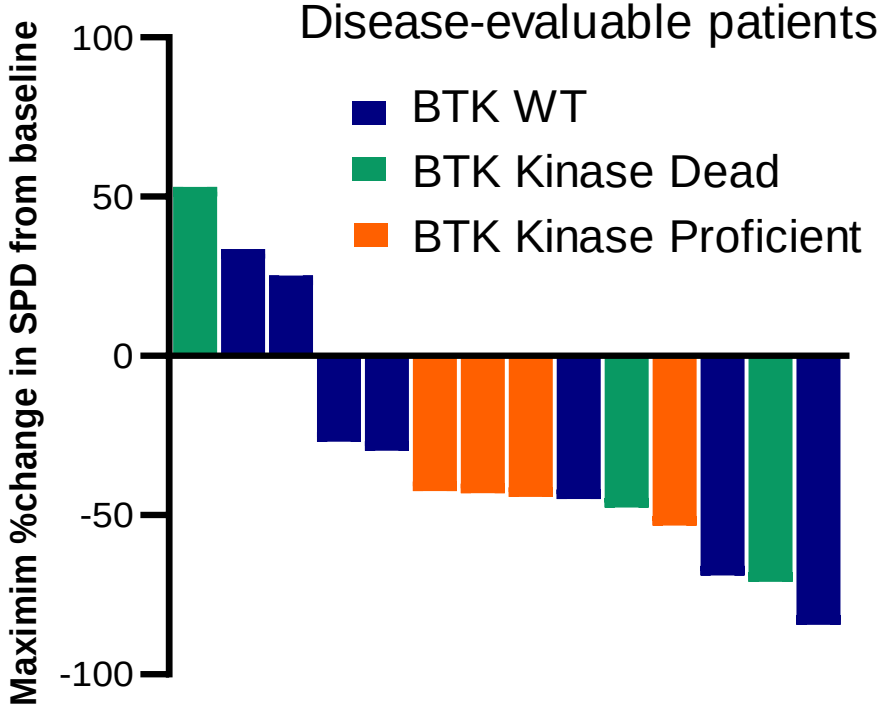
NX-2127 Preliminary Efficacy in Patients with CLL

BTK degradation in CLL patients with known BTK mutation status



Patients with kinase dead mutations are classified as kinase dead regardless of co-occurrence of kinase proficient mutations

Disease-evaluable patients



- BTK degradation of 80% achieved in CLL patients including those harboring BTK C481, T474, L528, and V416 resistance mutations

Two Heavily Pre-Treated Patients with Non-GCB DLBCL Enrolled in NX-2127 Phase 1 Dose-Escalation

	Patient #1	Patient #2
Subtype	Non-GCB (ABC subtype) Double-hit, BCL2/BCL6	Non-GCB (ABC subtype)
Dose	100 mg	300 mg
Time on Study	3.5 months	5 months and ongoing
Priors	4	4
Response(s)	Stable Disease (SD) at 8w → Progressive Disease (PD)	Complete Response (CR)* at 8w confirmed at 16w

Patient #2	Baseline demographic and disease characteristics
Age; Relevant medical history	84; aortic regurgitation, diastolic dysfunction, aspergillosis sinus infection
Cancer Diagnosis	1988: Waldenstrom's macroglobulinemia (WM) 2015: Diffuse large B-cell lymphoma (DLBCL) ABC subtype
Prior treatments for DLBCL	2015: Rituximab + CHOP followed by focal axillary irradiation 2017: Rituximab + ICE 2018: Rituximab, mogamulizumab (anti-CCR4), and magrolimab (anti-CD47) 2019: Rituximab, ibrutinib, and lenalidomide (RIL)
Disease features at study entry	Stage IV, MYD88 mutated and CXCR4 mutated
Time on study	Ongoing, Cycle #6 (5 months)

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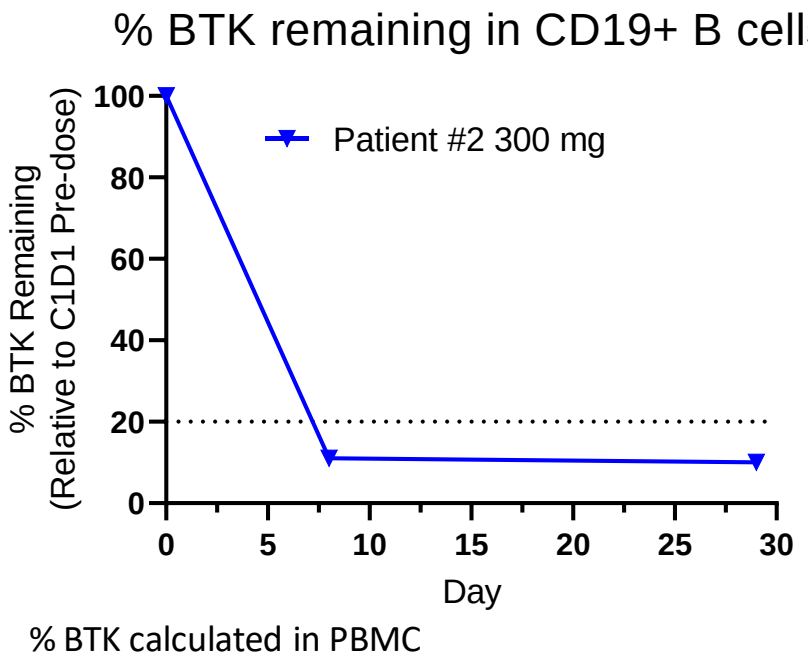
Data as reported October 26, 2022

*CR per Lugano criteria

Rapid BTK Degradation and Confirmed Complete Response Following NX-2127 Therapy

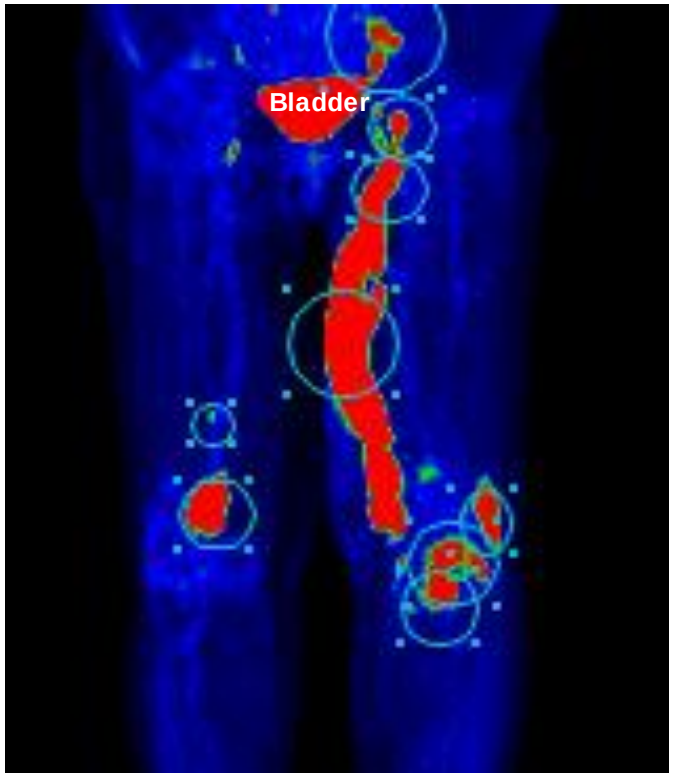


% BTK calculated in PBMC

Significant Ikaros and Aiolos degradation also confirmed by day 8

FDG-PET CT Scan Disease Assessment

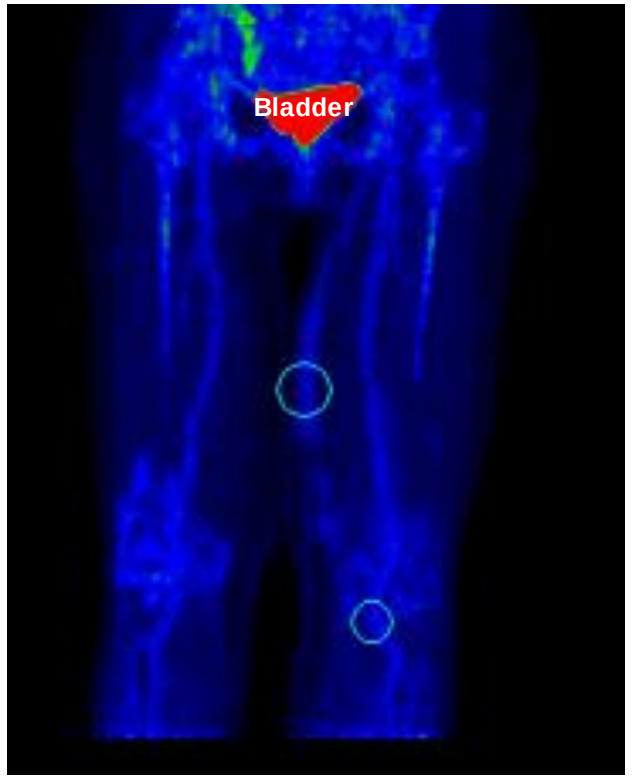
Baseline



Max SUV: 17.6
Deauville 5PS: 5

SUV: Standard Uptake Value

Week 16



Max SUV: 2.5
Deauville 5PS: 2

Normal SUV

- Complete response at first assessment (Week 8) and confirmed at subsequent assessment (Week 16)
- Safety: No DLT or SAE. Grade 3 neutropenia without infection, resolved with G-CSF. No Rx interruptions.

Data as reported October 26, 2022

NX-2127: First-in-Class BTK Degrader Demonstrates Early Signs of Meaningful Clinical Activity in Both CLL and NHL

Chronic lymphocytic leukemia (CLL)

- Objective responses observed in CLL patients who failed a median of 6 prior lines of therapy including patients who failed BTK inhibitors and BCL2 inhibitors
- Objective responses observed in patients whose tumors harbor BTK mutations known to cause resistance to both covalent and non-covalent BTK inhibitors

Next steps: Enrollment in Phase 1b is ongoing with clinical update planned for H2 2023

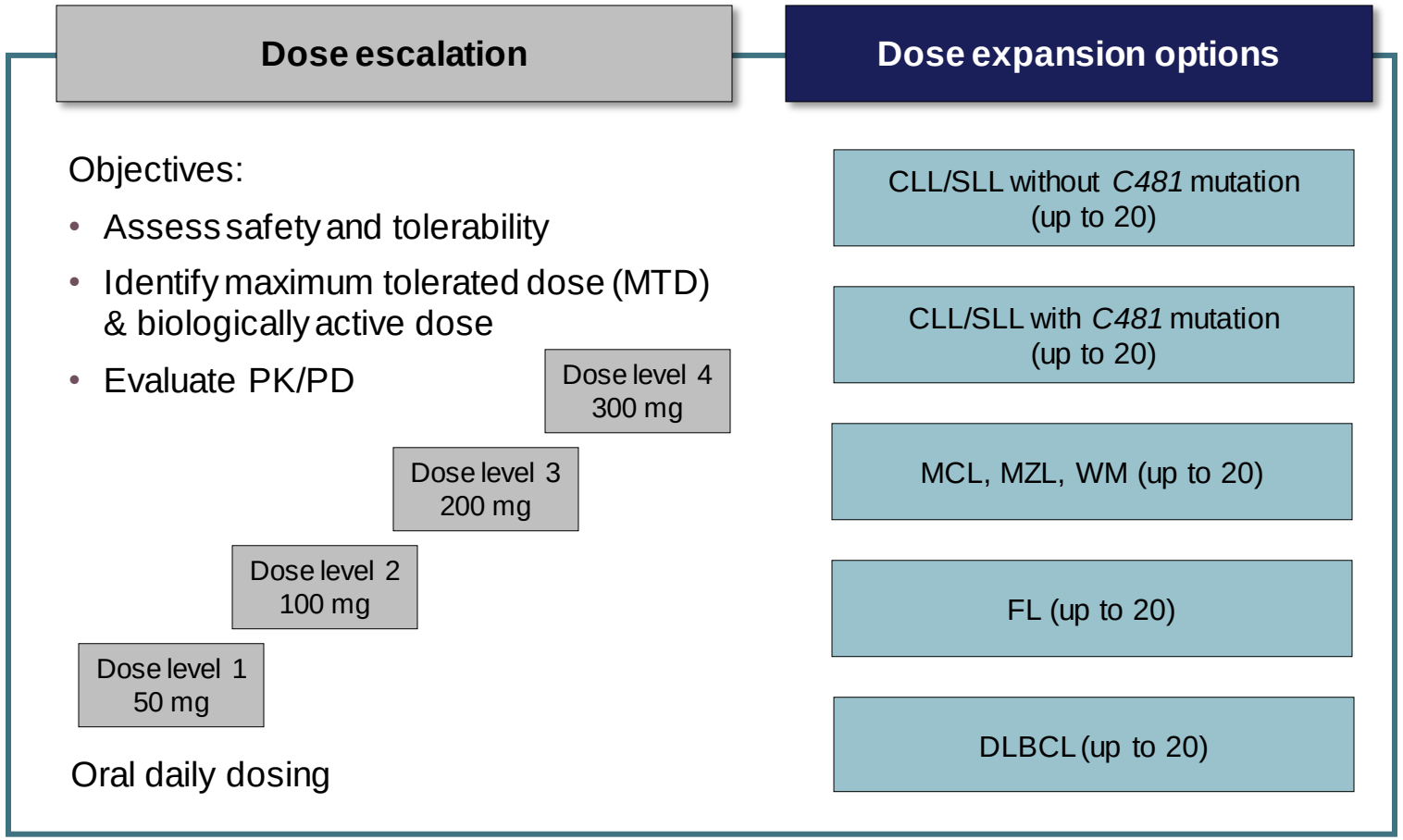
Non-Hodgkin lymphoma (NHL)

- Rapid and complete response in a patient with advanced relapsed/refractory non-GCB DLBCL following four prior lines of therapy

Next steps: Enrollment in Phase 1a is ongoing at the 200 mg and 300 mg doses in patients with NHL with clinical update planned for H2 2023.

NX-5948-301: Trial Design

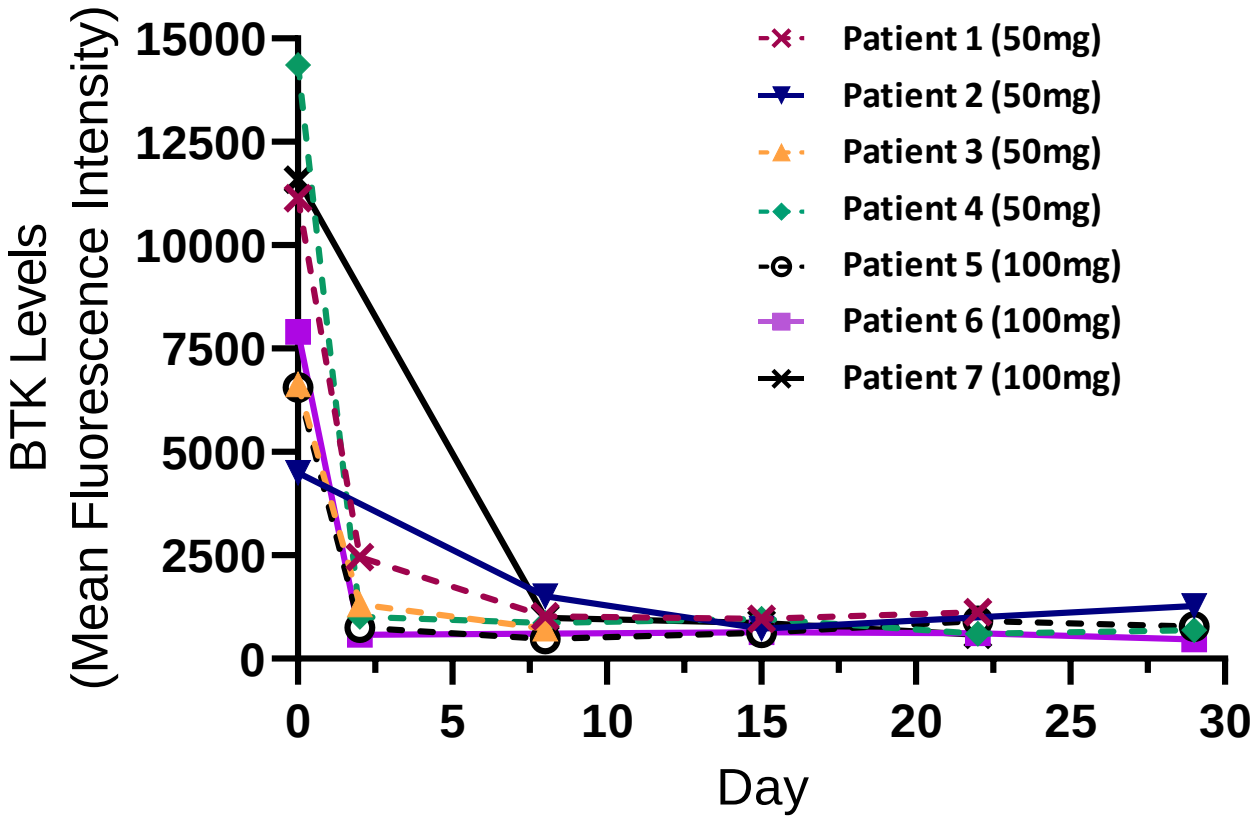
Phase 1 trial in adults with relapsed/refractory B-cell malignancies



- Phase 1a dose escalation is ongoing at clinical sites in the U.K.
- Plans to initiate U.S. sites in early 2023

CLL, chronic lymphocytic leukemia; **DLBCL**, diffuse large B-cell lymphoma; **FL**, follicular lymphoma; **MCL**, mantle cell lymphoma; **MZL**, marginal zone lymphoma; **PD,** pharmacodynamics; **PK,** pharmacokinetics; **WM**, Waldenstrom's macroglobulinemia

First Report of BTK Degradation with NX-5948 in Patients with B Cell Malignancies



BTK levels are evaluated in real time in a FACS-based assay on whole blood from patients treated with NX-2127

Initial proof of mechanism

- Rapid and sustained degradation of BTK
- Robust BTK degradation observed in all patients tested to date
- Dose escalation ongoing in patients with relapsed/refractory B cell malignancies

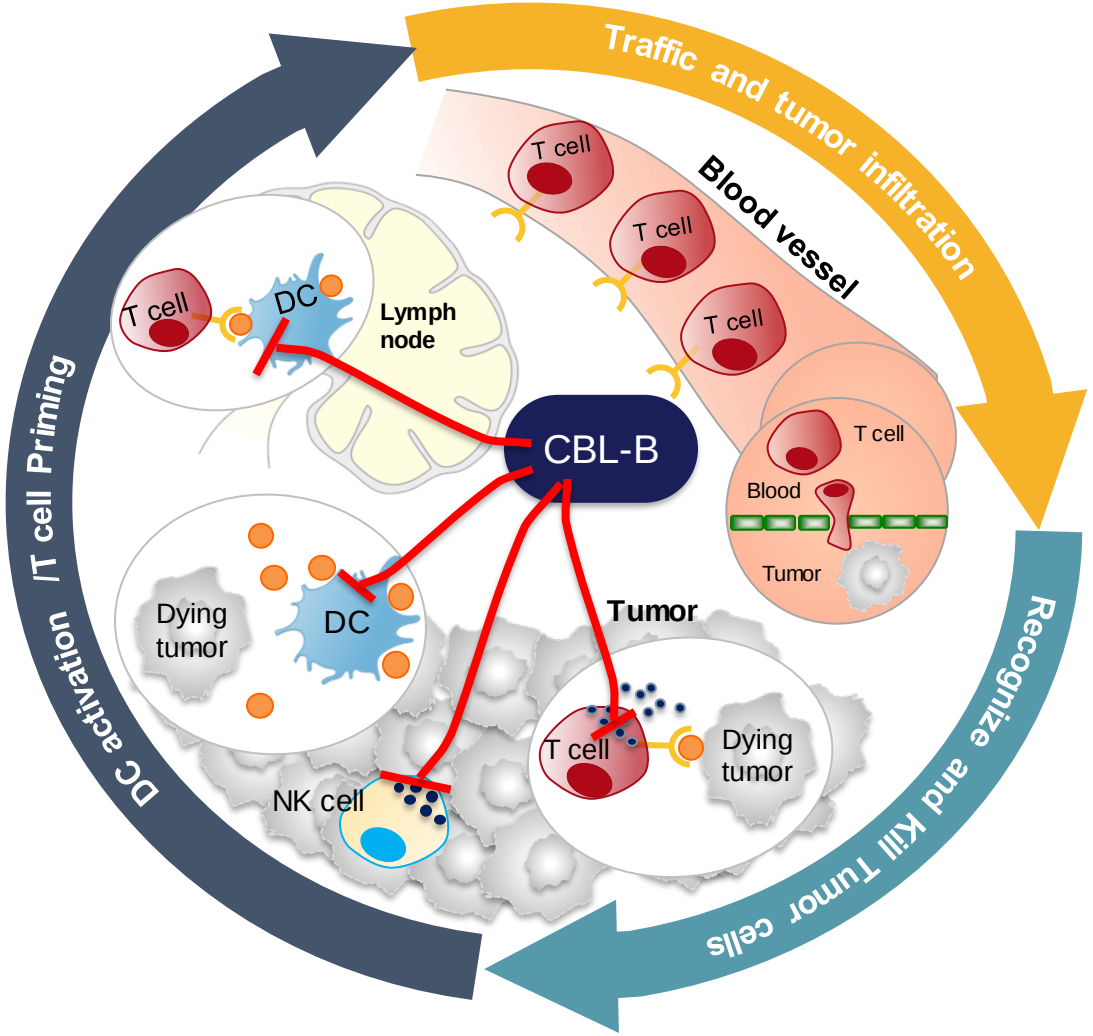
Targeting CBL-B Enhances Antitumor Response

A Master Orchestrator of the Immune System

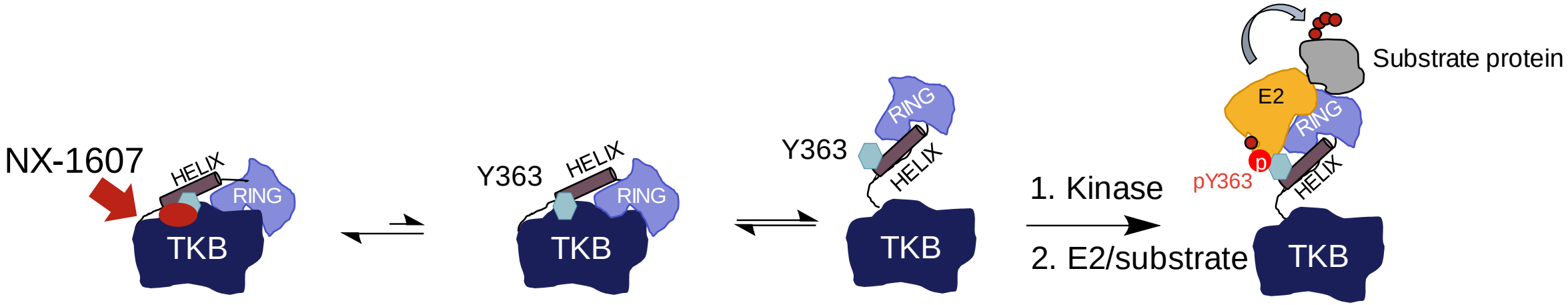
CBL-B mediated mechanisms strongly restrains a productive anti-tumor response

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



NX-1607 acts as an intramolecular glue forcing CBL-B in its folded **INACTIVE** state

Closed State **INACTIVE**

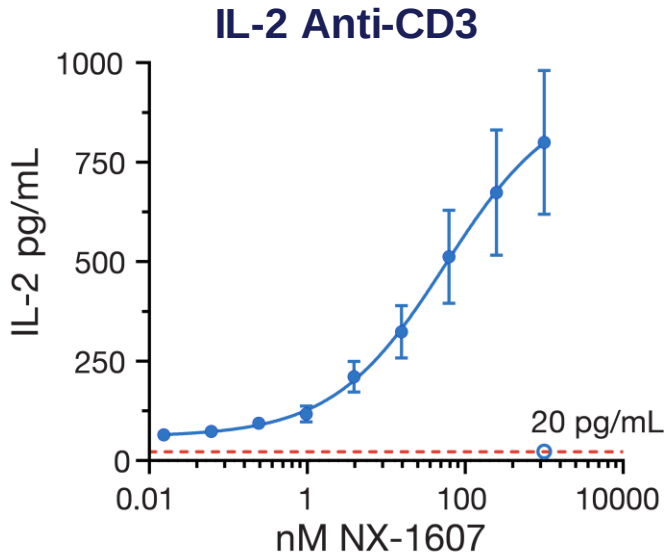
Opened State

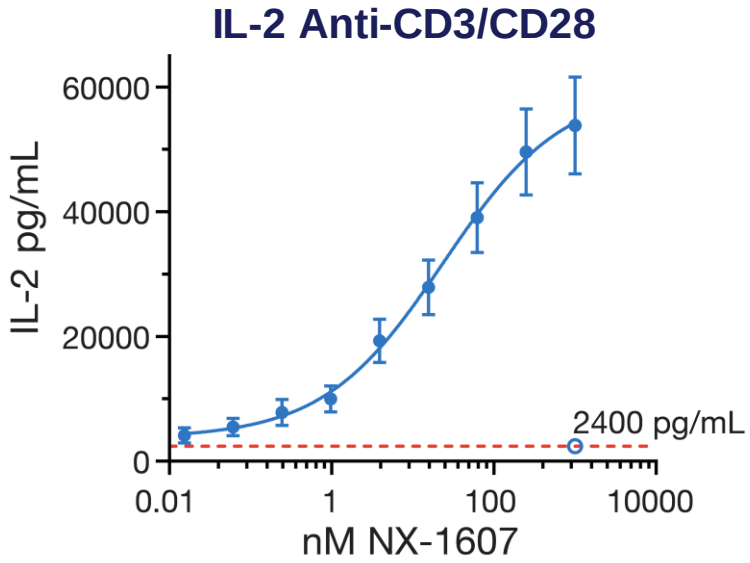
Phosphorylation locks CBL-B in the **ACTIVE** Conformation

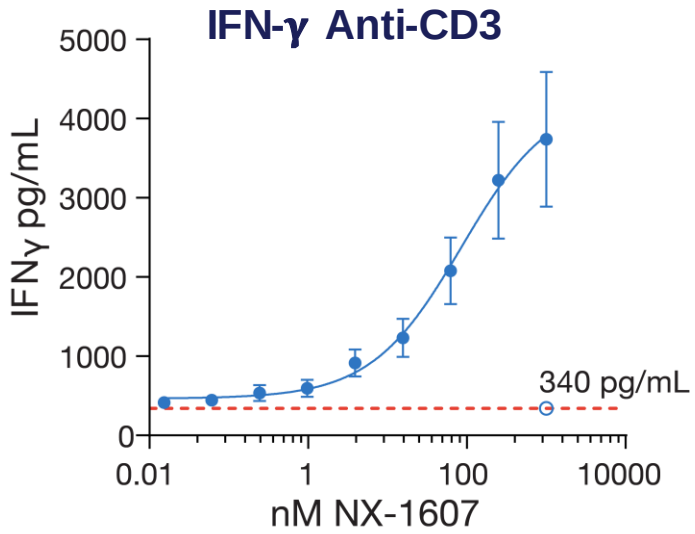
Immune Response

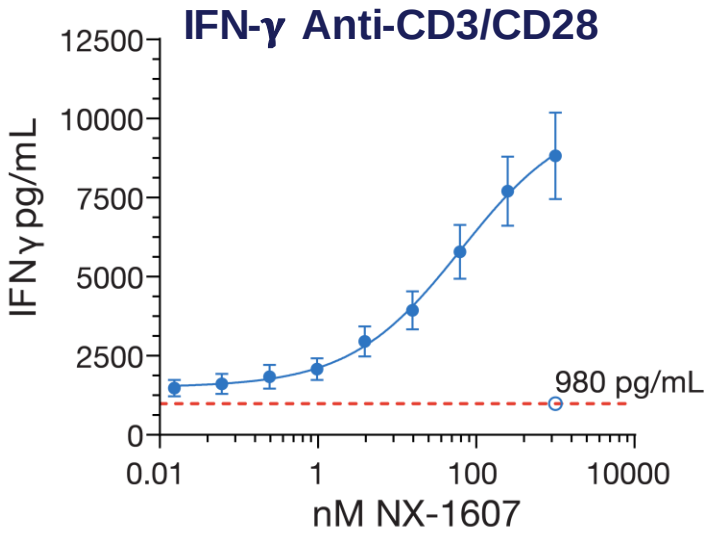
Immune Response

NX-1607 Increases IL-2 and IFN-γ Secretion in TCR Stimulated Primary Human T cells









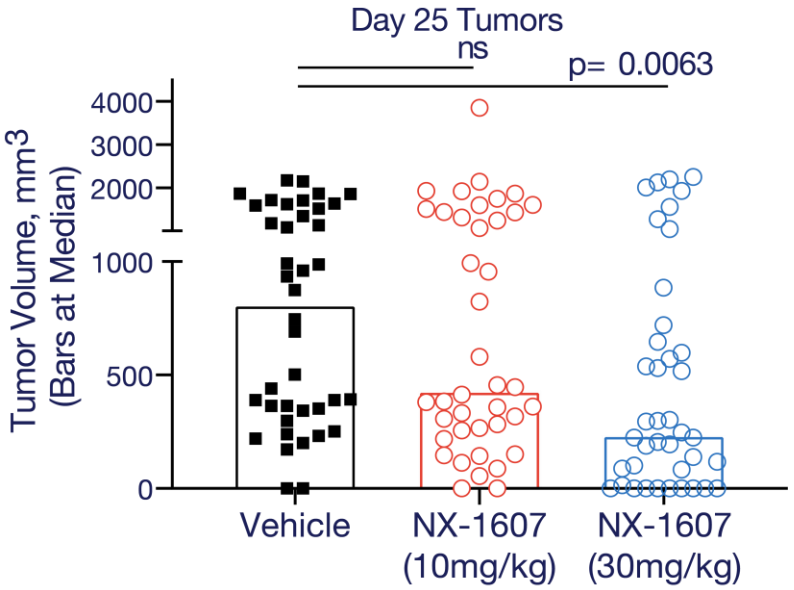
NX-1607 increases TCR stimulation-dependent production of IL-2 and IFN-γ in primary human T cells

NX-1607 has no impact in the absence of T cell stimulation as measured by proliferation, activation, or cytokine release

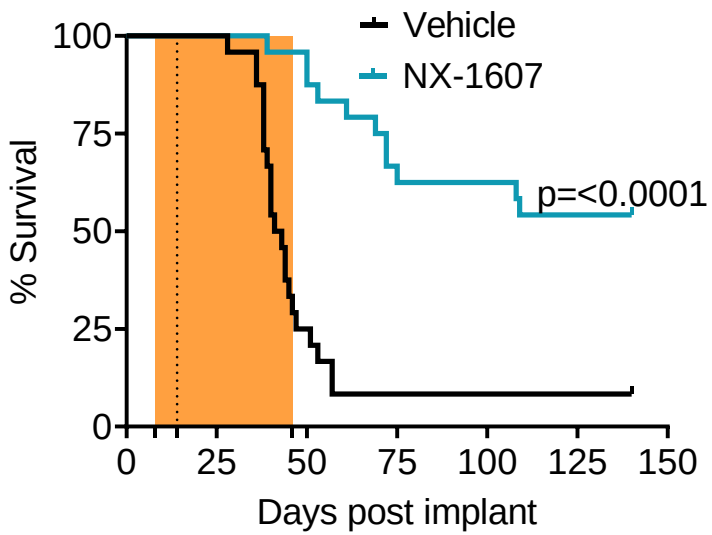
Cytokine Response
Baseline Response

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

NX-1607
Reduced Tumor Volume
Colorectal

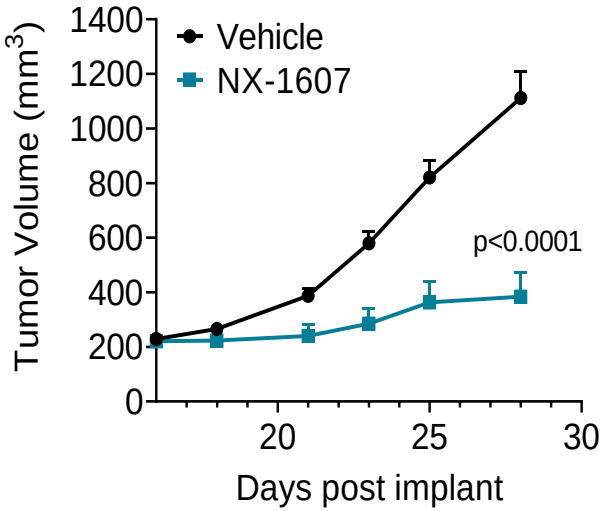


NX-1607
Prolonged Survival
Triple-Negative Breast



NX-1607 30 mg/kg day 7 to 46

NX-1607
Reduced Tumor Volume
B Cell Lymphoma

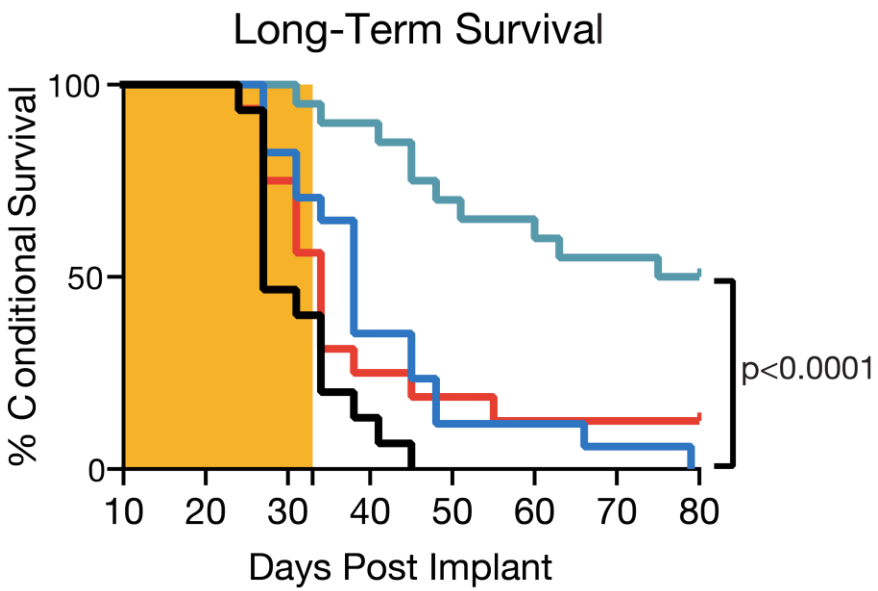


NX-1607 30 mg/kg day 16 to 28

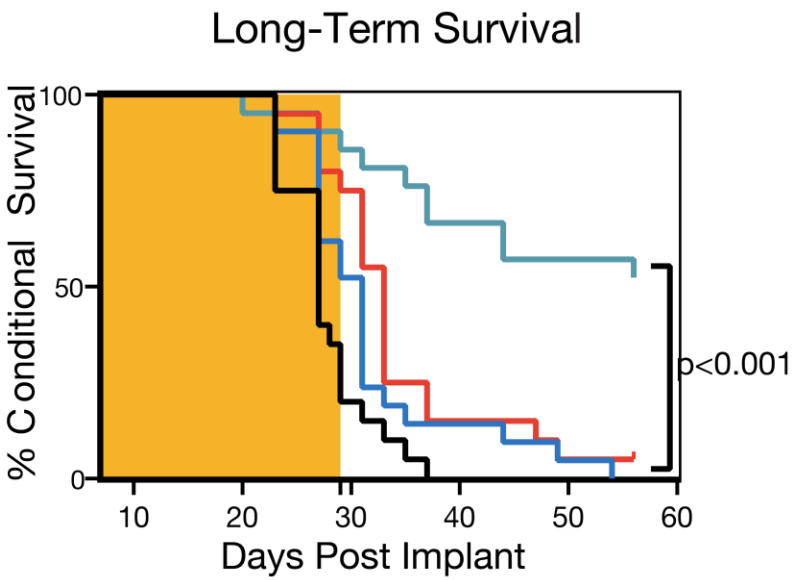
Shaded area indicates dosing period

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

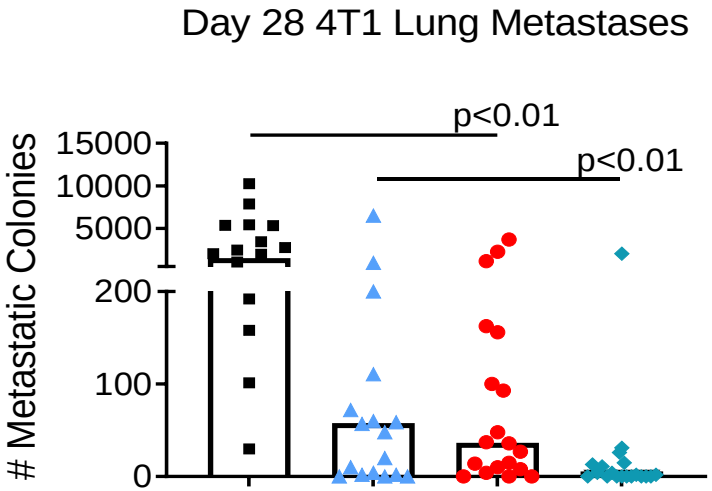
Colorectal (CT26)



Colorectal (MC38)



Triple-Negative Breast (4T1)

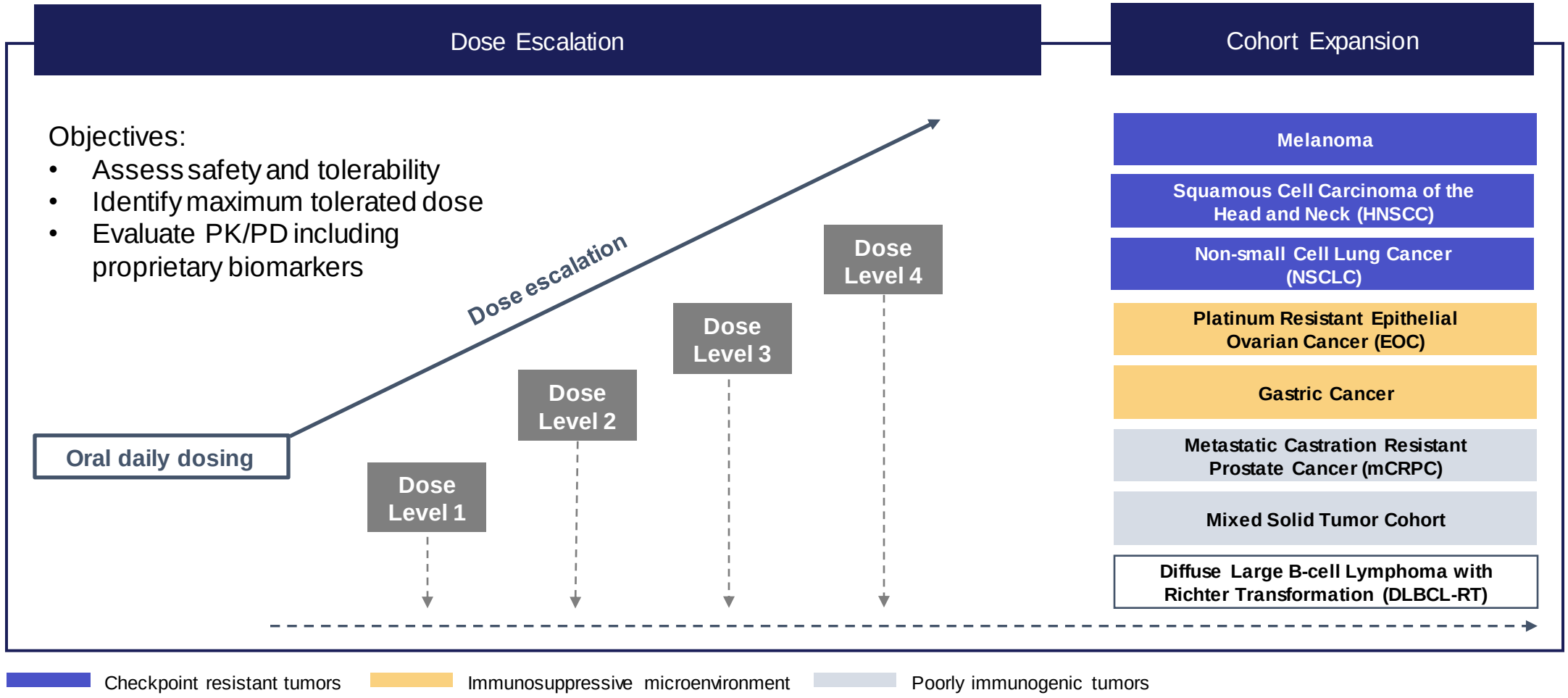


Vehicle NX-1607 anti-PD-1 NX-1607+anti-PD-1

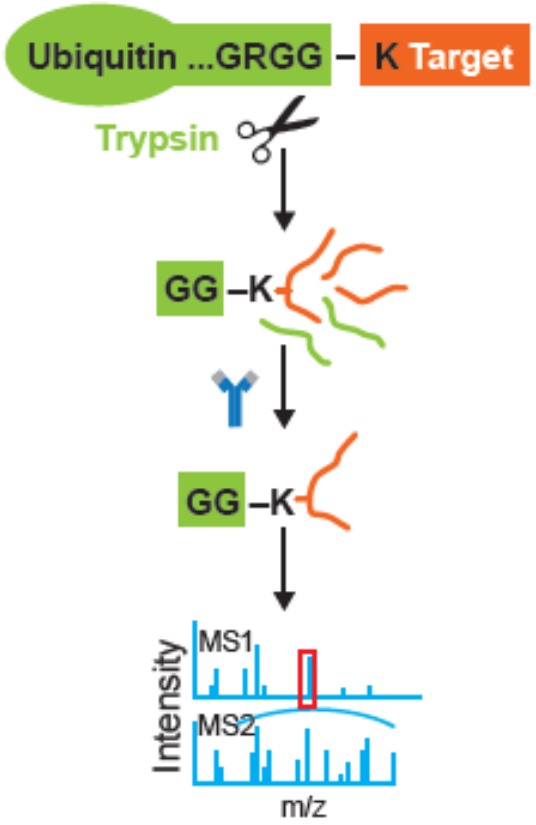
Shaded area indicates dosing period: NX-1607 (30 mg/kg, PO daily) and anti-PD-1 twice a week at 10 mg/kg dosing period

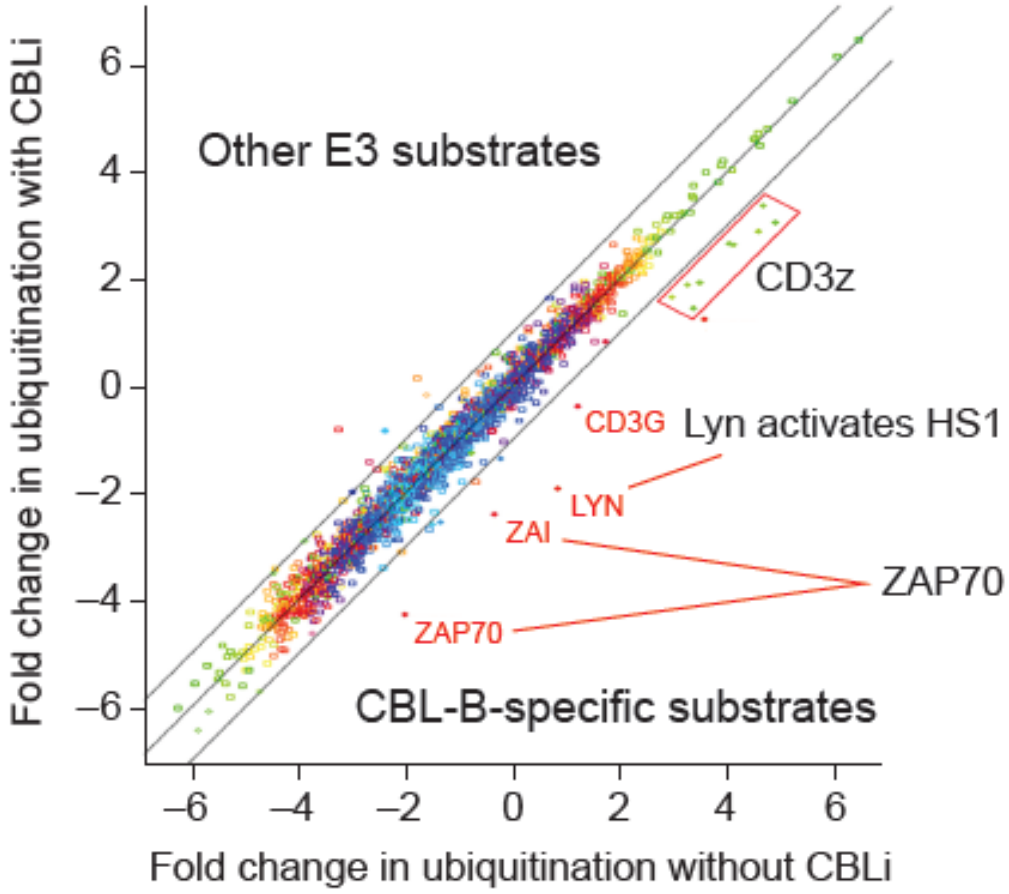
NX-1607-101: Phase 1 first-in-human clinical trial design

Two-Part Phase 1 Monotherapy Trial of NX-1607 in Relapsed or Refractory Tumors



UbiScan Identified Direct CBL Substrates Within the T Cell Receptor (TCR) Signaling Cascade

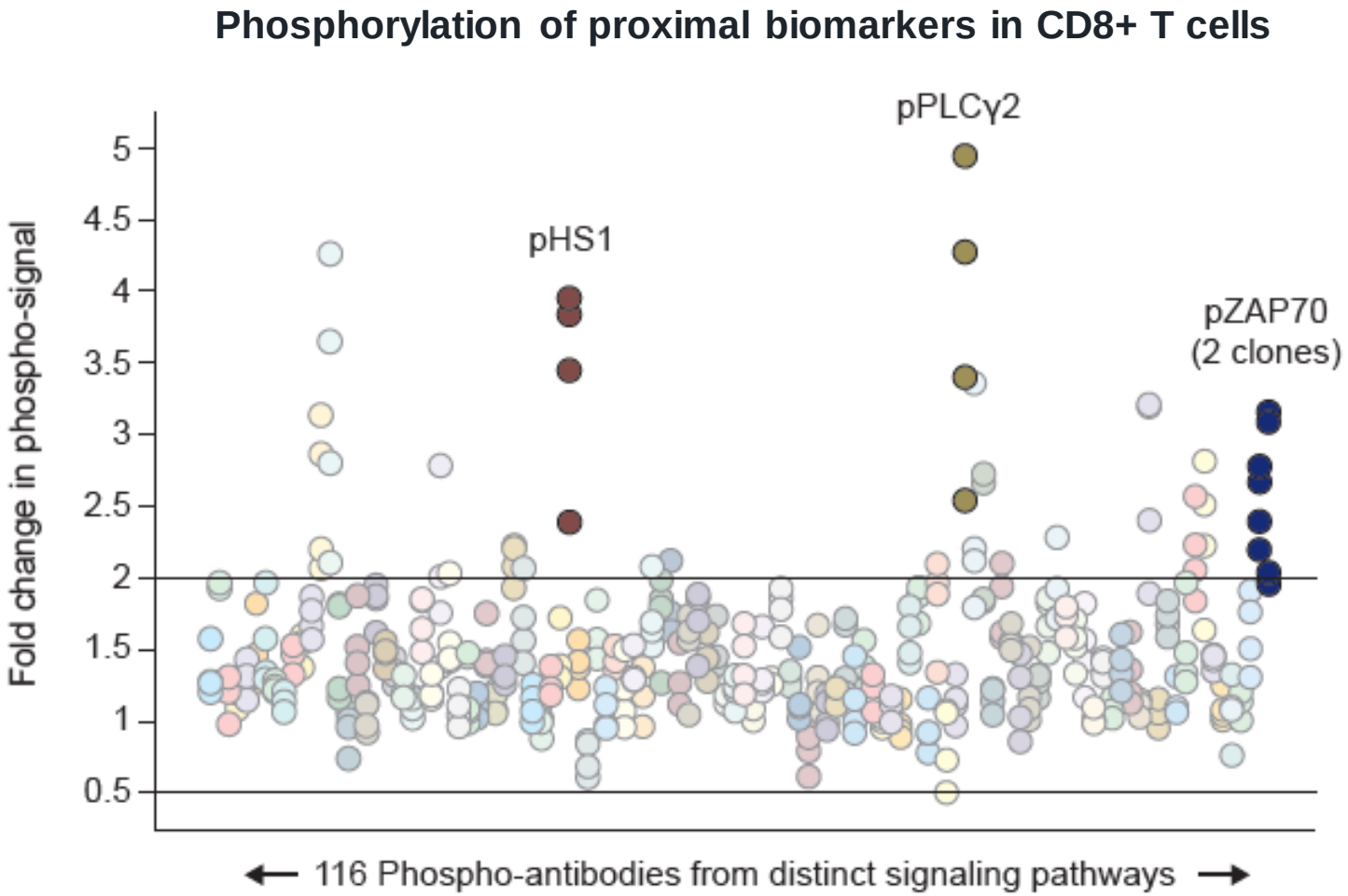




Decreased signal represents direct substrates ubiquitinated by CBL-B ligase activity

Inhibiting CBL-B decreases ubiquitination of important T Cell receptor signaling molecules

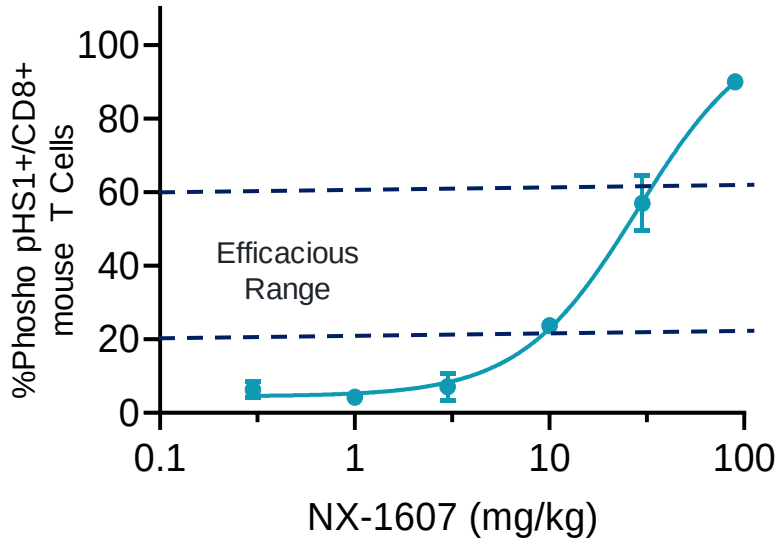
Phospho-Protein Flow Cytometry Assay Identified Proximal Biomarkers



- Stimulated human PBMCs with or without CBL-B inhibition
- Cells were stained with a panel of phospho-specific antibodies for proteins downstream the TCR signaling
- Expression levels were assessed by flow cytometry
- Overlapping results from orthogonal assays (Ubiscan) provided confidence in proximal biomarker signals

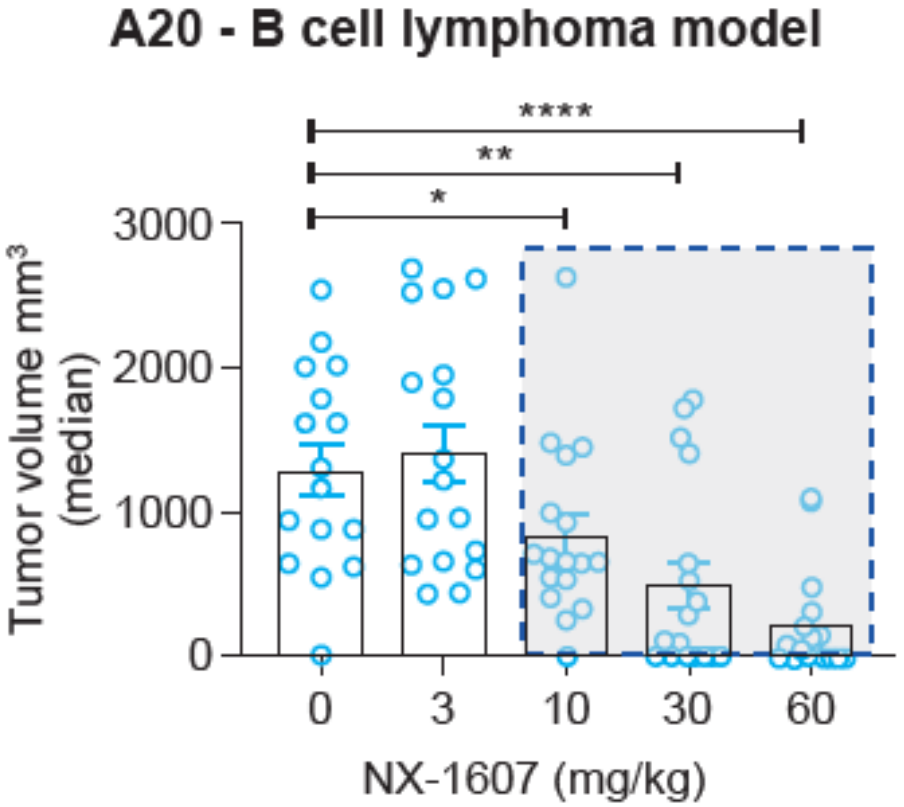
Dose Dependent Increases of CBL-B Proximal Biomarker Correlates with Antitumor Effects of NX-1607

Pharmacodynamic relationship in mice following NX-1607 dosing



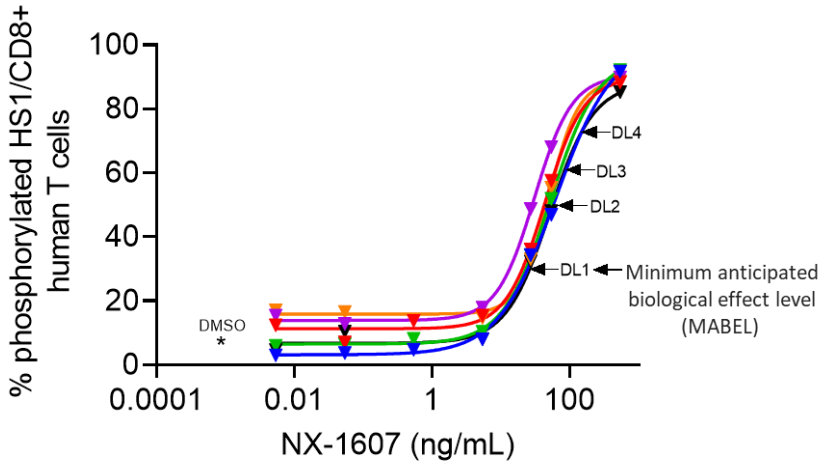
In vivo efficacy observed between 10-60 mpk which corresponds to ~20-60% pHS1+ CD8+ T Cells

NX-1607 reduced tumor volume



Characterization of a Novel Biomarker and First Evidence of Target Engagement for a CBL-B Inhibitor in the Clinic

Human whole blood and dose projection modeling

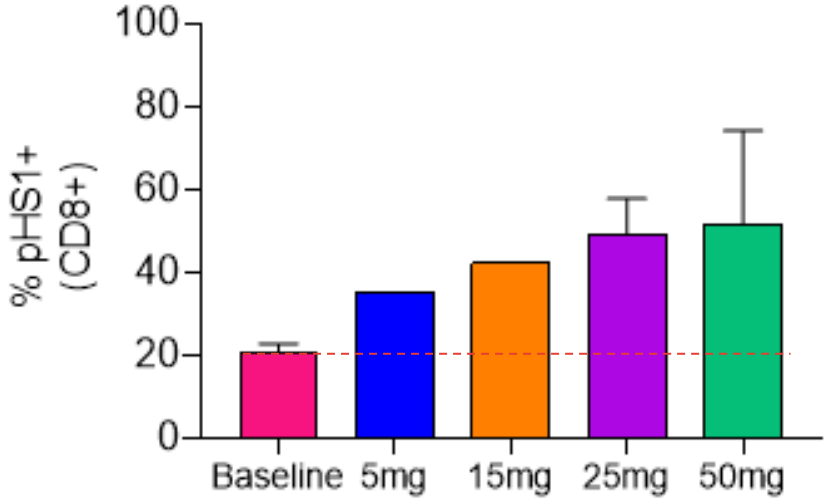


Proposed dose level[a]	NX-1607 dose (mg)	Estimated % HS1+/CD8+ T cells
-1	2.5	22.2
1[b]	5	30.0
2	15	49.7
3	25	60.6
4	50	74.0

[a]Dose levels in NX-1607-101.
[b]Minimum anticipated biological effect level (MABEL).

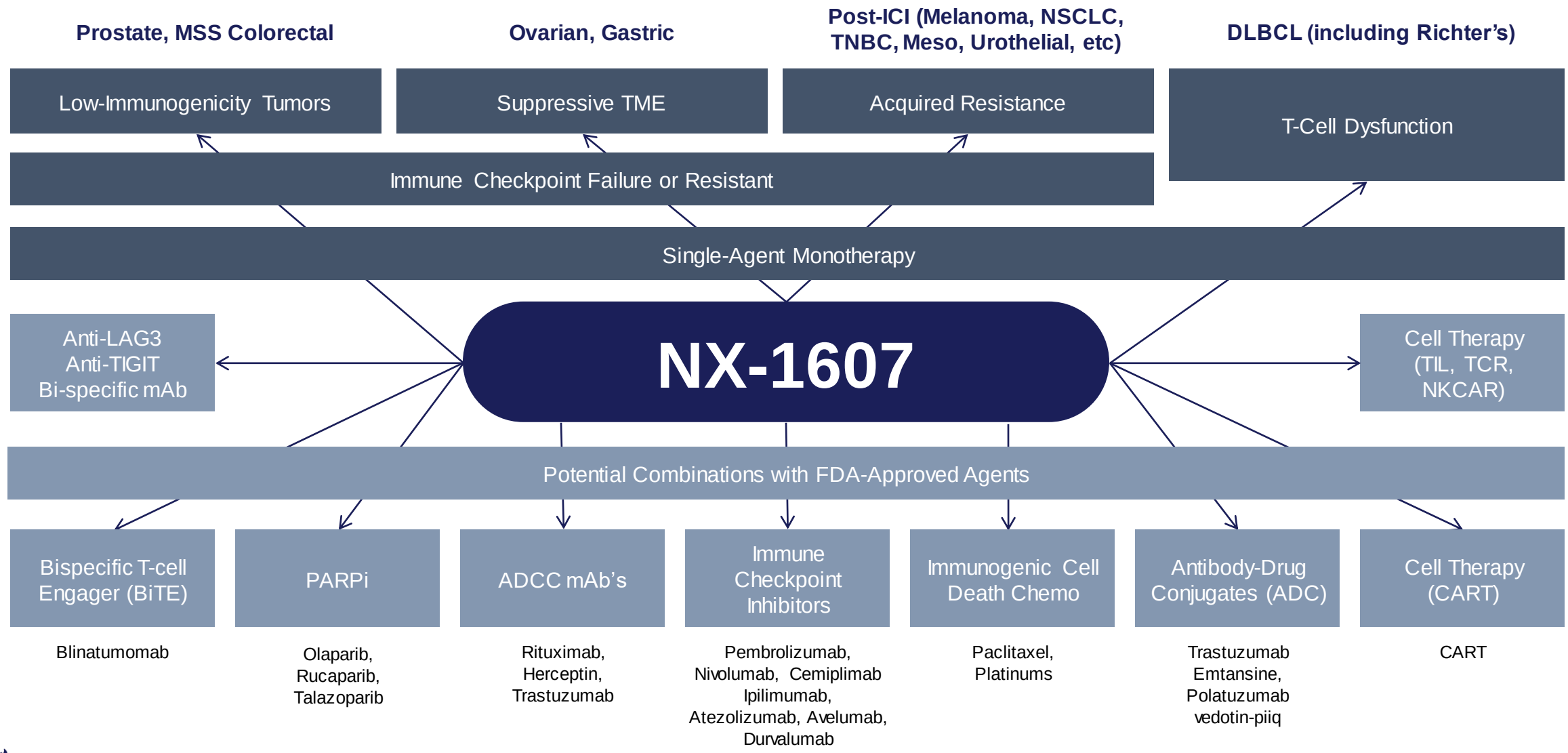
Clinical data

Maximal % pHS1+ expressing CD8+ T cells observed in C1D1



	Dose level 1 5mg	Dose level 2 15mg	Dose level 3 25mg	Dose level 4 50mg
Cycle 1, N:	1	1	6	2

CBL-B Inhibition Has the Potential To Be the Small Molecule Centerpiece of Immuno-Oncology Therapy



Defining Success in 2023

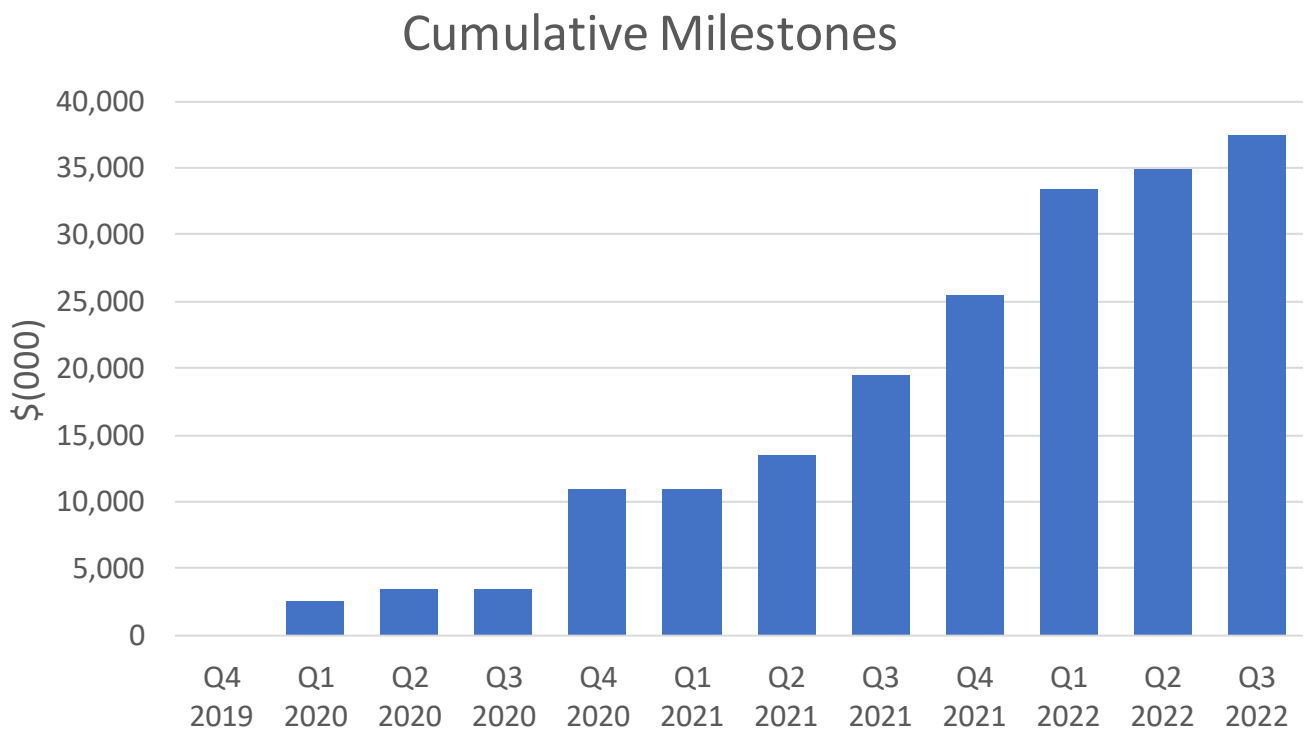
B-cell malignancies		Immune oncology	Platform & pipeline
NX-2127	**NX-5948**	**NX-1607**	**Research pipeline**
• Present updated Phase 1 clinical data in H2 2023 • Define regulatory strategy based on FDA feedback in H2 2023	• Present initial clinical data from Phase 1a in H2 2023 • Define Phase 1b dose for cohort expansion in H2 2023	• Present initial clinical data from Phase 1a in H2 2023 • Define Phase 1b dose for cohort expansion in H2 2023	• Select new targeted protein degrader development candidate • Achieve substantial research collaboration milestones throughout 2023

Note: All anticipated timing is based on calendar-year periods

Strong Financial Position

$414M in cash and investments as of August 31, 2022

- Funded through key readouts for all clinical programs
- Cash runway into Q4 2024 excluding any future potential milestones from collaborations



R&D collaboration details:

- Gilead $45M upfront and up to $2.3B in development, regulatory and sales milestones plus royalties
- Sanofi $77M upfront and expansion payments and up to $2.5B in development, regulatory and sales milestones plus royalties
- Nurix option for 50/50 U.S. co-development for two drug candidates per partner

Thank you

nurix