Leader in Targeted Protein Modulation

Nurix Therapeutics

Blazing a New Path in Medicine

J.P. Morgan Healthcare Conference Presentation

January 2023

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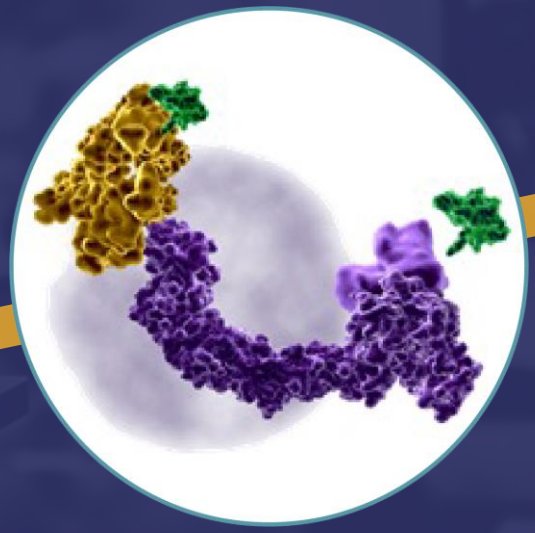
Nurix Drugs Engage Ligases for the Treatment of Cancer

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

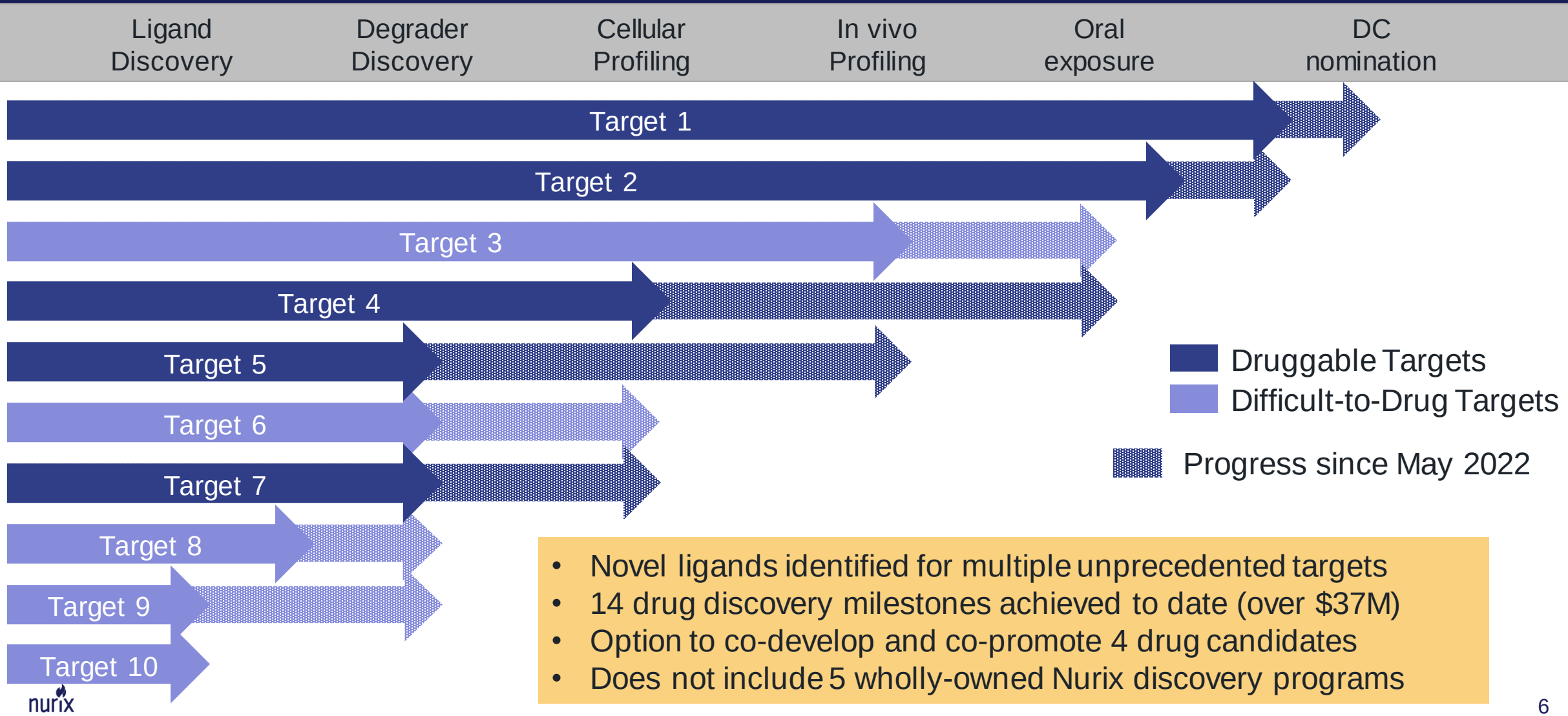
- First evidence of clinical benefit for patients with advanced B cell malignancies treated with a targeted protein degrader
- Target degradation can overcome treatment-emergent inhibitor resistance mutations
- First evidence that degraders uniquely address non-catalytic functions of proteins (e.g.,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

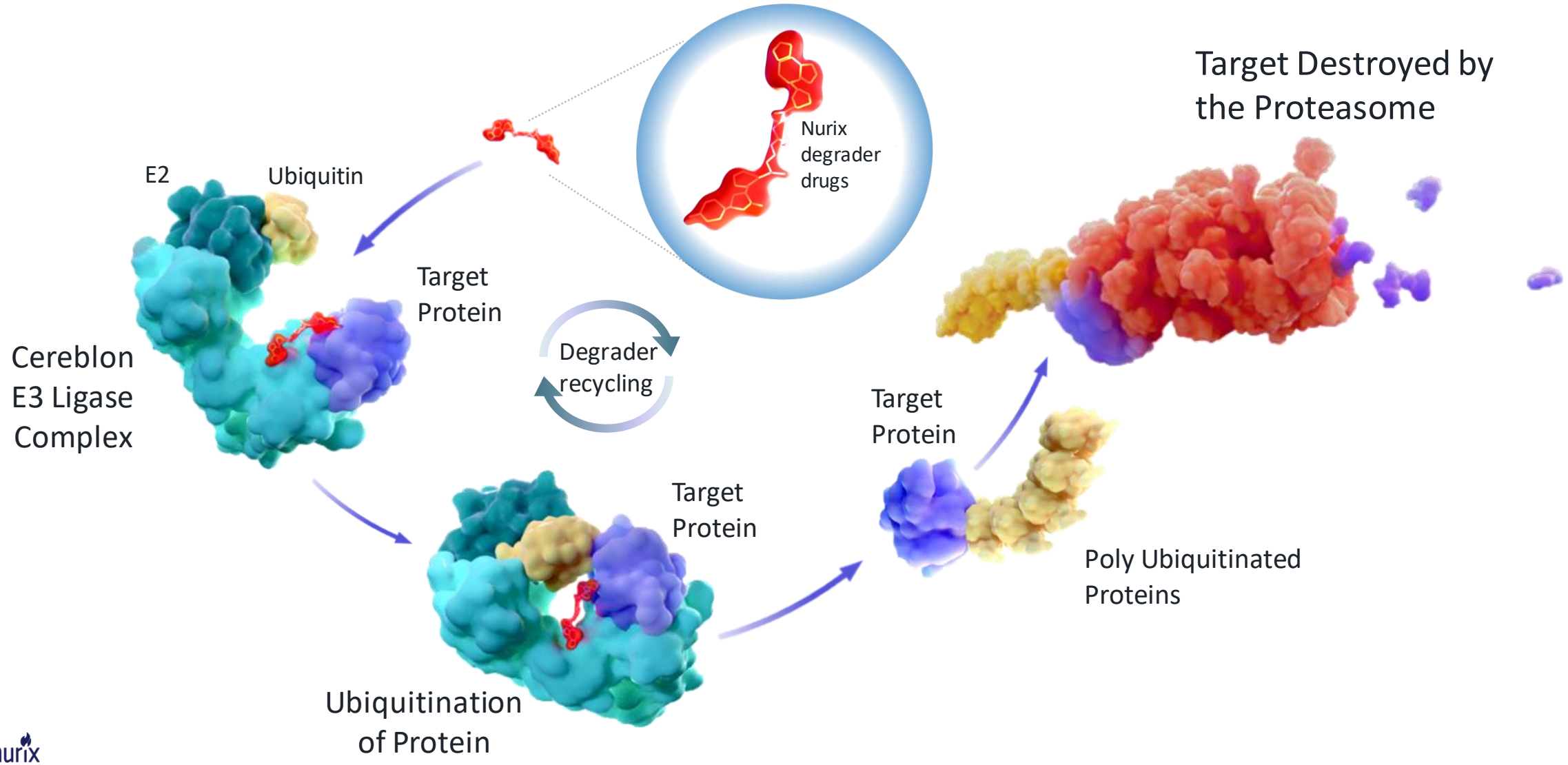
Broad Targeted Protein Degradation Pipeline Advancing Toward Clinical Development



- 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

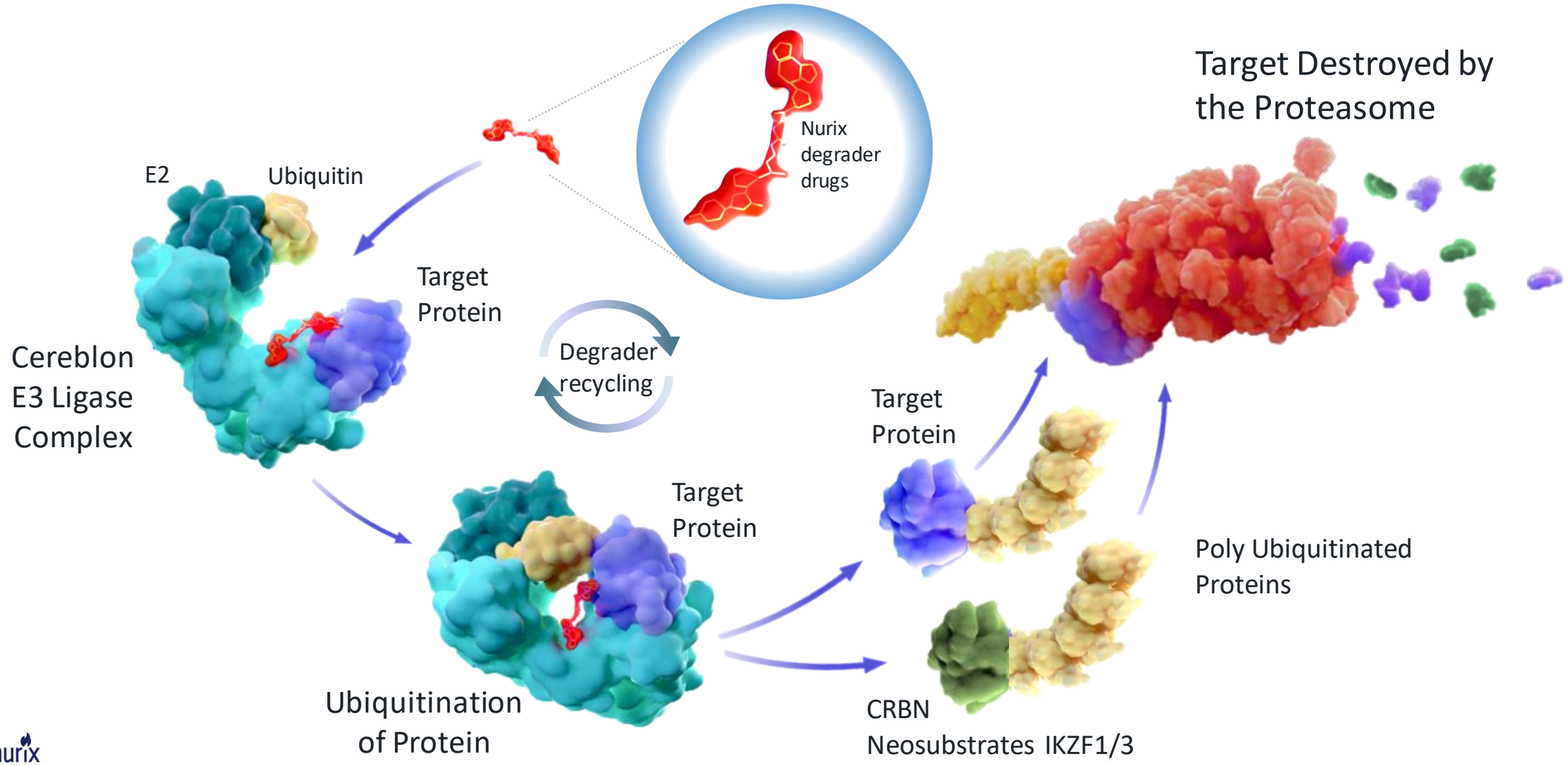
Targeted Protein Degradation

Harnessing the ubiquitin proteosome system to eliminate disease proteins



Dual Targeted Protein Degradation

Harnessing the ubiquitin proteosome system to address multiple complementary mechanisms

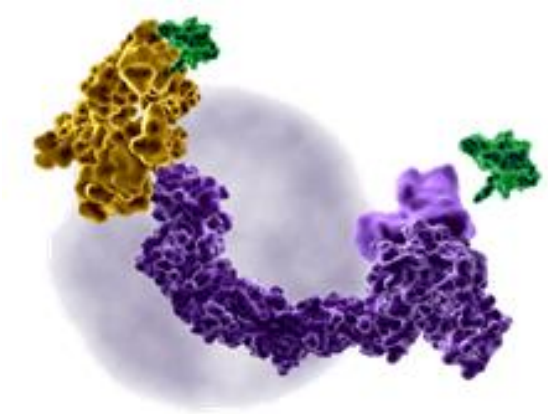


A First-In-Class Franchise of BTK Degraders:
NX-2127 & NX-5948

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

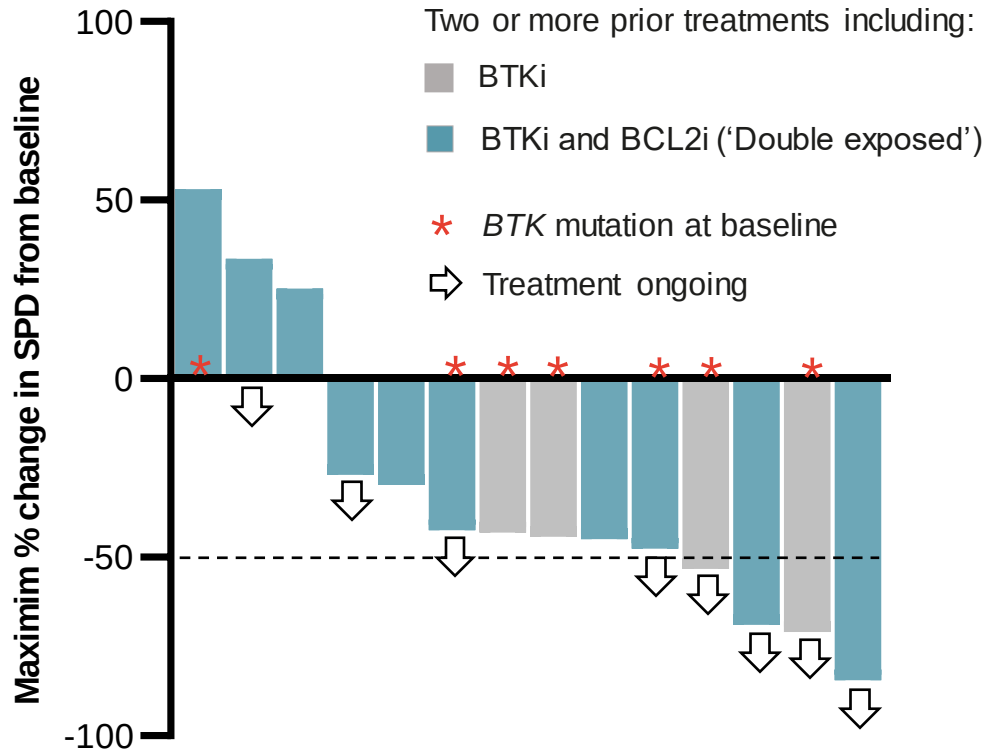
- Clinical evidence of potent BTK degradation in all patients tested
- Active in vitro against multiple BTK inhibitor-resistant mutations
- Crosses blood brain barrier and degrades BTK in brain-resident lymphoma cells and microglia in animal models
- Activity in multiple models of autoimmune disease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

First Demonstration of Clinical Activity of a Targeted Protein Degrader in Hematologic Malignancies

NX-2127 Preliminary Efficacy in Patients with 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



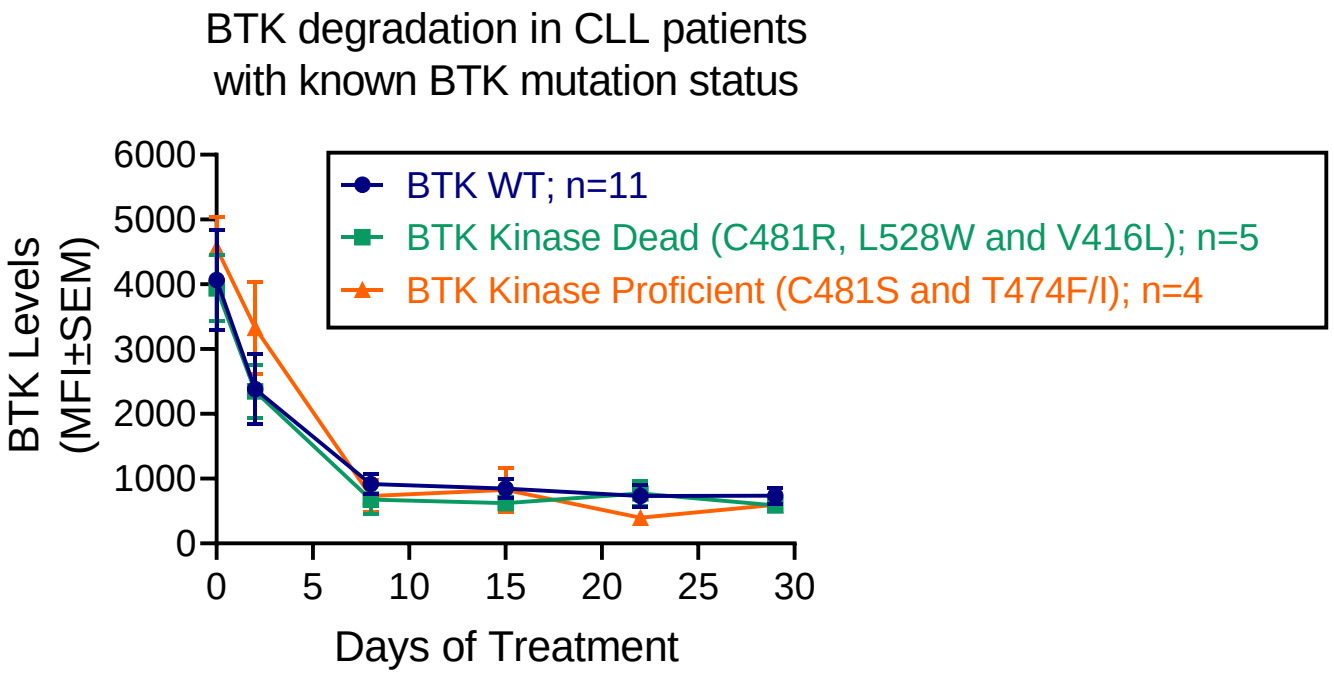
***One patient, not shown above, with prior BTKi and BCL2i treatment and with a *BTK* mutation detected at baseline, had no nodal disease at baseline. Their treatment is ongoing with a PR**

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

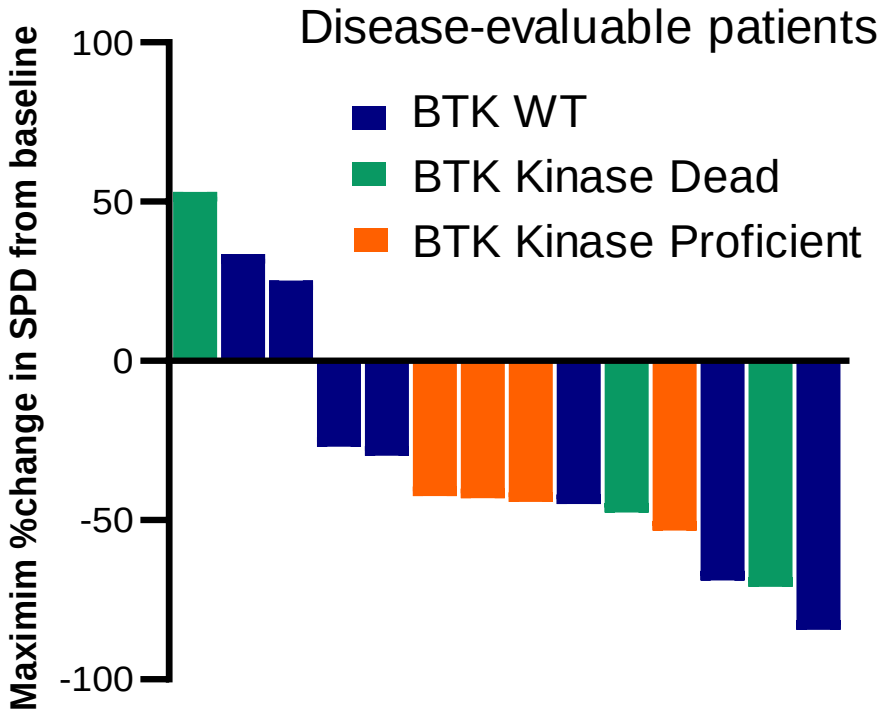
Data cutoff: September 21, 2022

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

NX-2127 Preliminary Efficacy in Patients with CLL



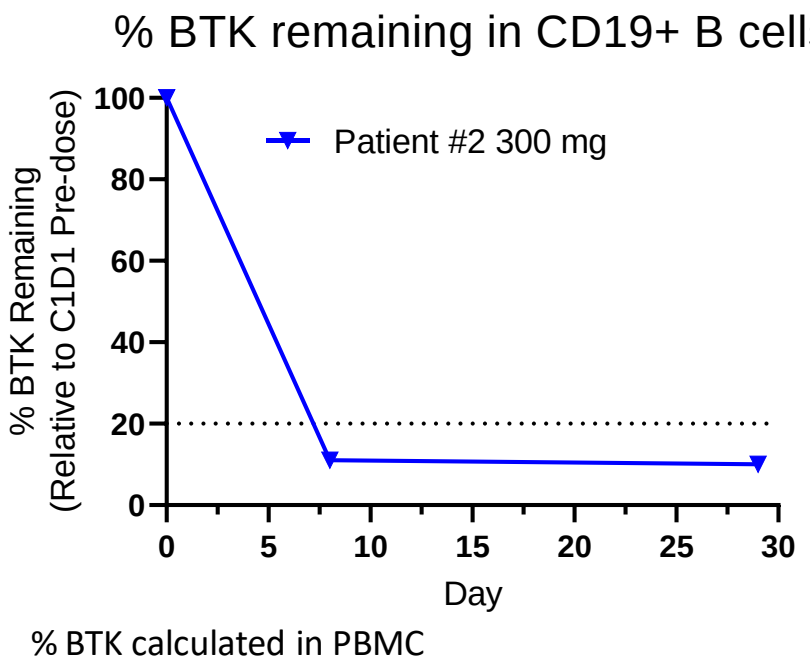
Patients with kinase dead mutations are classified as kinase dead regardless of co-occurrence of kinase proficient mutations



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

First Confirmed Complete Response in Diffuse Large B Cell Lymphoma with a BTK Degrader

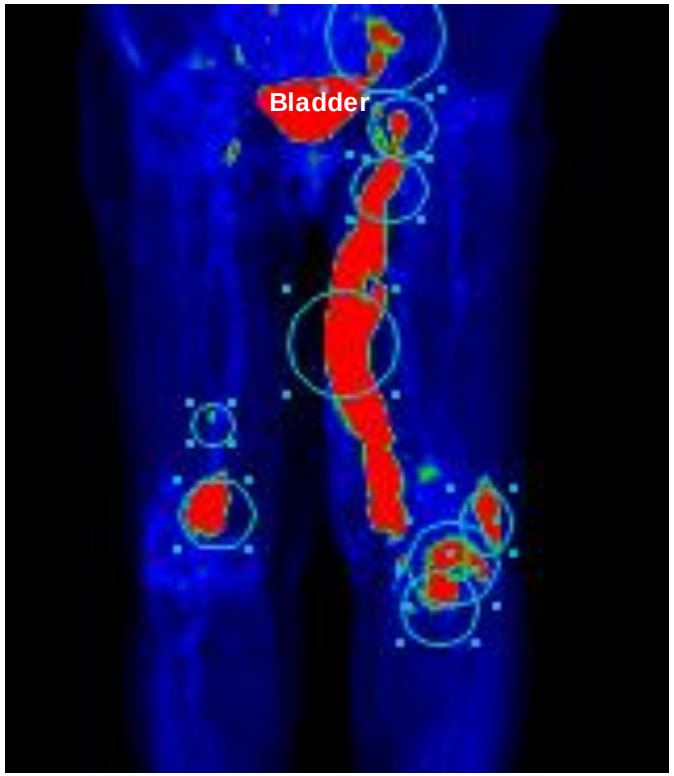
Case Study of NX-2127 as a single agent therapy in advanced DLBCL



% BTK calculated in PBMC

FDG-PET CT Scan Disease Assessment

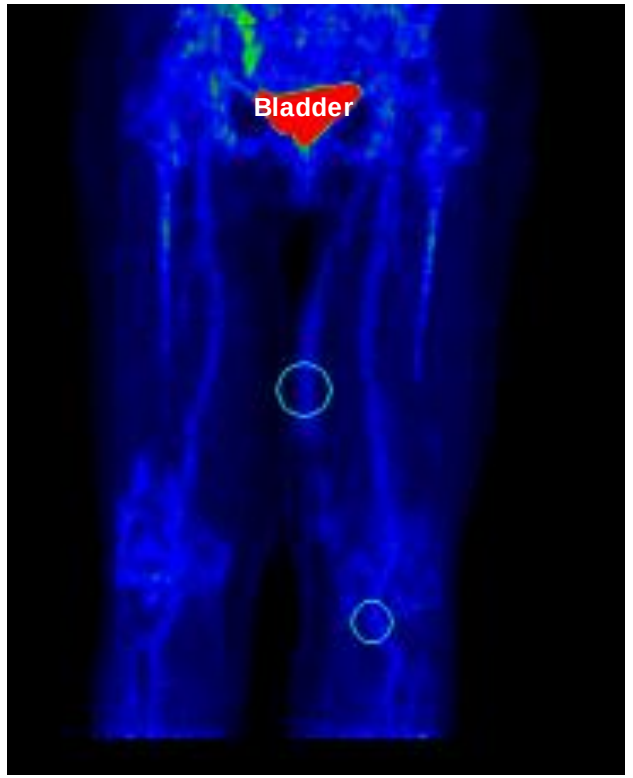
Baseline



Max SUV: 17.6
Deauville 5PS: 5

SUV: Standard Uptake Value

Week 16



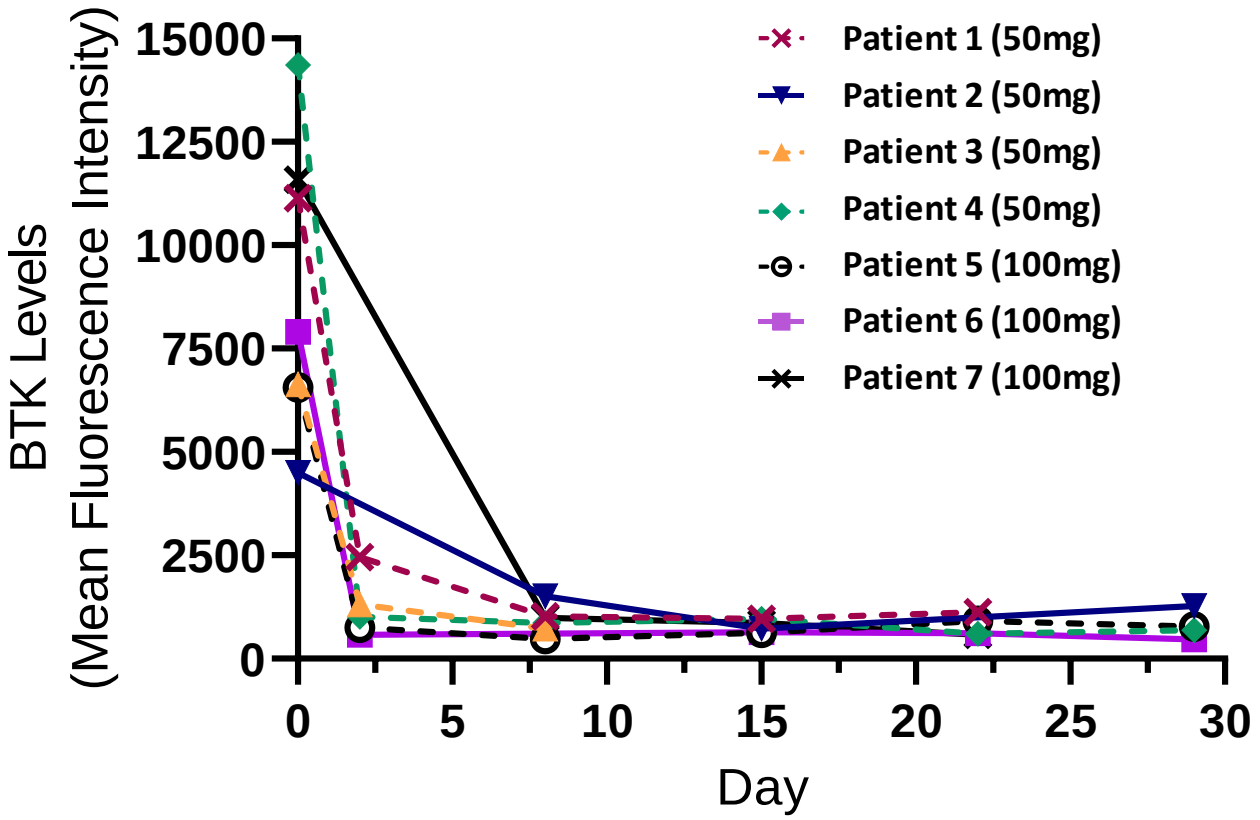
Max SUV: 2.5
Deauville 5PS: 2

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

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

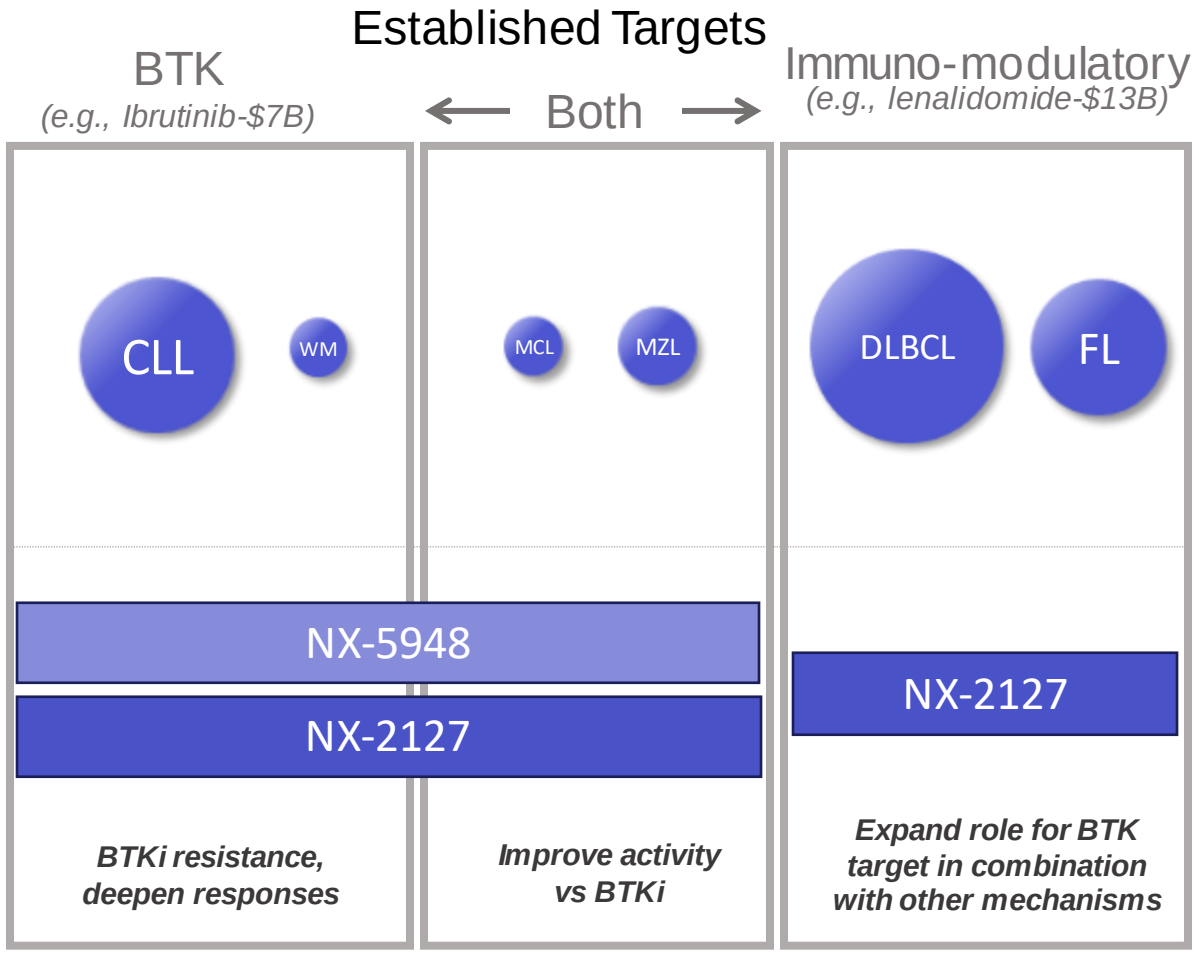
Initial proof of mechanism

- 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

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

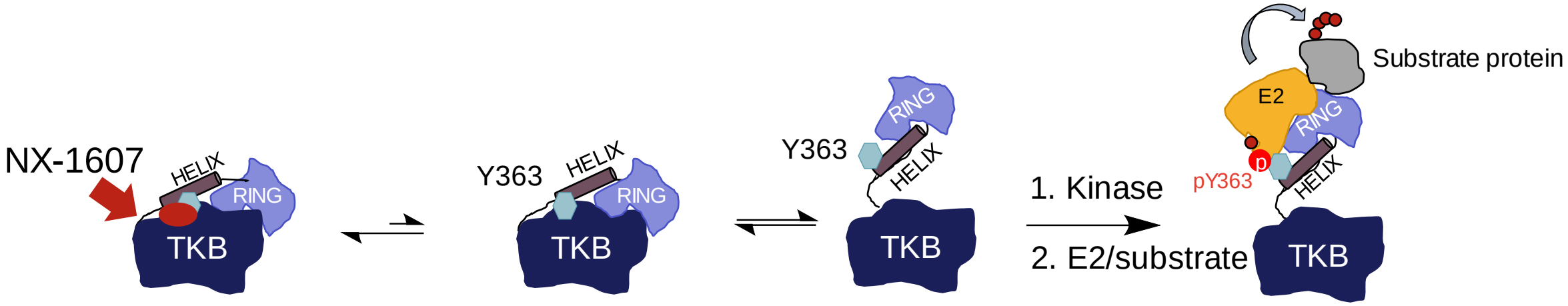
B-CELL MALIGNANCIES ANNUAL INCIDENCE (US & EU)	
Chronic Lymphocytic Leukemia (CLL)	39,700
Diffuse Large B-Cell Lymphoma (DLBCL)	55,100
Follicular Lymphoma (FL)	26,200
Mantle cell lymphoma (MCL)	6,200
Marginal Zone Lymphoma (MZL)	10,700
Waldenstrom's macroglobulinemia (WM)	6,300

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

First CBL-B Inhibitor to Enter Clinical Development: A New Small Molecule Immuno-Oncology Agent

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

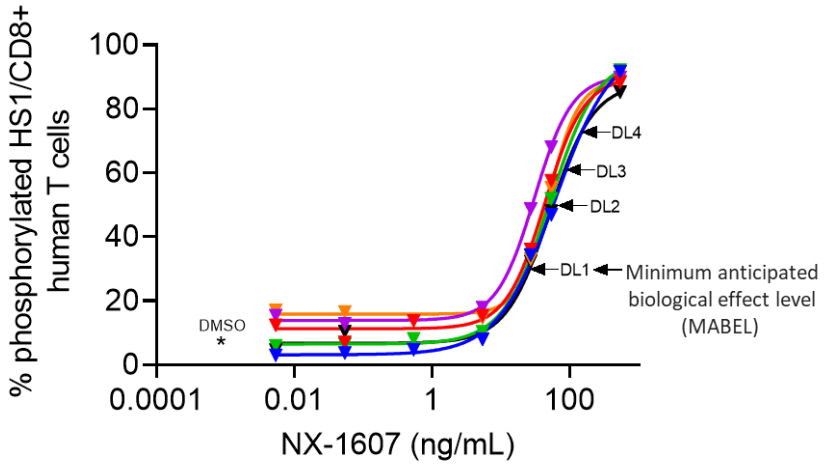
Phosphorylation locks CBL-B in the **ACTIVE** Conformation

Immune Response

Immune Response

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

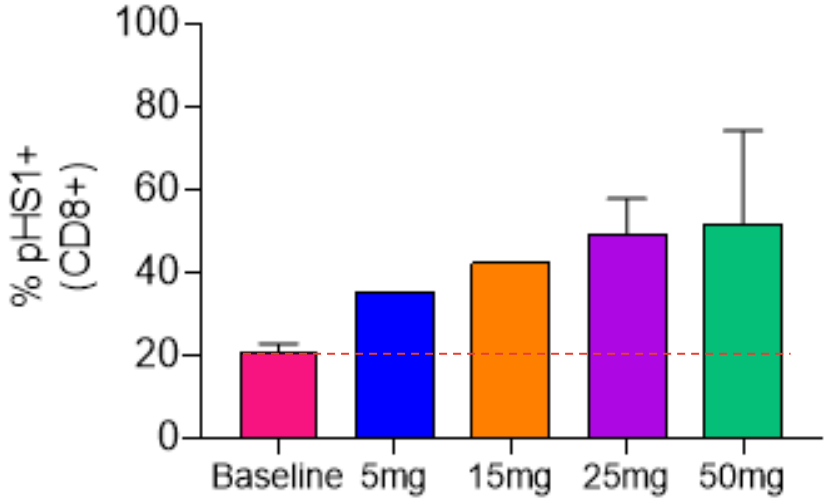


Proposed dose level[a]	NX-1607 dose (mg)	Estimated % HS1+/CD8+ T cells
-1	2.5	22.2
1[b]	5	30.0
2	15	49.7
3	25	60.6
4	50	74.0

[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

Defining Success in 2023

B-cell malignancies

NX-2127

- Present updated Phase 1 clinical data in H2 2023
- Define regulatory strategy based on FDA feedback in H2 2023

NX-5948

- Present initial clinical data from Phase 1a in H2 2023
- Define Phase 1b dose for cohort expansion in H2 2023

Immune oncology

NX-1607

- Present initial clinical data from Phase 1a in H2 2023
- Define Phase 1b dose for cohort expansion in H2 2023

Platform & pipeline

Research pipeline

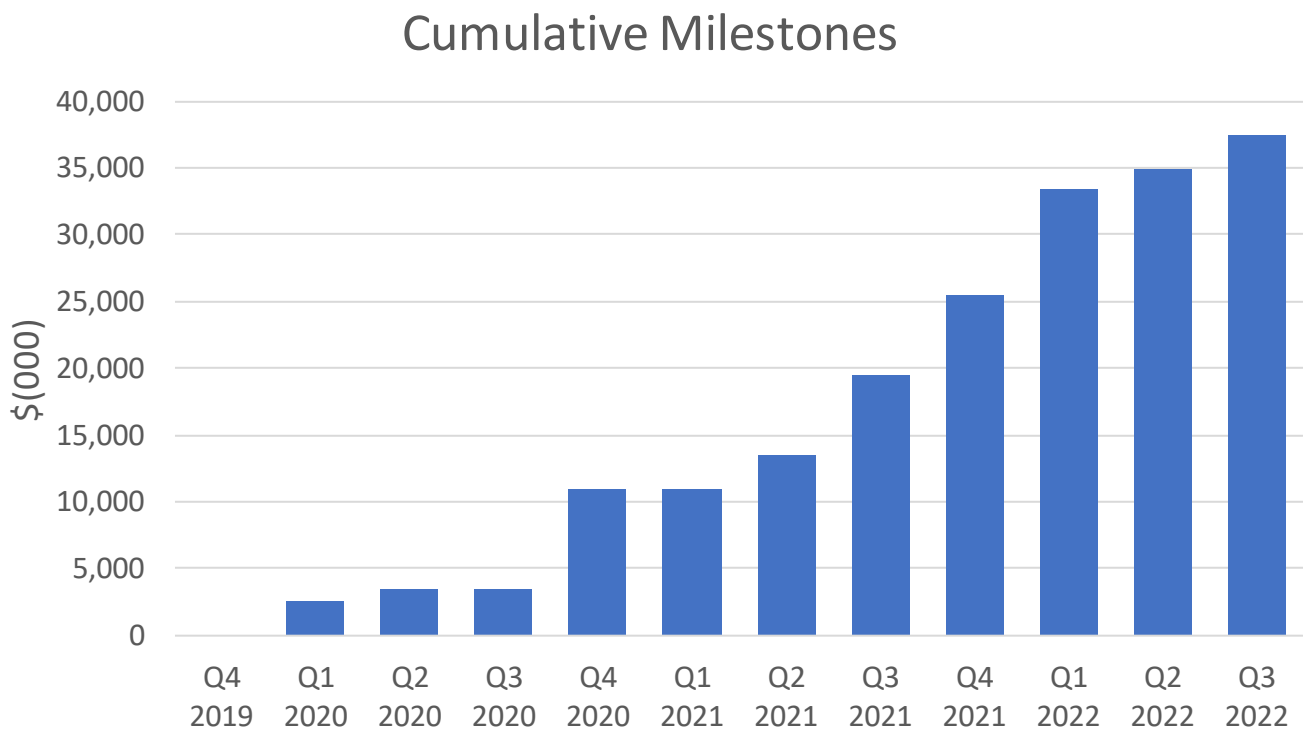
- Select new targeted protein degrader development candidate
- Achieve substantial research collaboration milestones throughout 2023

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