nurix

Leader in Targeted Protein Modulation

The First BTK Degraders in Hematologic Malignancies: The Latest from the Clinic

Arthur T. Sands, M.D., Ph.D.
President & CEO

5th Annual TPD Summit

Boston, MA

October 26th, 2022

Important Notice and Disclaimers

This presentation contains statements that relate to future events and expectations and as such constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. When or if used in this presentation, the words “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “outlook,” “plan,” “predict,” “should,” “will,” and similar expressions and their variants, as they relate to Nurix Therapeutics, Inc. (“Nurix,” the “Company,” “we,” “us” or “our”), may identify forward-looking statements. All statements that reflect Nurix’s expectations, assumptions or projections about the future, other than statements of historical fact, are forward-looking statements, including, without limitation, statements regarding our future financial or business plans; our future performance, prospects and strategies; future conditions, trends, and other financial and business matters; our current and prospective drug candidates; the planned timing and conduct of the clinical trial programs for our drug candidates; the planned timing for the provision of clinical updates and initial findings from our clinical studies; the potential advantages of our DELigase™ platform and drug candidates; the extent to which our scientific approach and DELigase™ platform may potentially address a broad range of diseases; the extent animal model data predicts human efficacy; and the timing and success of the development and commercialization of our current and anticipated drug candidates. Forward-looking statements reflect Nurix’s current beliefs, expectations, and assumptions. Although Nurix believes the expectations and assumptions reflected in such forward-looking statements are reasonable, Nurix can give no assurance that they will prove to be correct. Forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and changes in circumstances that are difficult to predict, which could cause Nurix’s actual activities and results to differ materially from those expressed in any forward-looking statement. Such risks and uncertainties include, but are not limited to: (i) risks and uncertainties related to Nurix’s ability to advance its drug candidates, obtain regulatory approval of and ultimately commercialize its drug candidates; (ii) the timing and results of clinical trials; (iii) Nurix’s ability to fund development activities and achieve development goals; (iv) the impact of the COVID-19 pandemic on Nurix’s business, clinical trials, financial condition, liquidity and results of operations; (v) Nurix’s ability to protect intellectual property and (vi) other risks and uncertainties described under the heading “Risk Factors” in Nurix’s Quarterly Report on Form 10-Q for the fiscal quarter ended August 31, 2022, and other SEC filings. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. The statements in this presentation speak only as of the date of this presentation, even if subsequently made available by Nurix on its website or otherwise. Nurix disclaims any intention or obligation to update publicly any forward-looking statements, whether in response to new information, future events, or otherwise, except as required by applicable law.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company’s own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal estimates and research are reliable, such estimates and research have not been verified by any independent source.

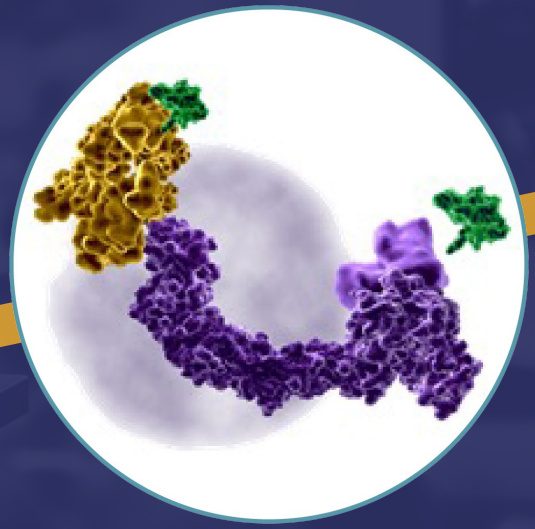
Nurix Drugs Engage Ligases for the Treatment of Cancer

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

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

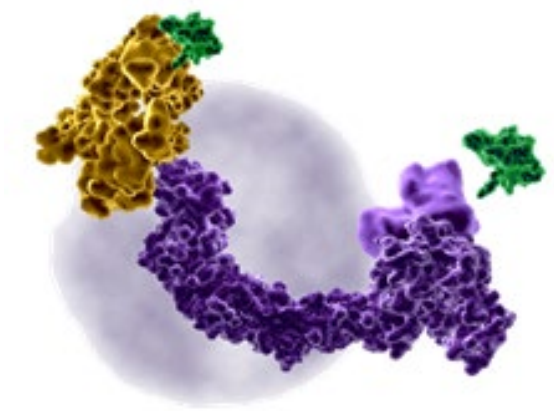
MOA	Drug program	Target/delivery	Therapeutic area	Preclinical	Phase 1	Phase 2	Phase 3
TPD	**NX-2127** Degrader	BTK-IKZF *Oral*	B-cell malignancies				
TPD	**NX-5948** Degrader	BTK *Oral*	B-cell malignancies				
TPE	**NX-1607** Inhibitor	CBL-B *Oral*	Immuno-Oncology				
TPE	**DeTIL-0255** Cell therapy	*Ex vivo CBL-B inhibition*	Gynecologic malignancies				
TPM	Wholly owned	5 targets	Multiple				
TPD	Gilead Sciences	5 targets	Multiple				
TPD	Sanofi	5 targets	Multiple				

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

NX-2127

BTK DEGRADATION & IMMUNOMODULATION

- Active against multiple BTK inhibitor-resistant mutations
- Robust BTK degradation and immunomodulatory activity observed across all dose levels to date
- Positive clinical activity in CLL patients, including responses in patients with BTK or BCL2 mutations
- Initiated cohort expansion for CLL patients
- Dose exploration is ongoing for patients with NHL



NX-5948

BTK DEGRADATION

- Active 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

Value Proposition for a BTK Degrader
Meeting the Unmet Need with NX-2127

Activity against resistance mutations to both covalent and non-covalent BTK inhibitors

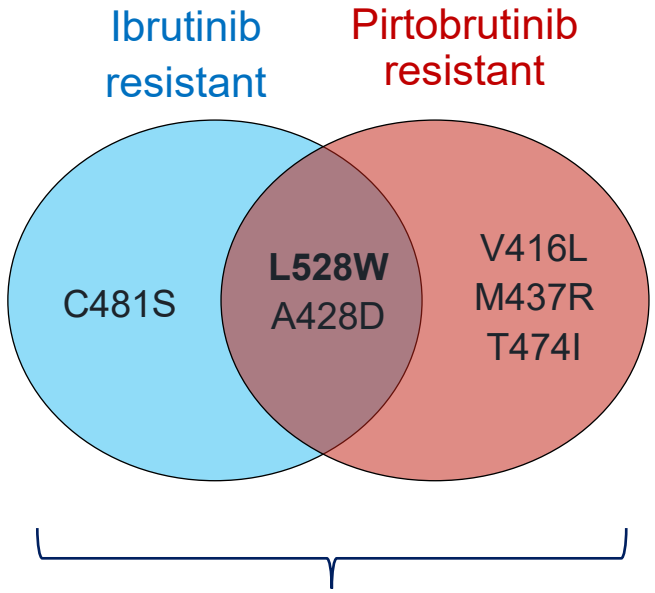
Degradation blocks all downstream signaling from BTK

Immunomodulatory activity adds second anti-tumor mechanism

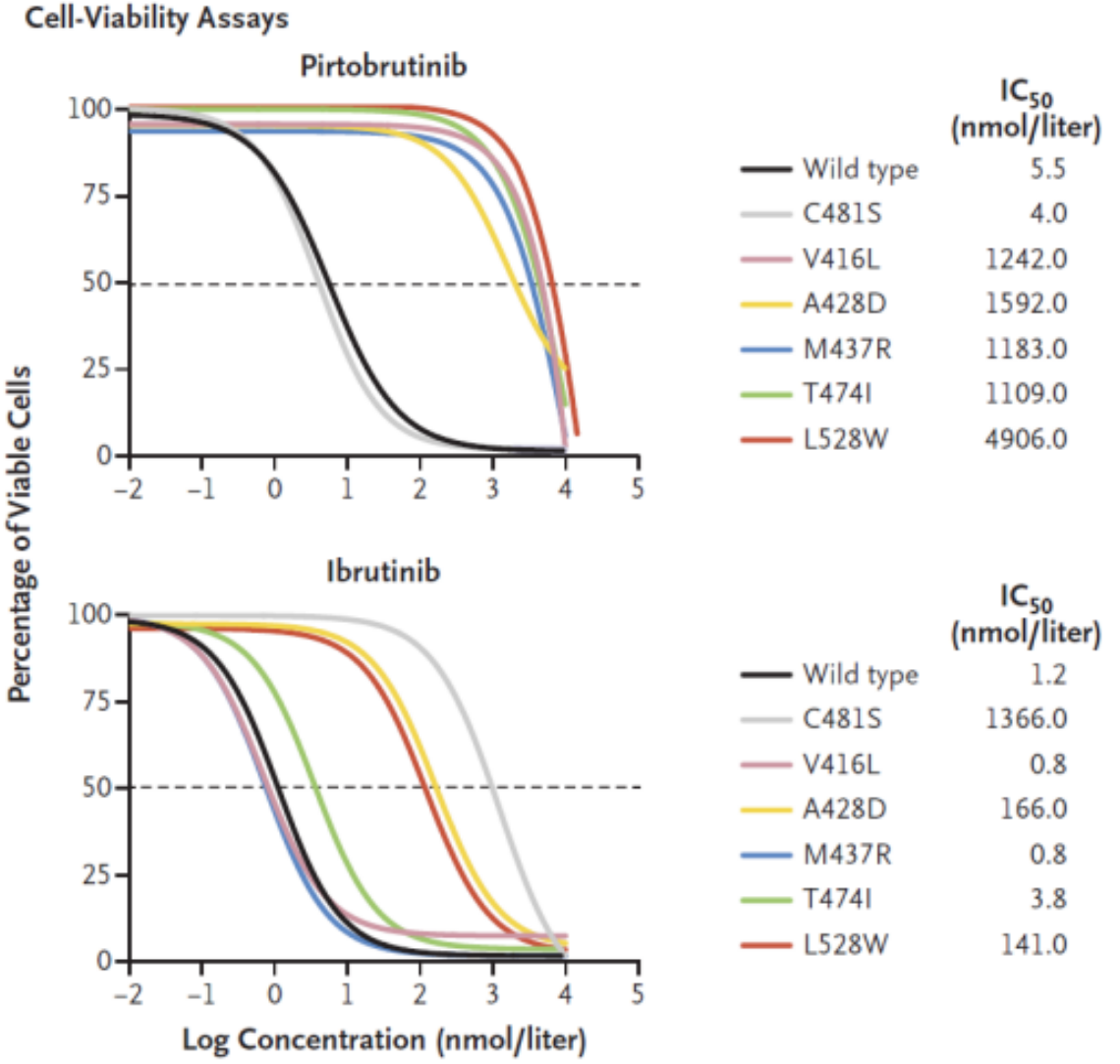
Emerging BTK Mutations Confer Resistance to Covalent and Non-Covalent BTK Inhibitors

The NEW ENGLAND JOURNAL of MEDICINE

"Our data suggest potential new therapeutic approaches to overcome the newly described BTK inhibitor resistance mechanisms. For example, these data provide a rationale for therapies aimed at addressing the potential scaffold function of BTK rather than inhibiting BTK kinase activity."



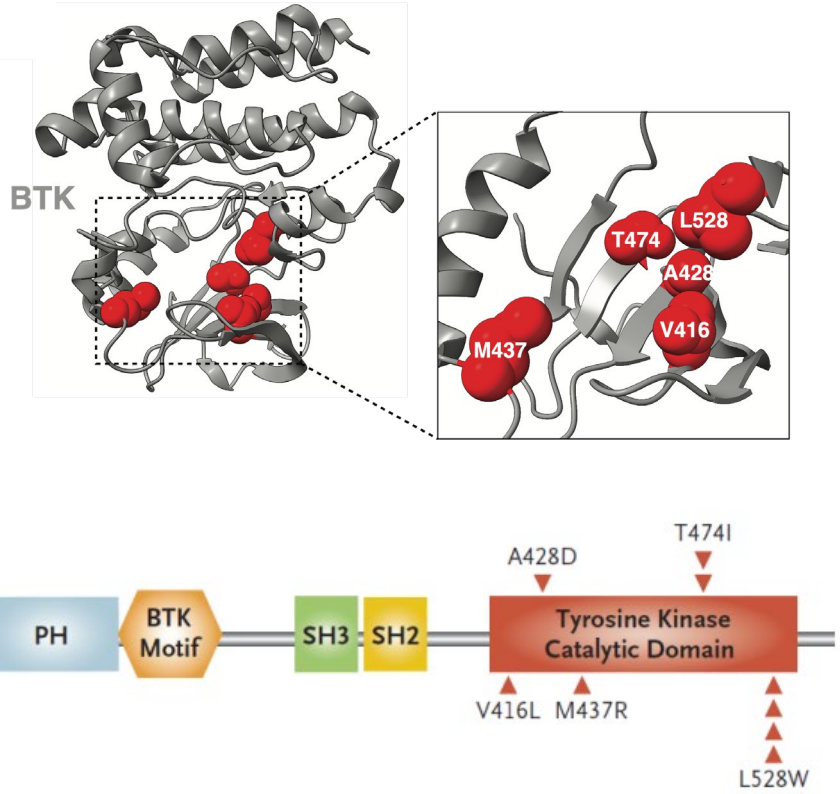
Opportunity for BTK degrader?



Wang E, et al. NEJM 2022

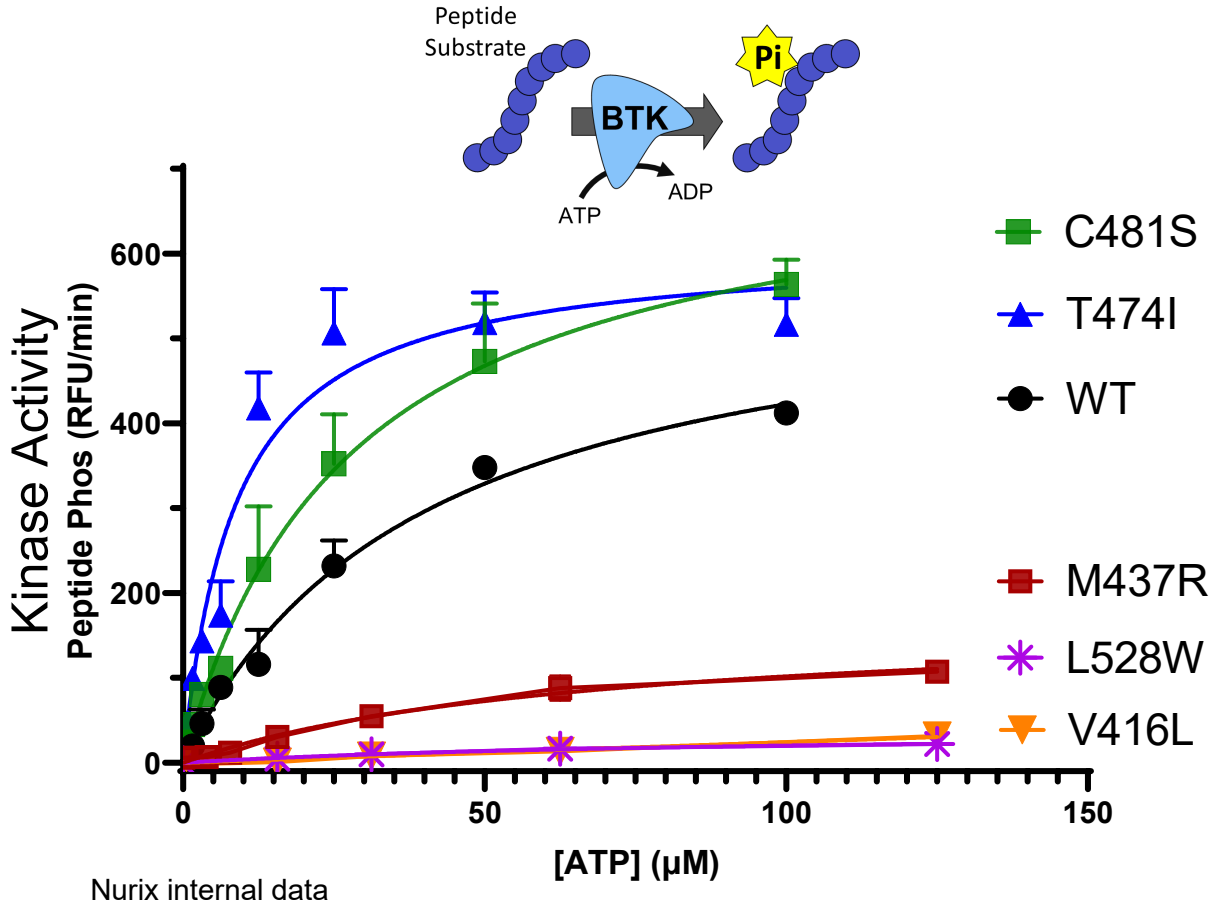
Nurix Degraders Directly Address Emerging Resistance Mutations and BTK Scaffolding Activity

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

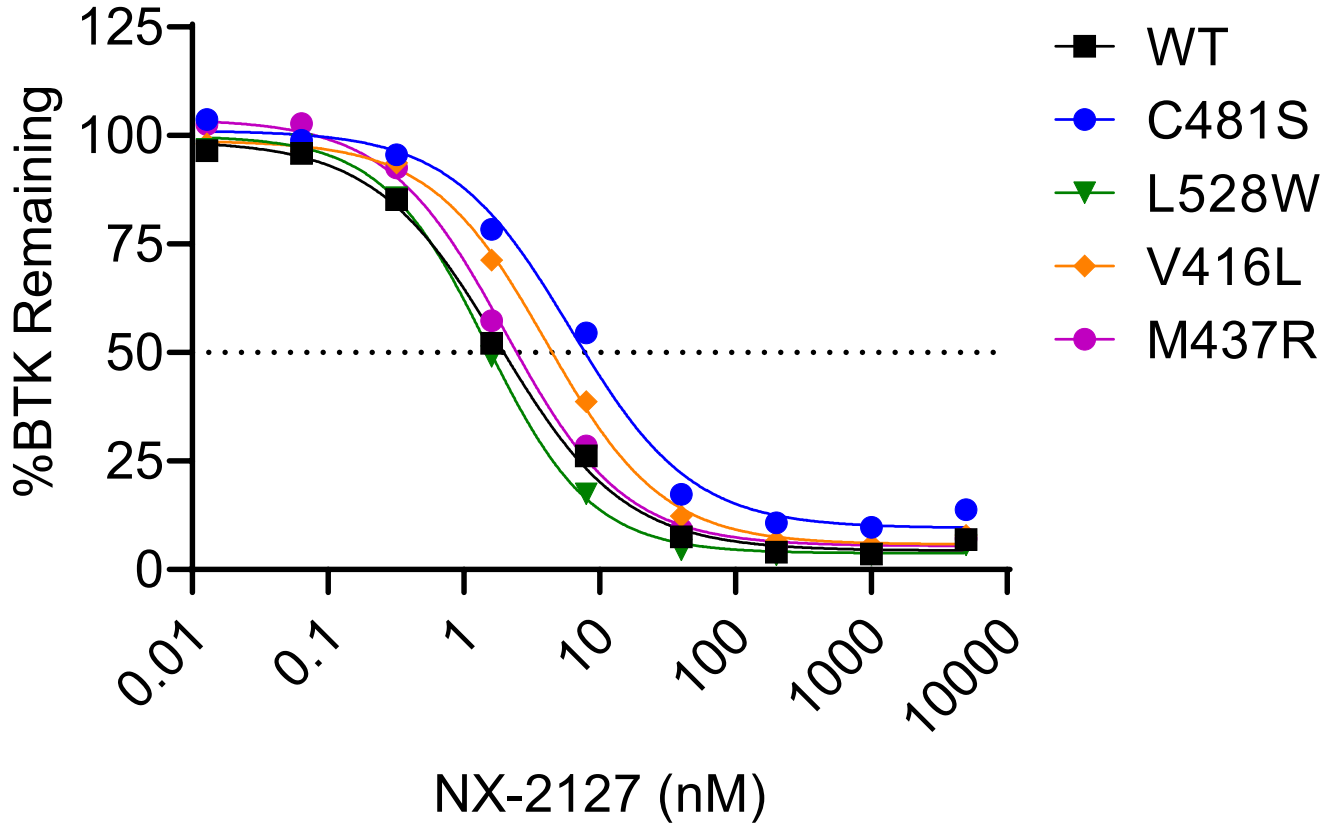


Nurix internal data

NX-2127 is Active Against Both Wildtype and Mutant BTK

Potential to treat patients who failed both covalent and non-covalent BTK inhibitors

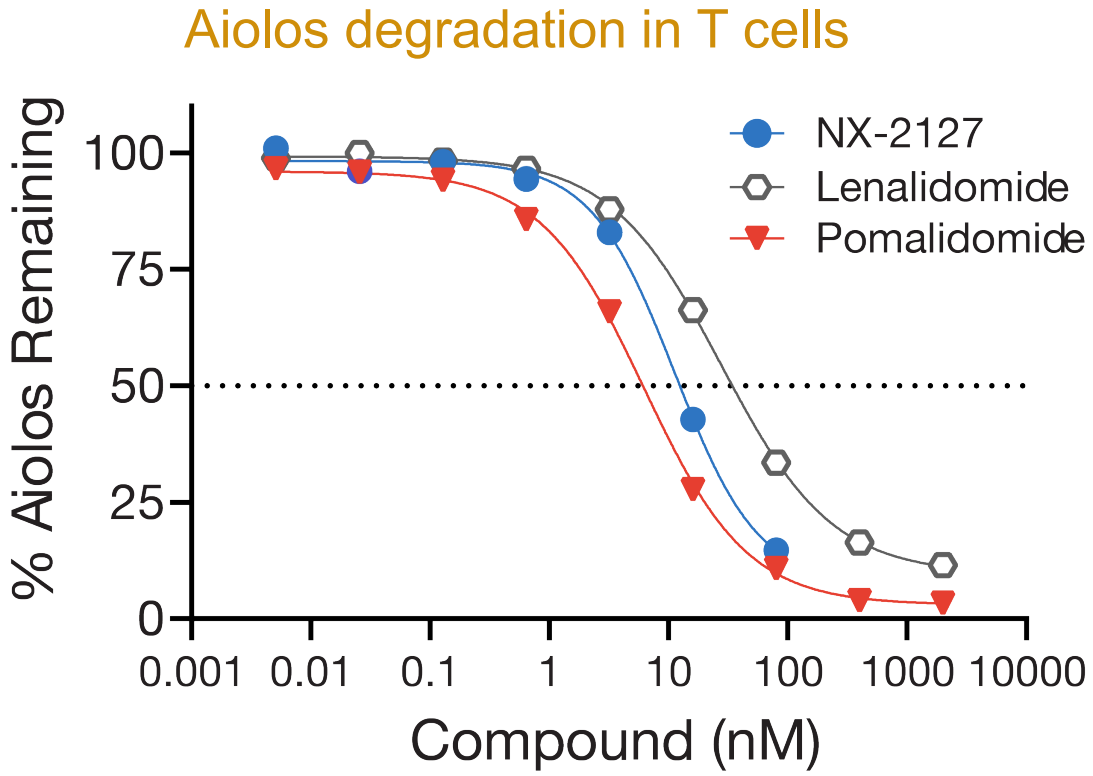
BTK degradation in TMD8 cells



NX-2127 is capable of degrading not only C481S, but also the novel BTK mutations observed post treatment with pirtobrutinib

TMD8: Human diffuse large B cell lymphoma cell line

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

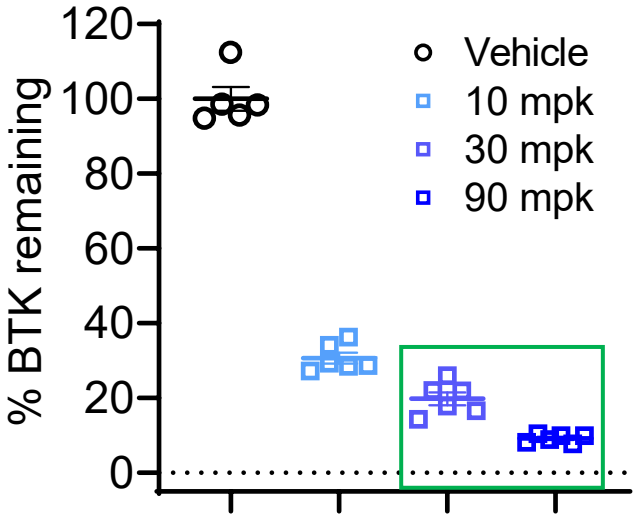


NX-2127 degradation of Aiolos in human T cells occurs at a similar potency to lenalidomide and pomalidomide

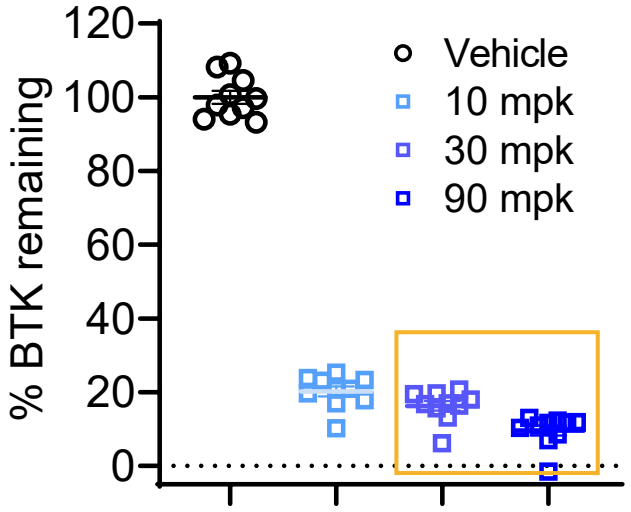
- Activity of NX-2127 is pegged to approved agents with well-established efficacy and safety
- Dual activity potentially addresses alternative resistance mechanism in CLL
- Emerging clinical data supports pathway combination approach in non-GCB-subtype DLBCL
- Dual mechanism shows strong benefit in MCL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

BTK Degradation of 80%+ Drives Potent Anti-Tumor Activity in Preclinical Models

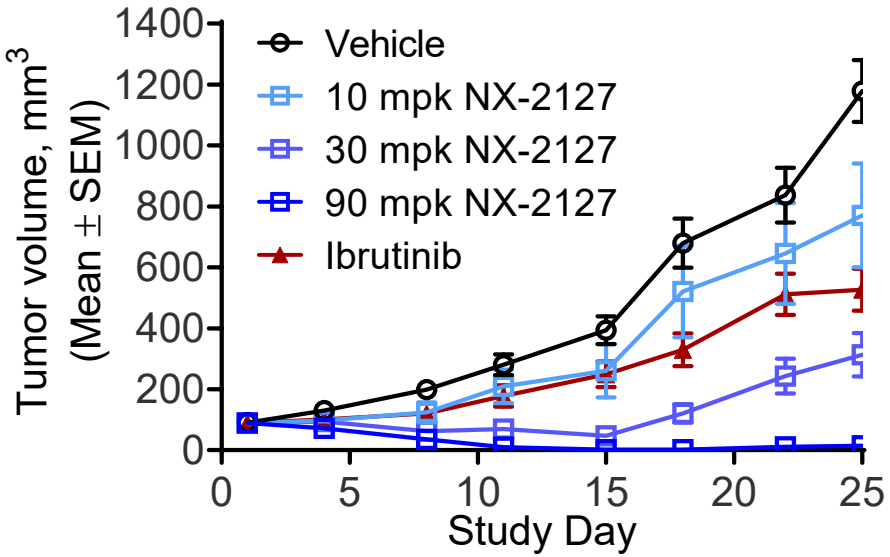
BTK degradation in Peripheral B cells



BTK degradation in TMD8 Tumor cells



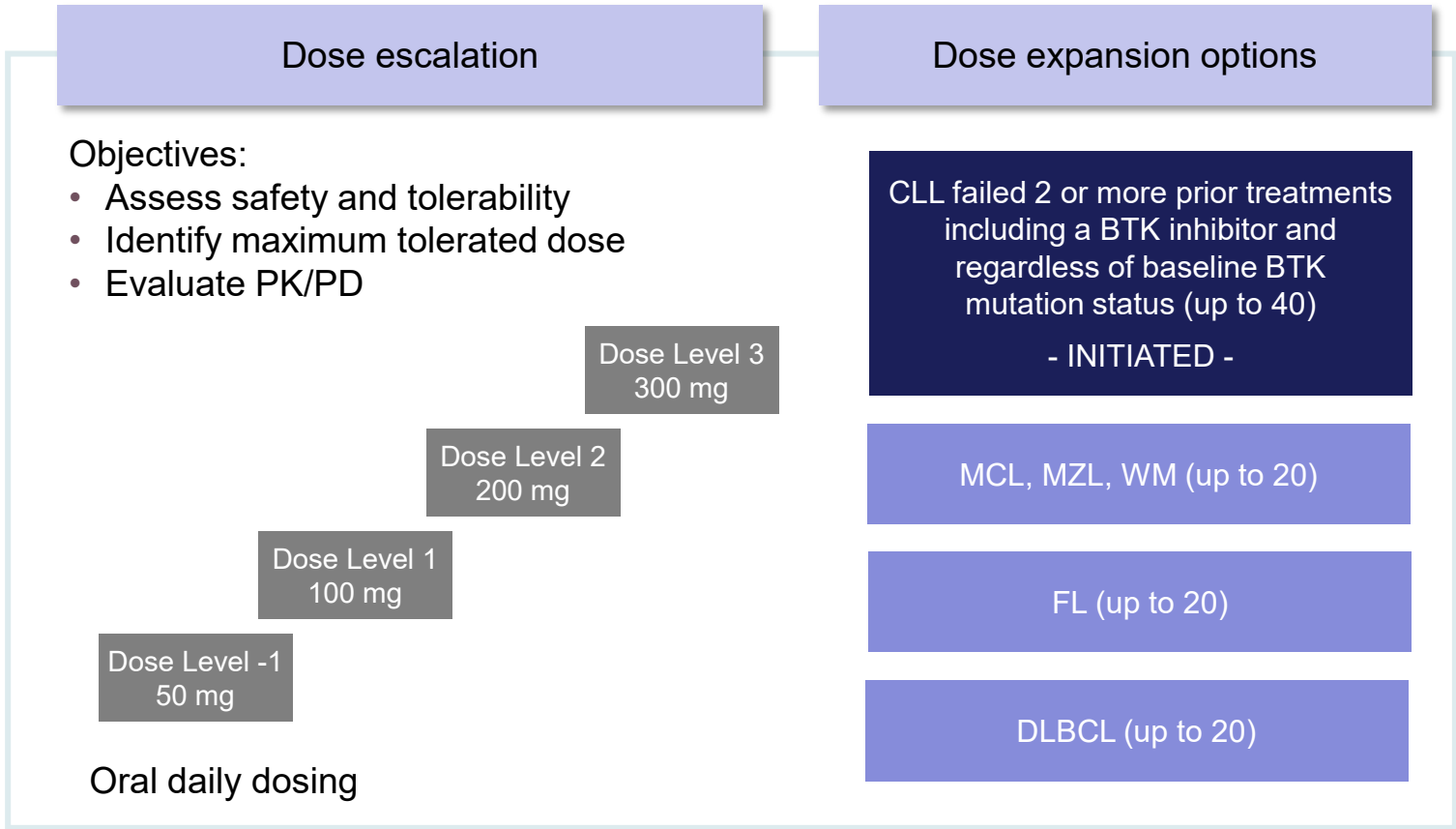
TMD8 Tumor Growth



Oral dose of NX-2127 (mg/kg)	10	30	90
% BTK degradation in peripheral B cells	69%	80%	91%
% BTK degradation in tumor tissue	79.8%	83.7%	90.4%
% Tumor growth inhibition vs Vehicle (Day 24)	58%	74%	100%

TMD8: Human diffuse large B cell lymphoma cell line

NX-2127-001
Phase 1a/1b Trial Design



CLL, chronic lymphocytic leukemia; DLBCL, diffuse large B cell lymphoma; FL, follicular lymphoma; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; WM, Waldenstrom's macroglobulinemia.

- CLL Phase 1b cohort expansion at 100 mg dose
- 50 mg CLL cohort opened to evaluate multiple doses for Project Optimus
- Phase 1a dose escalation is ongoing at 200 mg and 300 mg doses for patients with NHL

NX-2127-001: Heavily Pre-Treated Patient Population, Including Double-Refractory CLL Patients

Characteristics	Overall population (n=21)**	CLL (n=13)	Non-CLL (n=7)
Median age, years (range)	76.0 (61–92)	76 (65–86)	77 (67–92)
Female, n (%) Male, n (%)	7 (33.3) 14 (66.7)	7 (53.8) 6 (46.2)	0 7 (100)
Prior therapy*, median (range) BTK inhibitor, n(%) BCL2 inhibitor, n(%)	4.5 (1–8) 16 (76.2) 7 (33.3)	6.0 (2–8) 12 (92.3) 7 (53.8)	2.0 (1–5) 4 (57.1) 0

Type of Disease	Cohort 1 (100 mg) (n=12)	Cohort 2 (200 mg) (n=6)	Cohort 3 (300 mg) (n=3)	Total (n=21)
Chronic lymphocytic leukemia (CLL)	8 (66.7%)	3 (50%)	2 (66.7%)	13 (61.9%)
Mantle cell lymphoma (MCL)	1 (8.3%)	1 (16.7%)	1 (33.3%)	3 (14.3%)
Diffuse large B-cell lymphoma (DLBCL)	2 (16.7%)	1 (16.7%)	0 (0%)	3 (14.3%)
Waldenstrom's Macroglobulinemia (WM)	0 (0%)	1 (16.7%)	0 (0%)	1 (4.8%)
TBD***	1 (8.3%)	0 (0%)	0 (0%)	1 (4.8%)

Data cut April 8, 2022

*Prior therapies were not entered into the database for all enrolled patients at the time of datacut. Some data pending/ongoing
**One patient's disease type wasn't identified in the EDC at the time of extract, but disease type was coded based on source data
***One subject was screened into the study, but the indication and cohort weren't entered in the EDC at the time of data extract

NX-2127-001: Safety Observations By Dose (All Patients, Grade ≥3)

Adverse Event Preferred Term, Grade ≥3	100 mg (n=10) n (%)	200 mg (n=6) n (%)	300 mg (n=3) n (%)
Neutropenia	1 (10%)	3 (50%)	2 (66.7%)
Hypertension	0 (0%)	1 (16.7%)	0 (0%)
Dyspnea	0 (0%)	1 (16.7%)	0 (0%)
Anemia	1 (10%)	1 (16.7%)	0 (0%)
Pain in extremity	0 (0%)	0 (0%)	1 (33.3%)
Clostridium difficile colitis	0 (0%)	1 (16.7%)	0 (0%)
Clostridium difficile infection	0 (0%)	1 (16.7%)	0 (0%)
Cognitive disorder	0 (0%)	0 (0%)	1 (33.3%)
Upper respiratory tract infection	0 (0%)	1 (16.7%)	0 (0%)

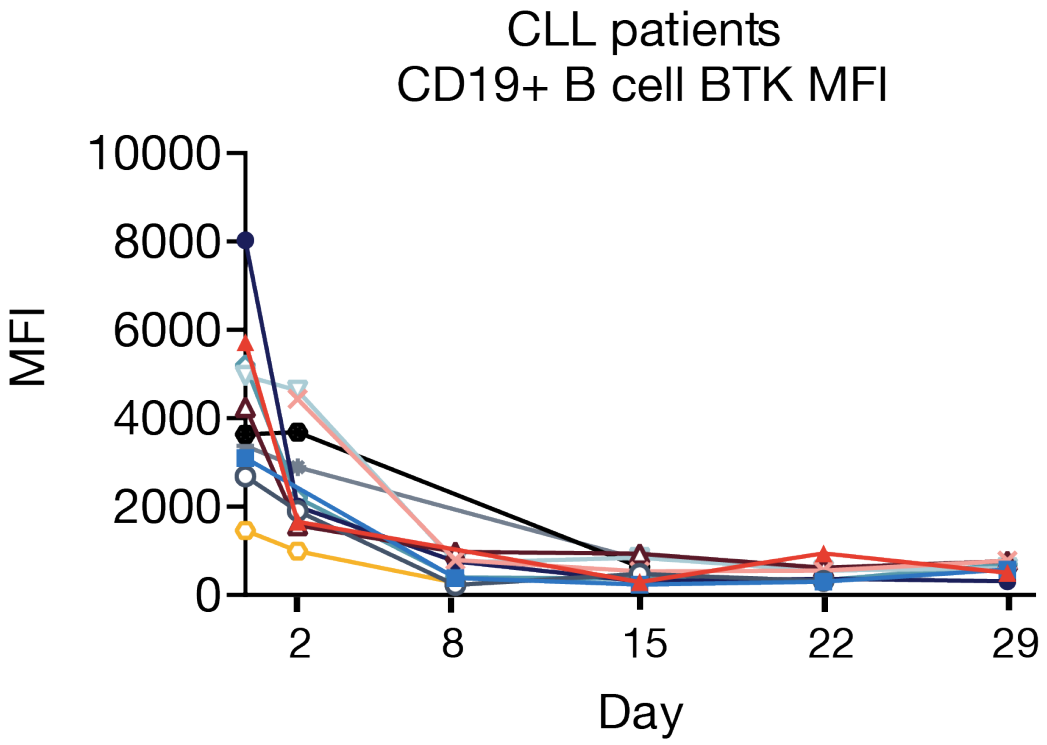
Safety population included 19 subjects. Two patients were assigned to the 100 mg cohort, but treatment was not entered in the EDC at time of extract

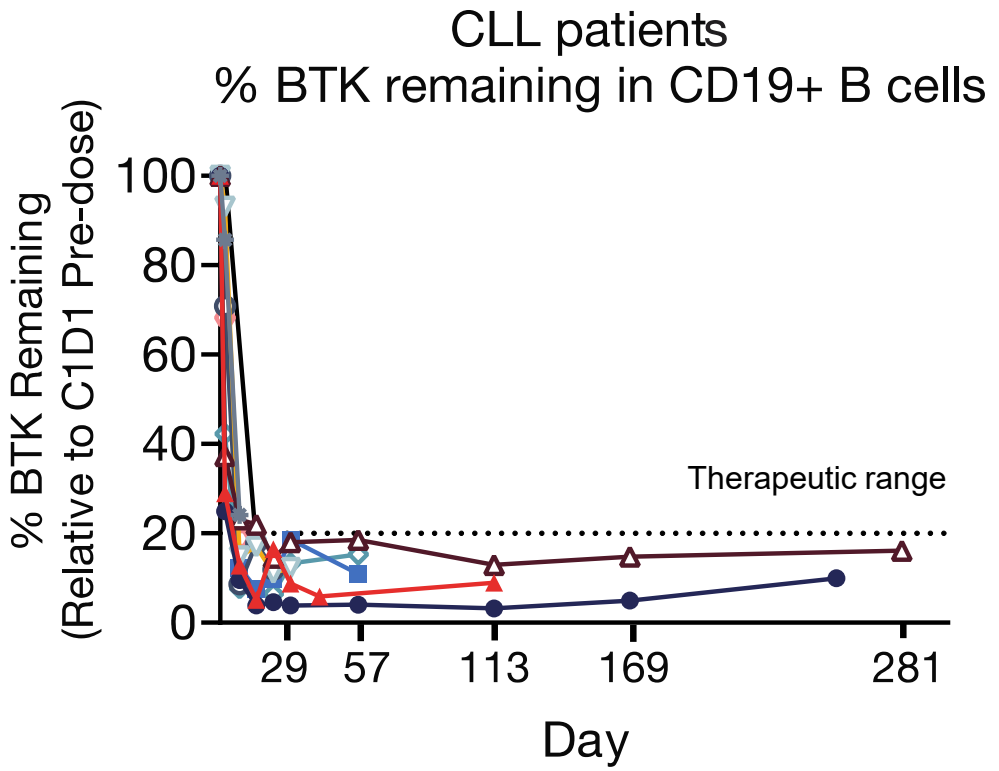
Data cut April 8, 2022

Additional safety observations:

- Dose-limiting toxicity observed at 300 mg in a patient with CLL; cognitive AE believed to be related to immunomodulatory activity
- Two AEs of lower grade atrial fibrillation were observed at 100 mg in a patient with MCL, and at 200 mg in a patient with CLL

NX-2127-001: Rapid and Sustained Degradation of BTK in Patients with CLL





Target BTK degradation achieved by Day 15 (steady state) for all starting BTK levels

BTK degradation is sustained

Data cut April 8, 2022

Case Study: Patient #1 (Presented at TPD 2021)

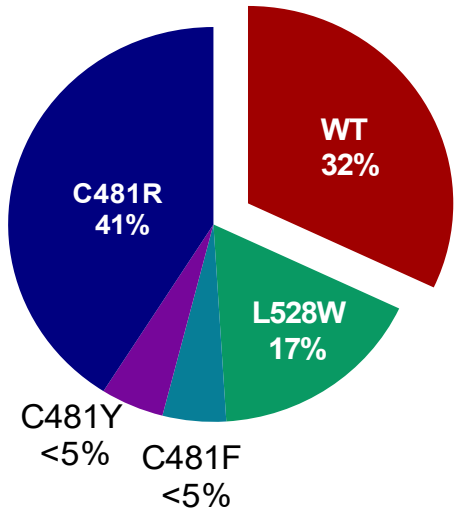
Patient history
78-year-old male
with stage IV CLL

Prior treatments
1. Rituximab, 2015
2. Ibrutinib, 2015-2021

Disease at study entry
Bone marrow involvement: 85.4%
Spleen: enlarged (15.7 cm)
Nodal lesions: several, largest 4.2 cm
Multiple resistance mutations

Safety	
Exposure	No dose interruptions or modifications
DLT's	None
SAE's	None
Grade 3 or > AE	Neutropenia (ANC = 860), resolved without intervention

Up to 68% of Leukemia Cells with BTK Mutations



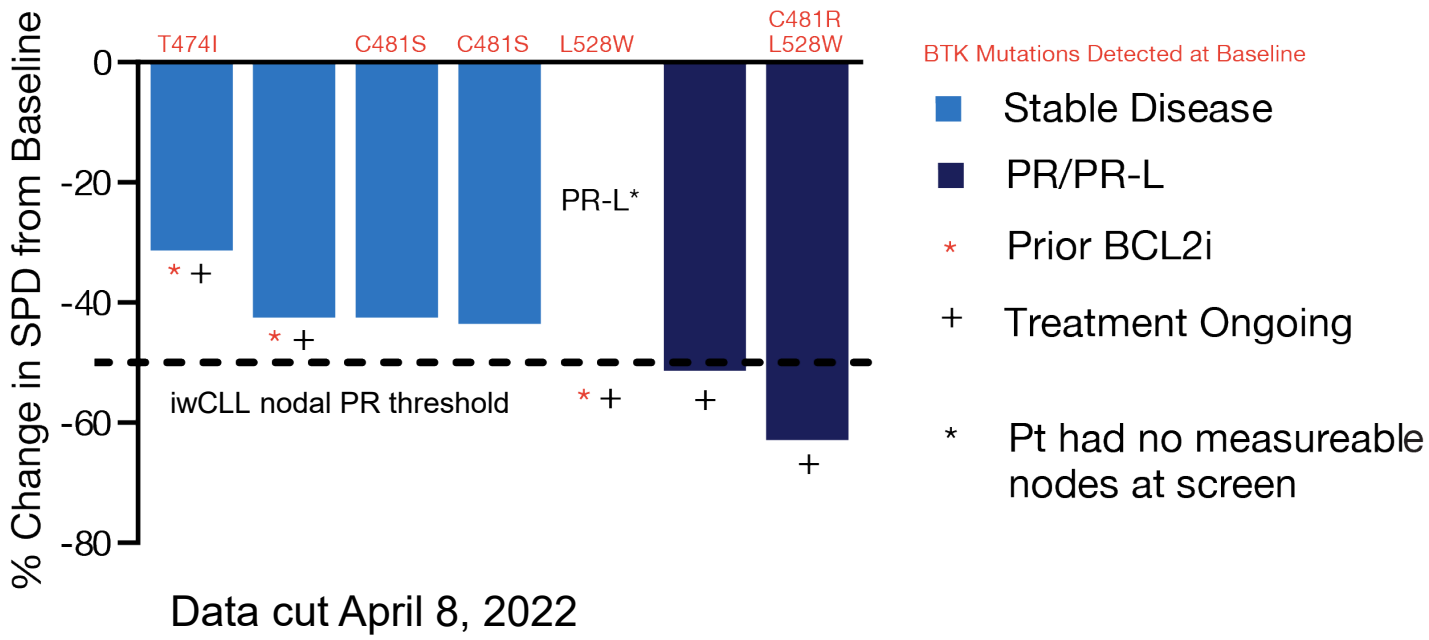
Disease assessment

Time Point	Hgb (g/dL)	Plt (K/uL)	ALC (K/uL)	Spleen (cm)	Spleen % change[a]	Lymph Node SPD (cm^2)	Nodal SPD % Change	Response[b]
Baseline	14.3	112	16.4	15.7	–	27.1	–	–
Week 8	13.2	133	36.9	14.8	–33%	13.4	–51%	Stable disease
Week 16	14.1	114	22.5	14.2	–56%	10.8	–60%	Partial remission with lymphocytosis

[a]Spleen % change is the percent change to a reference "normal" of 13 cm
[b]Response for this patient as per International working group on chronic lymphocytic leukemia (iwCLL)
[c]Listed as partial remission in database
DLT: dose limiting toxicity; SAE: serious adverse event; AE: adverse event; ANC: absolute neutrophil count; Hgb: hemoglobin, Plt: platelet count, ALC: absolute lymphocyte count, SPD: sum of product diameters

NX-2127-001 Phase 1a: Positive Initial Findings in Heavily Pretreated CLL Patients

Best Nodal Response On Study (CLL)



Data cut April 8, 2022

Next clinical update on CLL patients at ASH 2022

- Meaningful clinical benefit in CLL patients with a median of 6 prior lines of therapy
- Biologic activity including nodal reductions and/or lymphocytosis observed in all patients treated
- Responses in patients with resistance mutations to covalent and non-covalent BTK inhibitors
- Responses include a double-refractory patient who had prior BCL2 inhibitor therapy

SPD, sum of the product of diameters; iwCLL, international Workshop on CLL

Clinical Update

Initial experience in non-GCB DLBCL patients

CASE STUDY

First Report of Targeted Protein Degrader NX-2127 in Diffuse Large B cell Lymphoma (DLBCL)

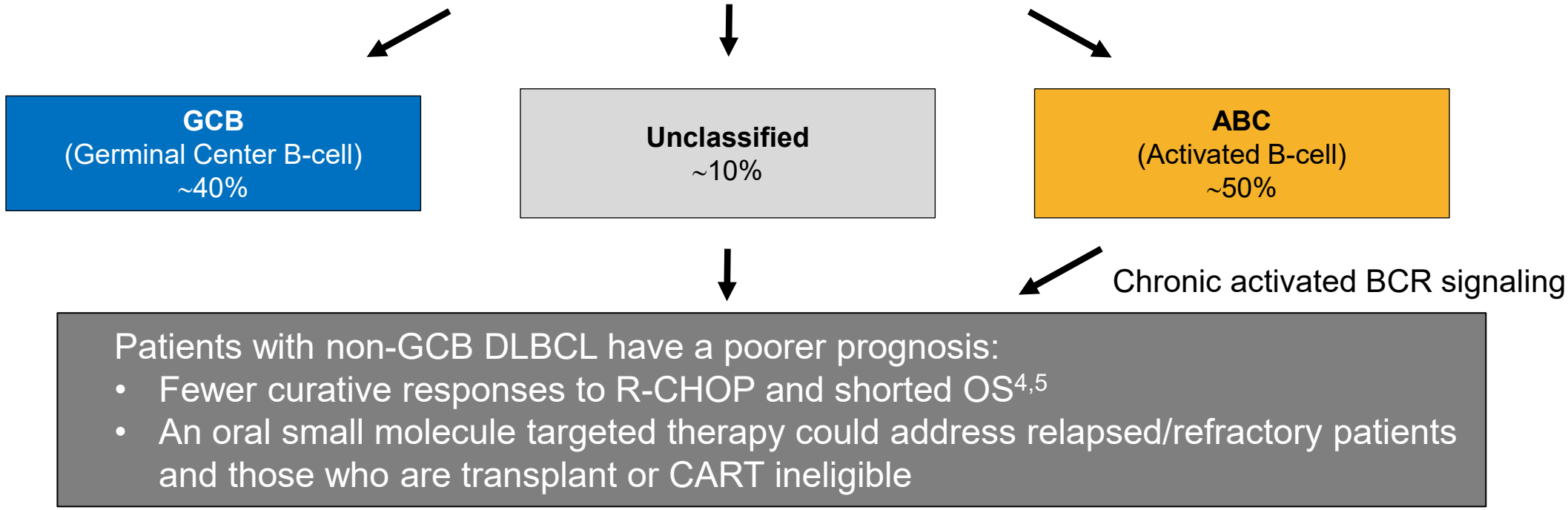
Robert Brown, M.D.
Executive Vice President
Clinical Development
Nurix Therapeutics

October 26, 2022

Non-GCB DLBCL Represents an Important Unmet Medical Need

- DLBCL is the most common form of lymphoma, representing ~30% of all NHL diagnoses[1,2]
- ~24,000 people diagnosed in the United States each year, with ~60% 5-year survival[1,2,3]

DLBCL treatments are the same for all patients, even though it is a biologically heterogeneous disease[4]



[1]American Cancer Society. Cancer Facts & Figures 2022. Atlanta, Ga: American Cancer Society; 2022. https://www.cancer.org/cancer/non-hodgkin-lymphoma/about/key-statistics.ntml#references
[2]NCCN, B-Cell Lymphomas; April 2021 https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf; [3]https://seer.cancer.gov/statfacts/html/dlbcl.html
[4]Mareschal et al. Hematologica 2011;96:1888–90; [5]Schmitz et al. N Engl J Med 2018;378:1396–407

Mechanistic Rationale for Dual Degrader in DLBCL

CLINICAL TRIALS AND OBSERVATIONS

Comment on Goy et al, page 1024

Ibrutinib and lenalidomide: when 1+1 = >2

Jason Westin | MD Anderson Cancer Center

Hyper-activated BCR (CD79b-mut) and TLR (MyD88-mut) signaling are hallmarks of non-GCB DLBCL:

- NX-2127 targets both BCR and TLR signaling through BTK degradation
- NX-2127 targets non-BTK dependent TLR signaling through its immunomodulatory activity

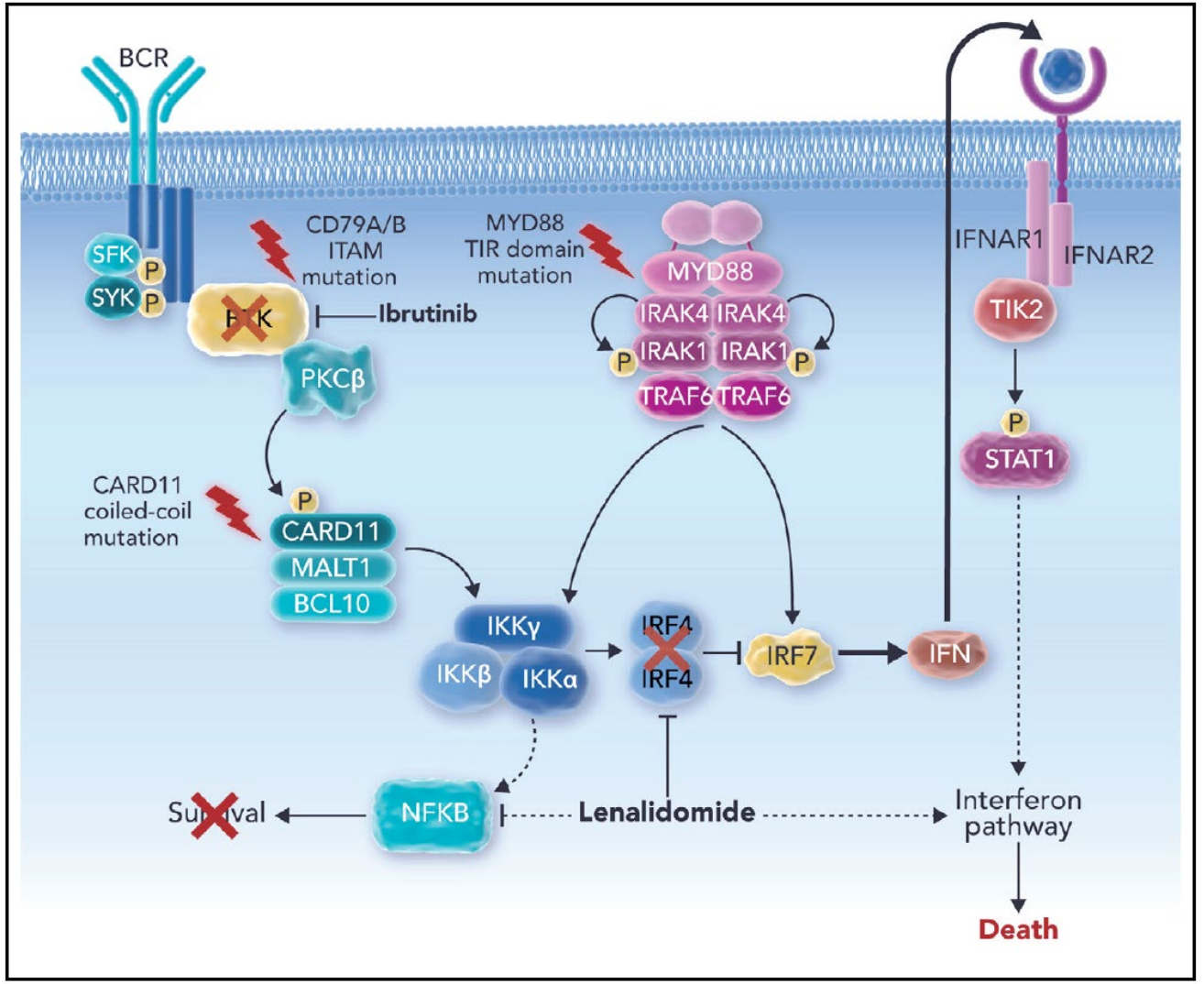


Figure from Westin J. Blood 2019;134:996–8

Dual Targeting of BTK and Immunomodulatory Activity Has Demonstrated Clinical Activity in Both Relapsed and First-Line Non-GCB DLBCL

CLINICAL TRIALS AND OBSERVATIONS

Ibrutinib plus lenalidomide and rituximab has promising activity in relapsed/refractory non–germinal center B-cell–like DLBCL

Andre Goy,[1] Radhakrishnan Ramchandren,[2] Nilanjan Ghosh,[3] Javier Munoz,[4] David S. Morgan,[5] Nam H. Dang,[6] Mark Knapp,[7] Maria Delioukina,[8] Edwin Kingsley,[9] Jerry Ping,[10] Darrin M. Beaupre,[10] Jutta K. Neuenburg,[10] and Jia Ruan[11]

ORIGINAL REPORTS | Hematologic Malignancy

Smart Start: Rituximab, Lenalidomide, and Ibrutinib in Patients With Newly Diagnosed Large B-Cell Lymphoma

Jason Westin, MD, MS[1]; R. Eric Davis, MD[1]; Lei Feng, MS[2]; Fredrick Hagemeister, MD[1]; Raphael Steiner, MD[1]; Hun Ju Lee, MD[1]; Luis Fayad, MD[1]; Loretta Nastoupil, MD[1]; Sairah Ahmed, MD[1]; Alma Rodriguez, MD[1]; Michelle Fanale, MD[1,3]; Felipe Samaniego, MD[1]; Swaminathan P. Iyer, MD[1]; Ranjit Nair, MD[1]; Yasuhiro Oki, MD[1]; Nathan Fowler, MD[1]; Michael Wang, MD[1]; Man Chun John Ma, PhD[1]; Francisco Vega, MD[4]; Timothy McDonnell, MD[4]; Chelsea Pinnix, MD, PhD[5]; Donna Griffith, RN[1]; Yang Lu, MD[6]; Sanjit Tewari, MD[6]; Ryan Sun, PhD[2]; David W. Scott, MBChB, PhD[7]; Christopher R. Flowers, MD[1]; Sattva Neelapu, MD[1]; and Michael R. Green, PhD[1,8]

Goy A, et al. Blood 2019;134:1024–36
Westin J, et al. J Clin Oncol 2022;Aug 11 (epub ahead of print)

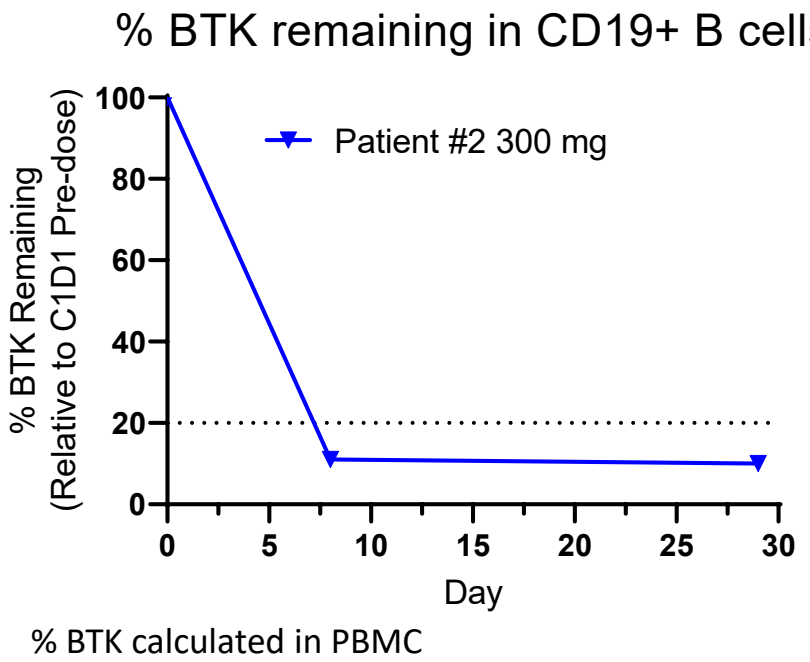
Two Heavily Pre-Treated Patients with Non-GCB DLBCL Enrolled in NX-2127 Phase 1 Dose-Escalation

	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)

*CR per Lugano criteria

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

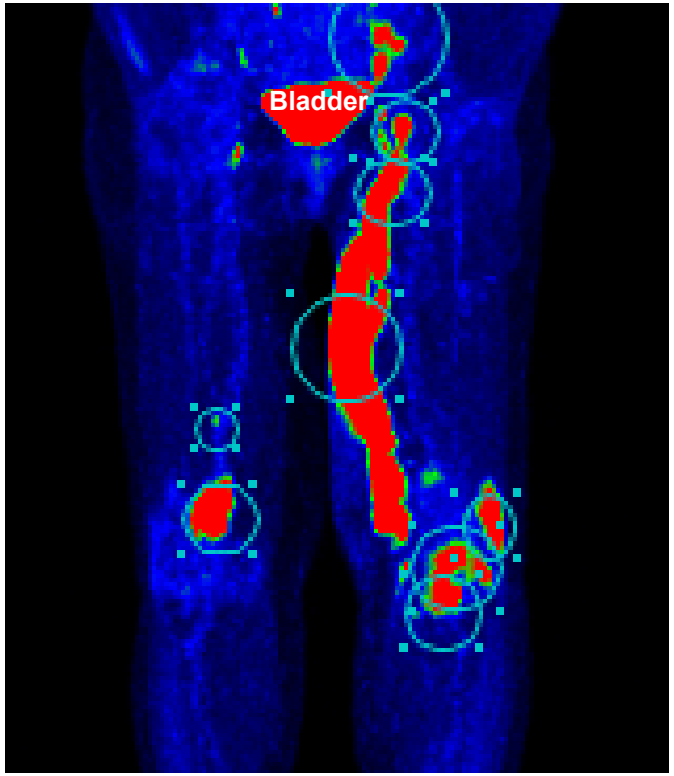


% BTK calculated in PBMC

Significant Ikaros and Aiolos degradation also confirmed by day 8

FDG-PET CT Scan Disease Assessment

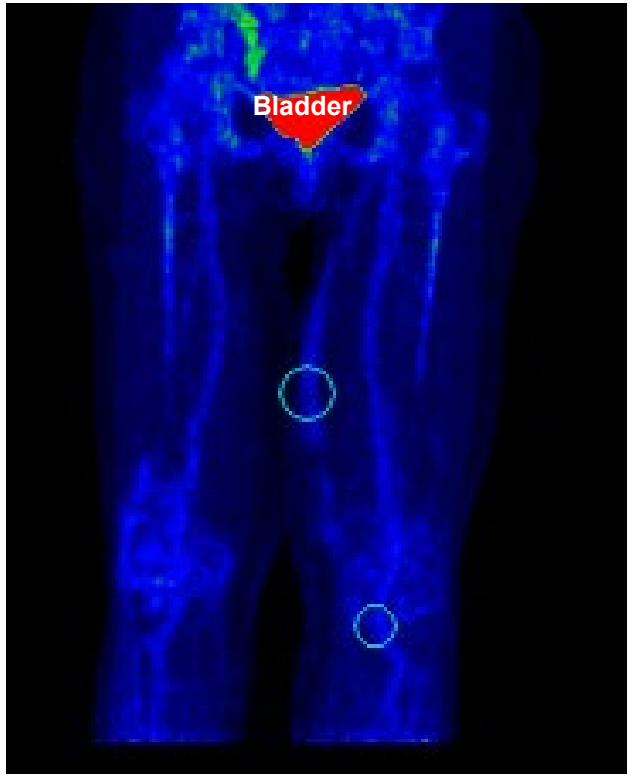
Baseline



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.

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 the American Society of Hematology (ASH) Annual Meeting in December 2022

Non-Hodgkin lymphoma (NHL)

- Rapid and complete response in patient with advanced relapsed/refractory non-GCB DLBCL
- Complete response ongoing 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 2023

Thank you