Nurix Therapeutics

European Protein Degradation Congress

September 2021

Important Notice and Disclaimers

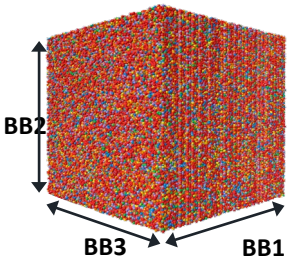
This presentation contains information relating to Nurix Therapeutics, Inc. (the “Company,” “we," "us" or "our") and forward-looking statements within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical results and other future conditions. All statements, other than statements of historical fact, contained in this presentation are forward-looking statements, including statements regarding our future financial or business performance, conditions, plans, prospects, trends or strategies and other financial and business matters; our current and prospective drug candidates; the timing of our planned IND submissions for our drug candidates; the planned timing and conduct of our clinical trial programs for our drug candidates, preclinical activities, research and development costs, current and prospective collaborations; 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 anticipated drug candidates, including our DeTIL and DeCART opportunities. In addition, when or if used in this presentation, the words “may,” “could,” “should,” “anticipate,” “believe,” “estimate,” “expect,” “intend,” “plan,” “predict” and similar expressions and their variants, as they relate to the Company may identify forward-looking statements. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Readers are cautioned that actual results, levels of activity, performance or events and circumstances could differ materially from those expressed or implied in our forward-looking statements due to a variety of factors, including risks and uncertainties related to our ability to advance our drug candidates; our ability to obtain regulatory approval of and ultimately commercialize our product candidates; the timing and results of preclinical and clinical trials; our ability to fund development activities and achieve development goals; the impact of the COVID-19 pandemic on our business; our ability to protect intellectual property; and other risks and uncertainties described under the heading “Risk Factors” in our Annual Report on Form 10-K for the fiscal year ended November 30, 2020 filed with the Securities and Exchange Commission (the “SEC”) on February 16, 2021, our Quarterly Report on Form 10-Q for the fiscal quarter ended May 31, 2021 filed with the SEC on July 13, 2021, and other filings we make from time to time with the SEC. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein.

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 is reliable, such estimates and research have not been verified by any independent source.

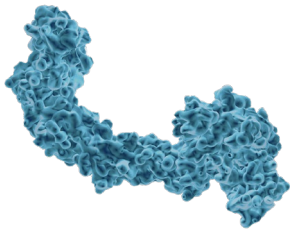
Targeted Protein Degradation is Only the Beginning
Controlling Protein Fate to Treat Disease

- Nurix can modulate specific protein levels up or down with its drug discovery platform
- DELigase™ is a versatile drug discovery platform comprised of massive DNA-encoded libraries to screen an expanded universe of E3 ligases and proteins previously thought to be undruggable
- Four wholly-owned oncology and immunology drug candidates expected to enter the clinic in 2021*
- Revenue generating drug discovery partnerships with Sanofi and Gilead fuel future pipeline
- Applying targeted protein modulation to create new adoptive cell therapies for cancer and to discover anti viral drugs

Protein Modulation Platform



Proprietary DNA-Encoded Libraries, >10^9 compounds



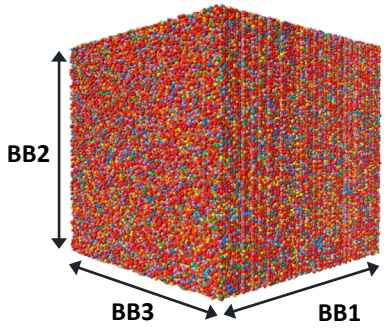
>30 E3 ligases currently in discovery

Chimeric Targeting Molecules (CTMs) ***Decrease*** **specific protein levels**

Ligase Inhibitors ***Increase*** **specific protein levels**

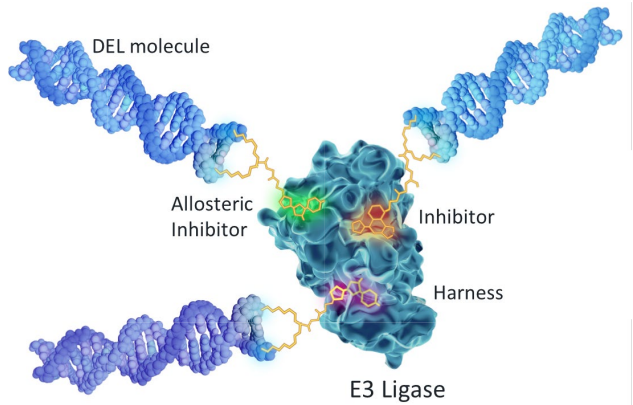
*Expected Phase 1 clinical trial timing based on calendar-year periods

DEL is at the Center of Nurix's Discovery Platform



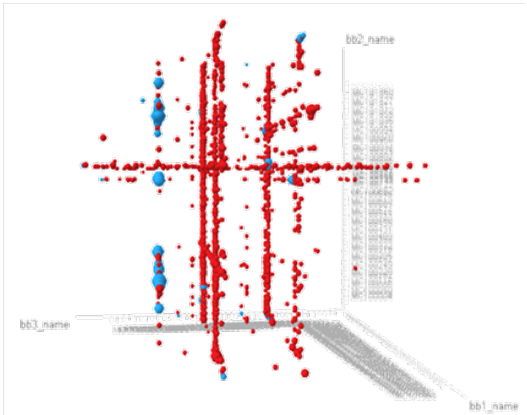
DNA-Encoded library

- > 1 billion compounds represented in DEL "cube"
- Combinatorial 3D matrix of >1,000 building blocks
- Allows massively parallel screening
- Identifies novel binders to both ligases and target proteins



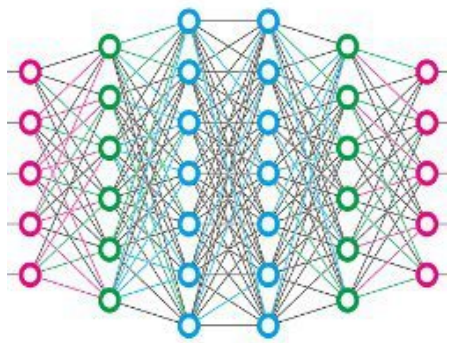
Finding novel binders to difficult targets

- Screening complex mixtures without a biochemical assay
- Binders identified by unique DNA tag using PCR
- Assays run under multiple conditions to find competitive inhibitors, allosteric inhibitors, and binders



DEL generates matrix of hit series

- Hits can be visualized based on position within the DEL cube
- Multiple hits identified in single reaction
- Clusters of hits provide insight into structure activity relationship



Machine learning

- Information-rich DEL output can be analyzed using machine learning
- Artificial intelligence used to identify hits outside of our library
- Synthesis of in-silico hits have a remarkably high rate of target interaction

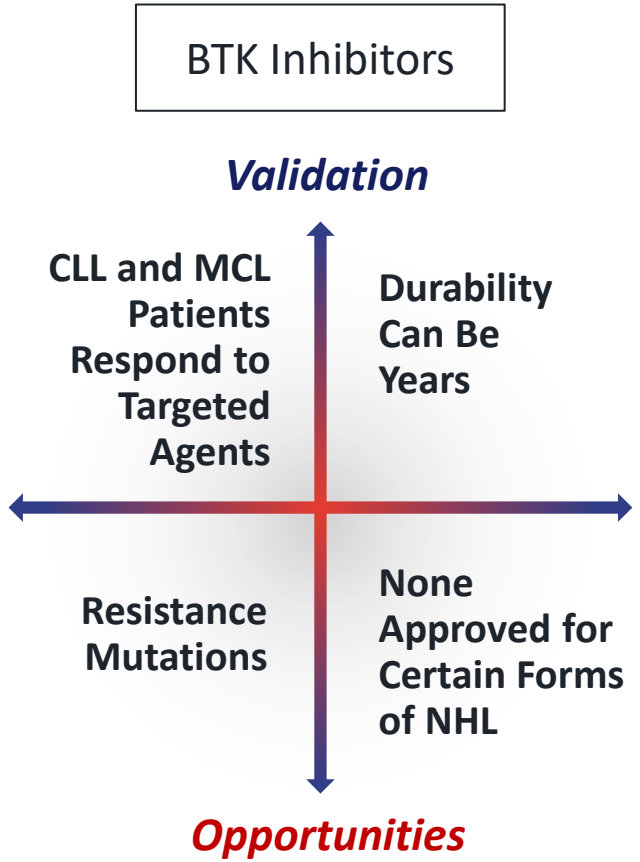
Nurix's Wholly-Owned Targeted Protein Modulation Drug Pipeline: Four Clinical Programs Expected This Year

Drug Candidate	Target / Delivery	Therapeutic Area	Discovery	Lead Optimization	Preclinical	Phase 1	Phase 2	Phase 3
Protein Degradation Chimeric Targeting Molecule (CTM) Portfolio								
NX-2127	BTK + IMiD activity *Oral*	B-cell Malignancies						
NX-5948	BTK *Oral*	B-cell Malignancies and Autoimmune Diseases				Commence in H2 2021*		
KINASE-CTM3	T Cell Kinase	T-cell Malignancies and Autoimmune Diseases						
COVID-CTM	Intracellular SARs COV-2 proteins	Anti-viral						
Ligase Inhibition Portfolio								
NX-1607	CBL-B *Oral*	Immuno-oncology				Commence in H2 2021*		
DeTIL-0255	CBL-B (NX-0255) *ex vivo*	Adoptive Cell Therapy (ACT)				Commence in H2 2021*		
LIGASE-INH2	Undisclosed	Immuno-oncology						

* Expected timing of commencement of Phase 1 clinical trials based on calendar-year periods

BTK Degraders: A Differentiated Approach to B-Cell Malignancies in BTK Inhibitor Failures

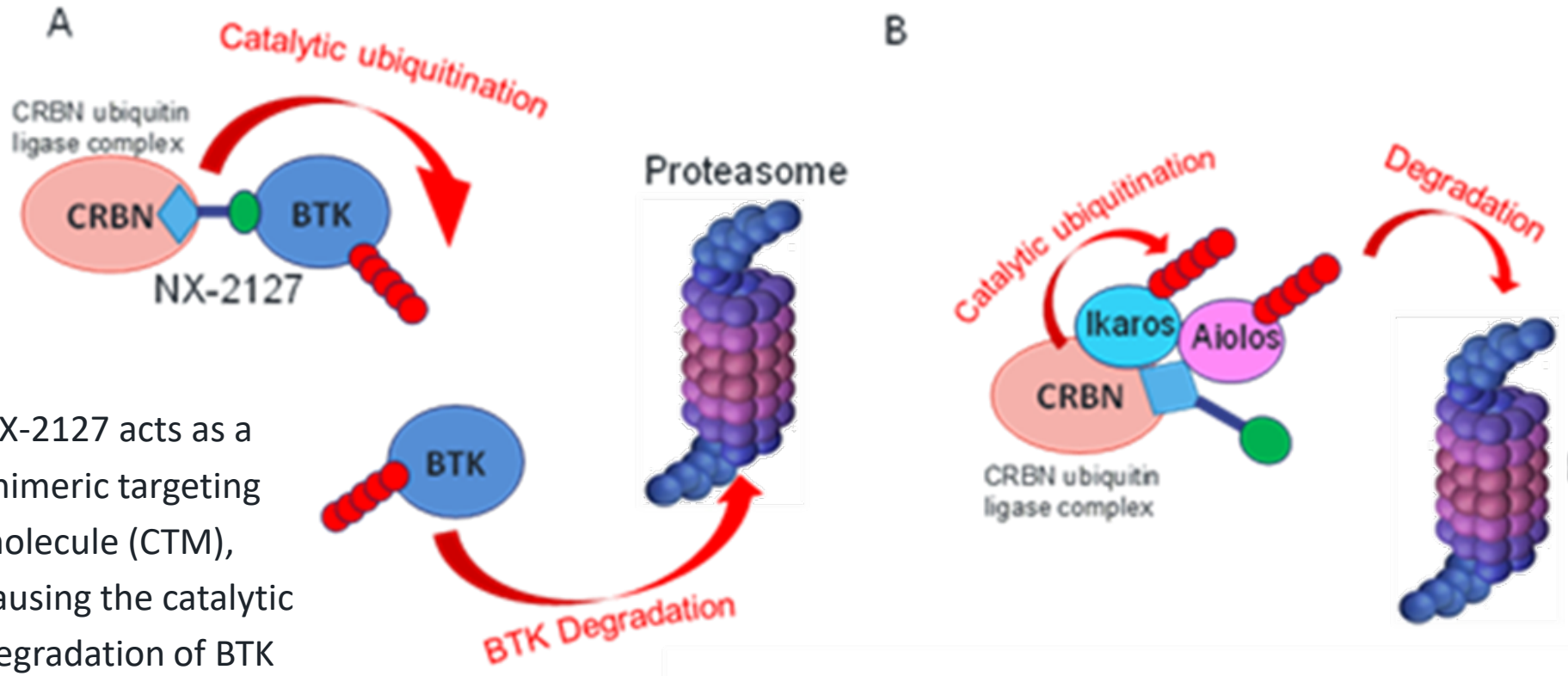
- **BTK is a validated target**
  - Global sales of BTK inhibitors were approximately $7.1 billion in 2020
  - BTK inhibitors are approved by the FDA for five different diseases across multiple lines of therapy (CLL/SLL, mantle cell lymphoma, Waldenstrom's, marginal zone lymphoma, GVHD)
- **Fast to market strategy and future expansion**
  - Initial focus on fast to market opportunity as a potentially superior treatment for relapsed and resistant chronic lymphocytic leukemia (CLL) and C481S resistance to ibrutinib
  - Expand beyond CLL: An estimated 77,000 people in the United States were diagnosed with Non-Hodgkin's Lymphoma (NHL) in 2020 and 85% of NHLs are a result of B-cell malignancies
  - Opportunities: Follicular lymphoma and diffuse large B-cell lymphoma (DLBCL), areas where BTK inhibitors have not been approved nor proven successful



NX-2127: BTK degrader with IMiD activity. Developing for B-cell malignancies benefiting from combination activity.

NX-5948: BTK degrader without IMiD activity. Developing for B-cell malignancies and autoimmune diseases with potential CNS activity.

Dual Function of NX-2127 Combines Two Mechanisms of Action: BTK Degradation plus IMiD Activity

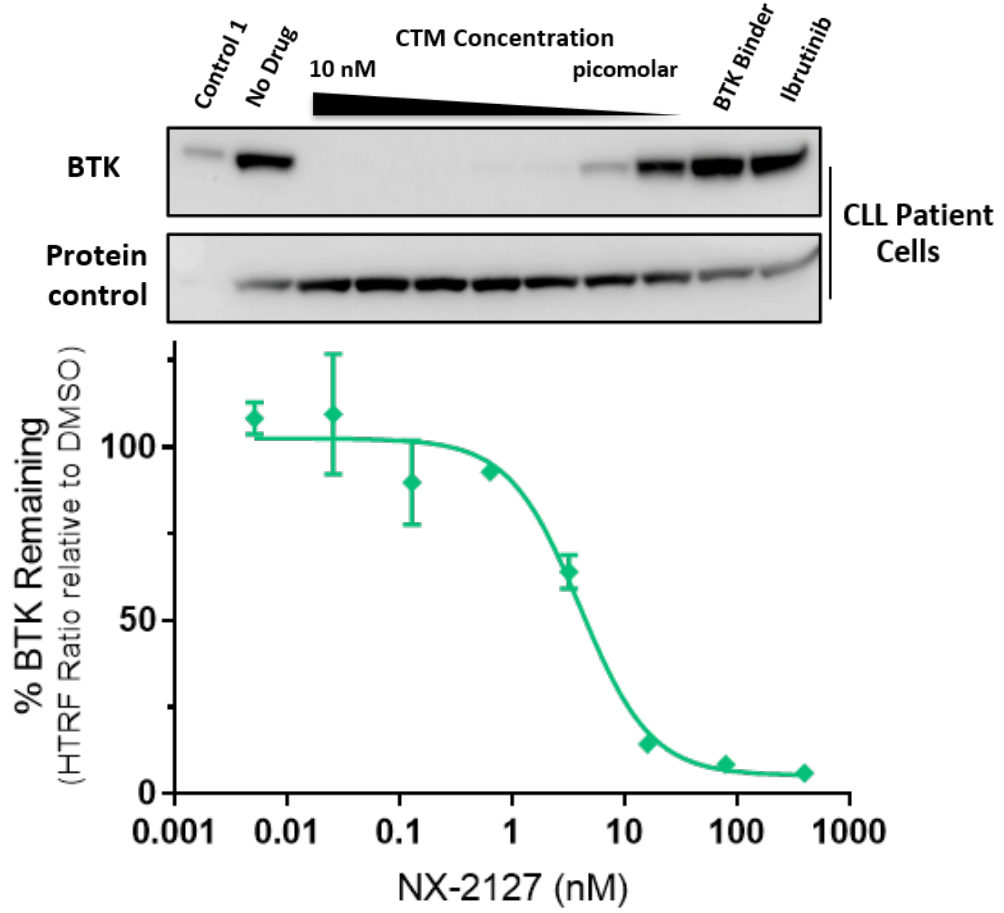


- NX-2127 acts as a chimeric targeting molecule (CTM), causing the catalytic degradation of BTK and Aiolos

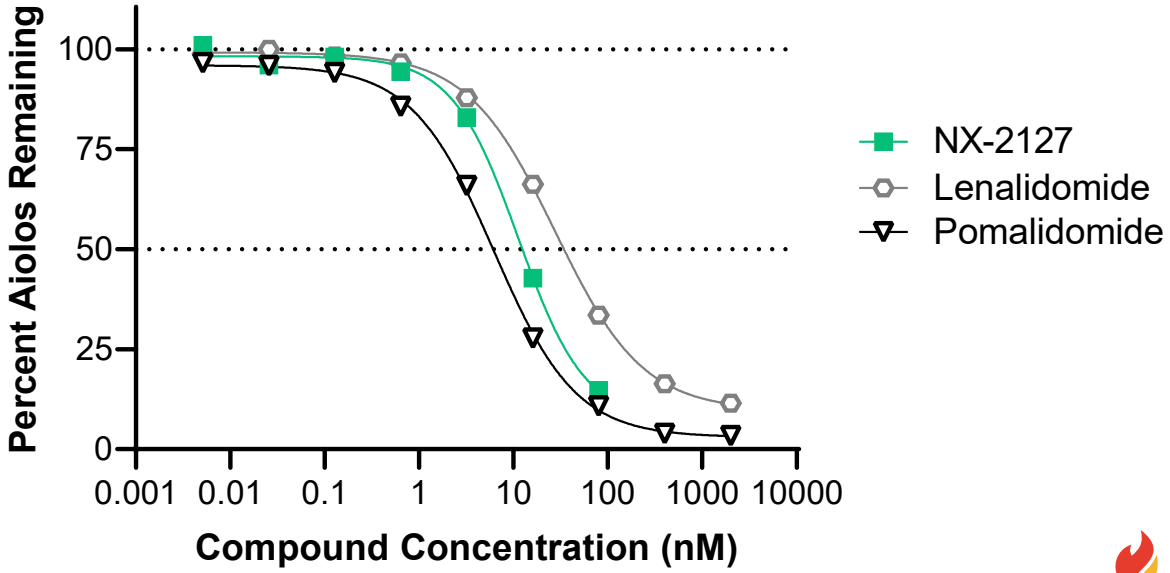
- NX-2127 utilizes a "harness" that retains the molecular glue activity of the IMiD class of drugs, causing the catalytic degradation of Ikaros and Aiolos
- The dual activity gives NX-2127 a unique profile relative to both BTK inhibitors and to IMiDs

NX-2127 Degrades Both BTK and Aiolos

NX-2127 shows potent BTK degradation in CLL patient cells and TMD8 cells (human DLBCL cell line)



NX-2127 IMiD Activity: Aiolos Degradation in Naïve Human T Cells at similar potency to Pomalidomide and Lenalidomide



BTK / IMiD Combination Therapeutic Advantage

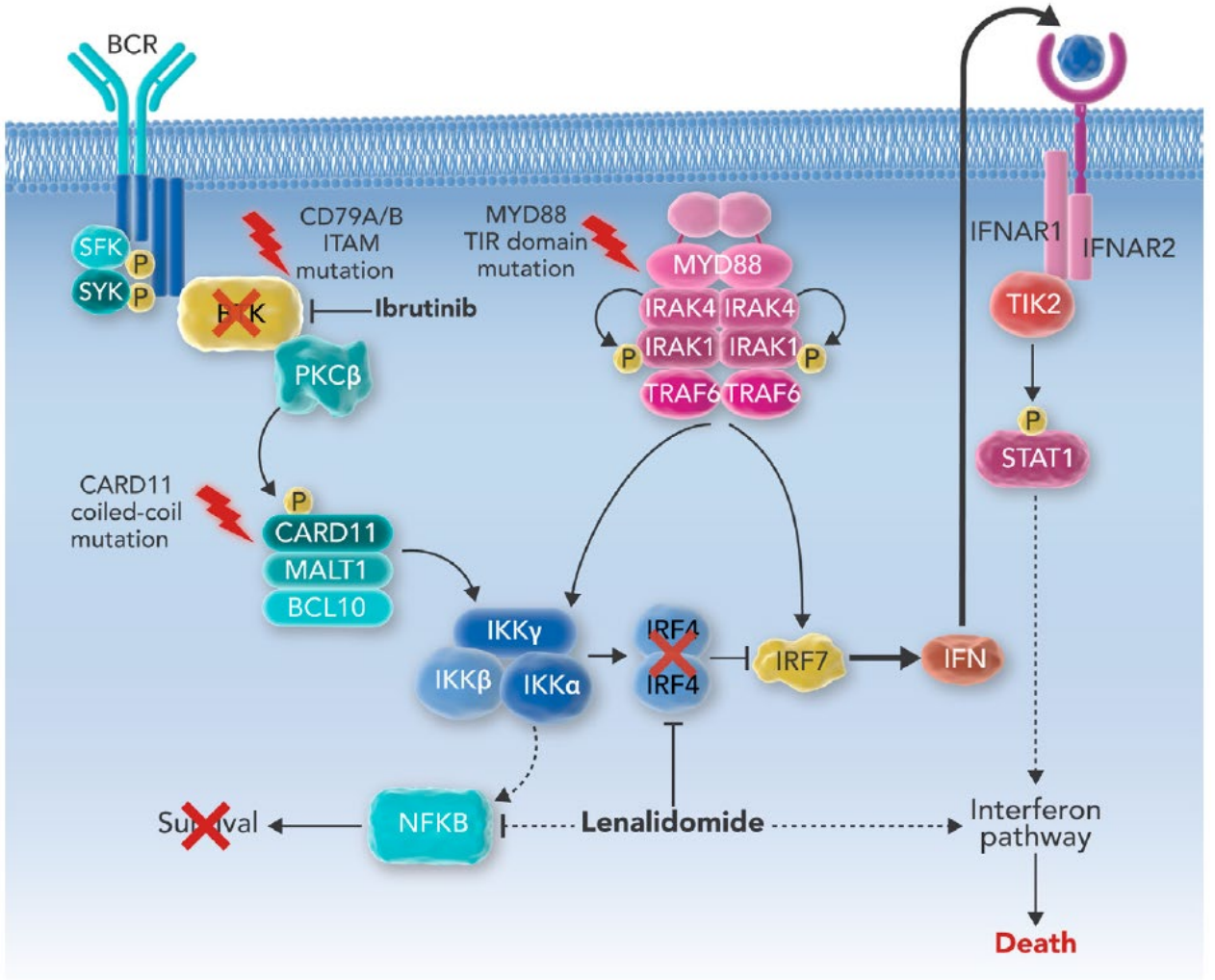
CLINICAL TRIALS AND OBSERVATIONS

Comment on Goy et al, page 1024

Ibrutinib and lenalidomide: when 1+1 = >2

Jason Westin | MD Anderson Cancer Center

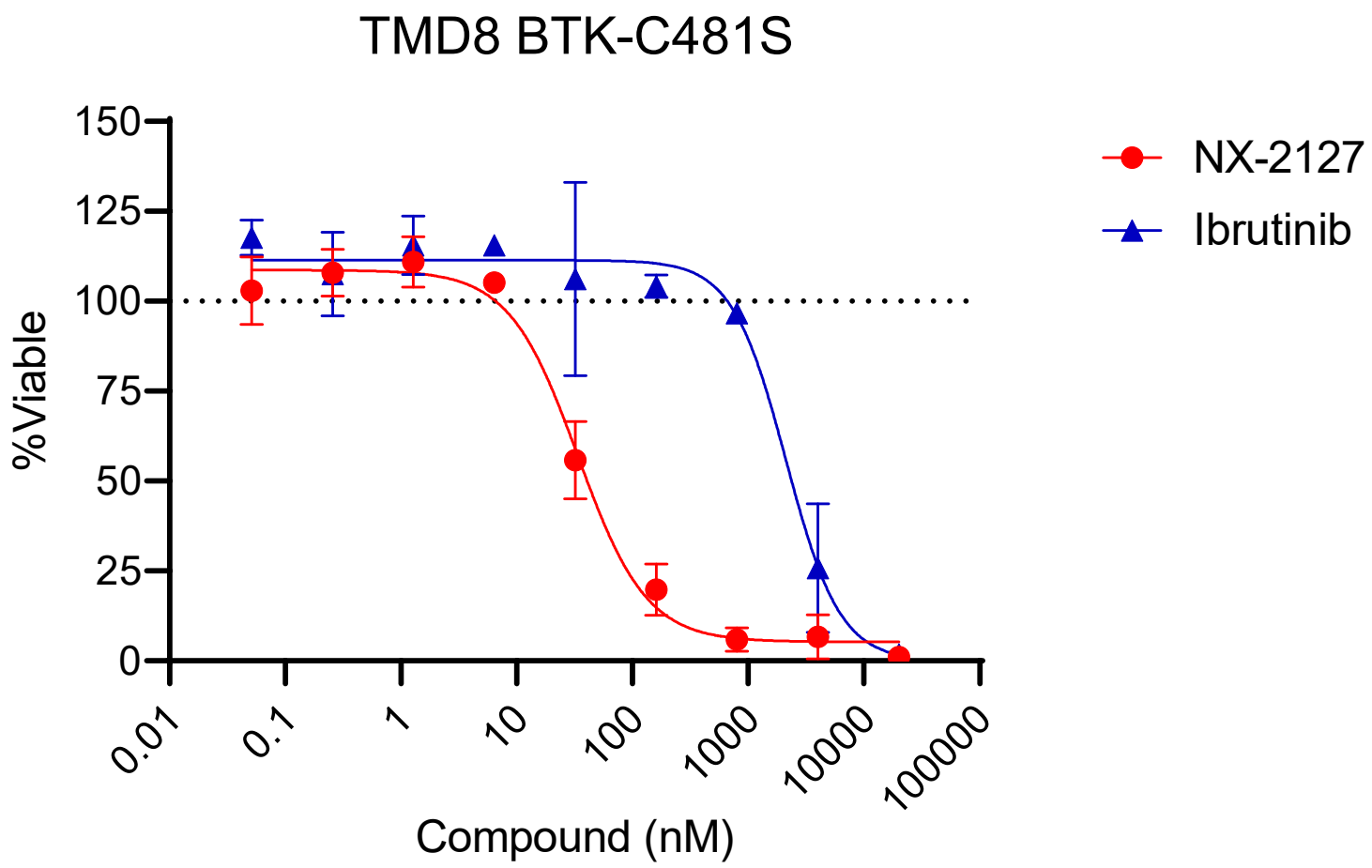
- IMiDs and BTK inhibitors are both approved as single agents in mantle cell lymphoma, suggesting a drug with both activities may provide added benefit to either alone
- In DLBCL (diffuse large B cell lymphoma), there is *in vitro* evidence of synthetic lethality of BTK inhibitors and IMiDs through blockade of IRF4 (interferon regulatory factor 4) and the upregulation of interferon pathway, which is toxic for the ABC subtype of DLBCL*
- IMiDs activate T cells, which may deepen and prolong the anti-tumor activity of a BTK degrader, potentially across multiple B-cell malignancies



* Westin, *Blood,* 2019, 134 (13), p. 996-998.

NX-2127 Potently Inhibits Growth of Ibrutinib-Resistant Tumor Cell Lines

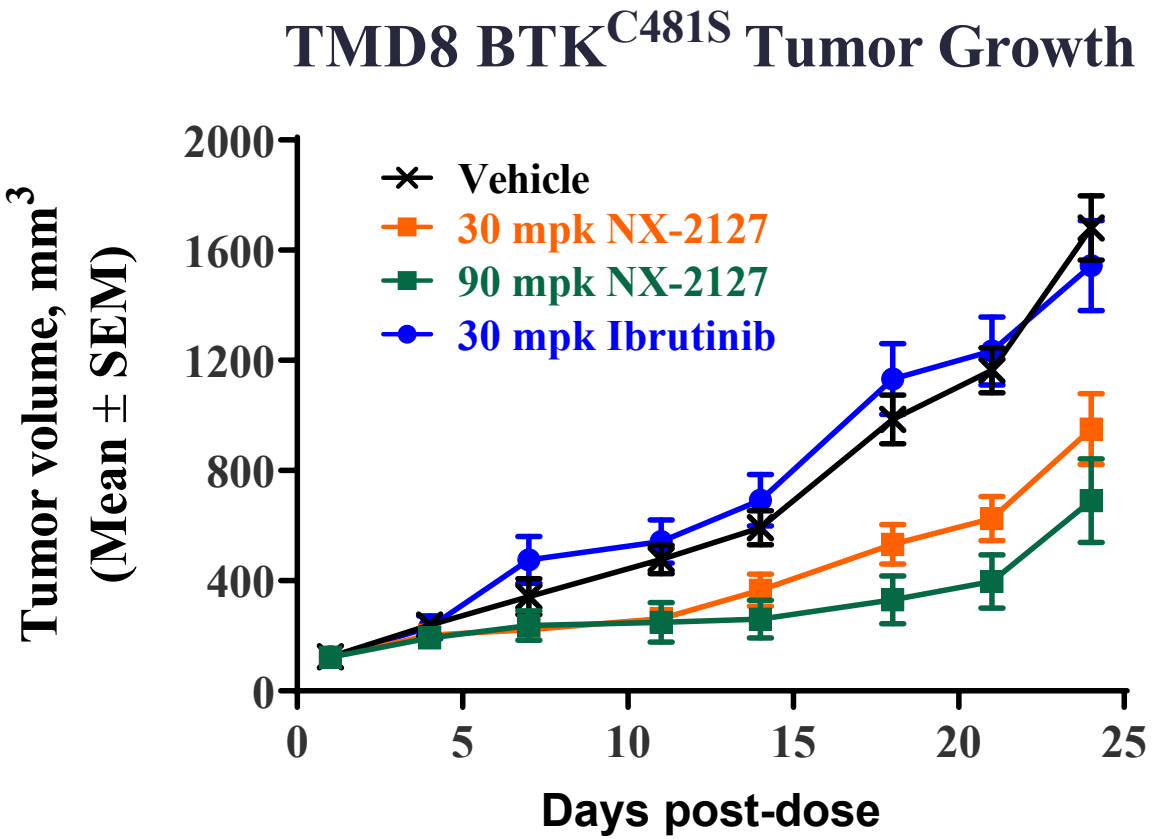
Growth inhibition of ibrutinib-resistant DLBCL lymphoma cell line



- NX-2127 retains potent growth inhibition activity relative to BTK inhibitors in a tumor cell line carrying the C481S mutation
- Degradation of BTK with NX-2127 may offer a therapeutic option for patients who develop resistance to BTK inhibitors
- NX-2127 also shows superior activity to BTK inhibitors in wild-type TMD8 cells

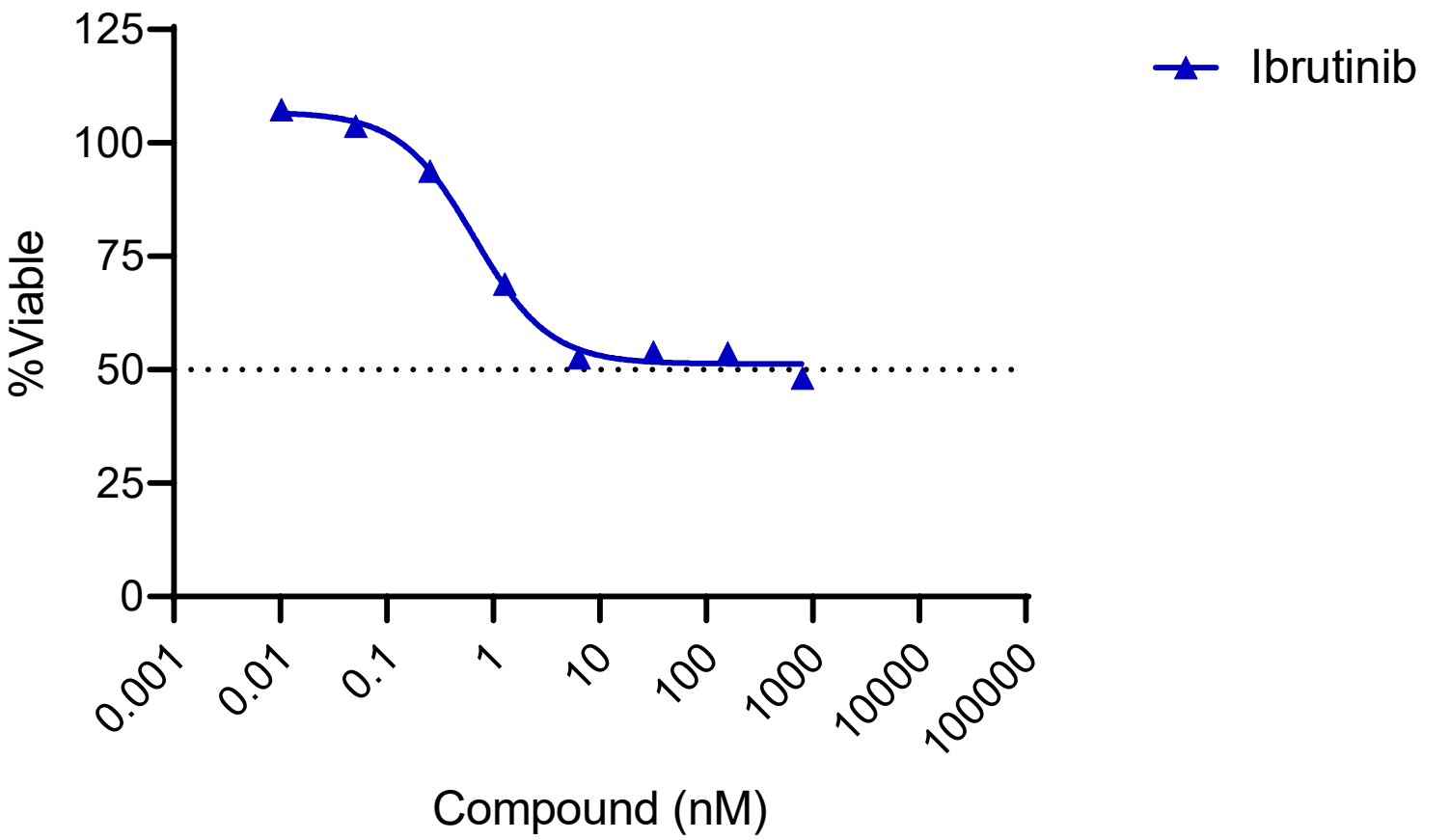
Oral NX-2127 Demonstrates Cancer Growth Inhibition in BTK Resistant Mouse Tumor Models

Tumor Growth Inhibition in Xenograft Model of Mutant Ibrutinib-Resistant Lymphoma



- NX-2127 shows potent tumor growth inhibition in a model of ibrutinib-resistance due to the C481S mutation, the most common human resistance mutation in the BTK target protein
- NX-2127 also shows superior anti-tumor activity versus ibrutinib in cell lines with wild-type BTK

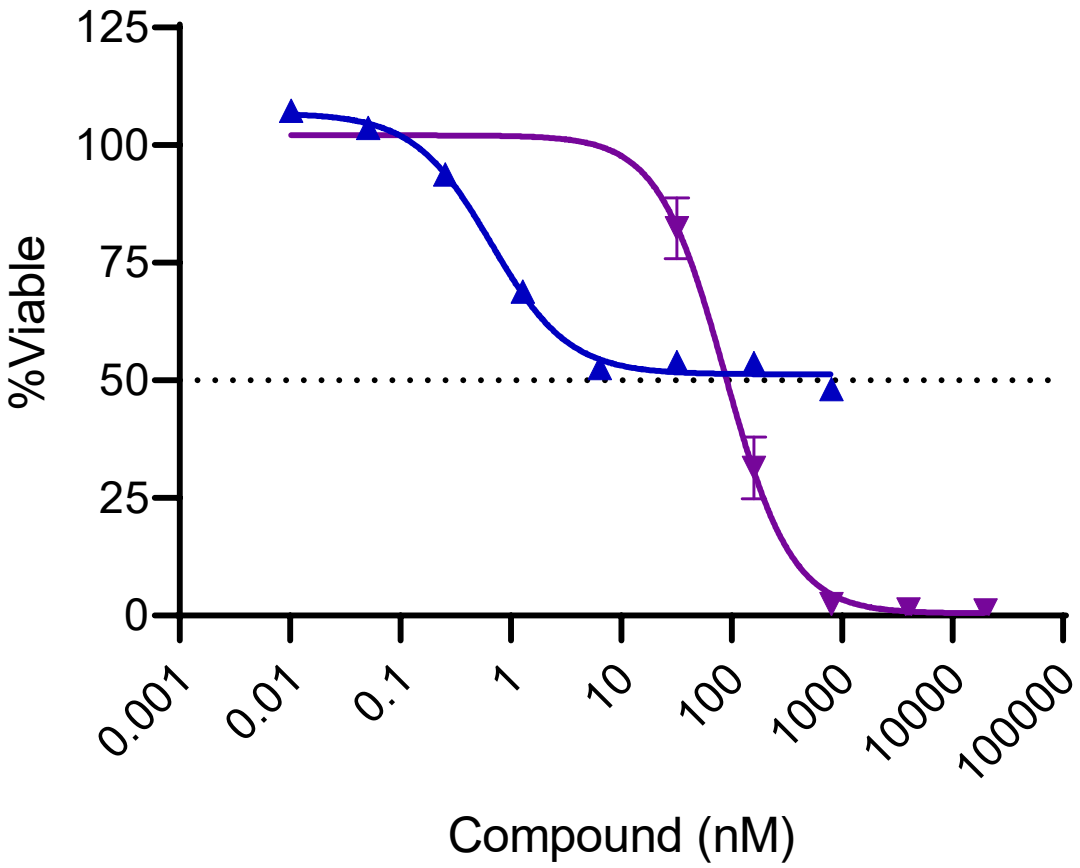
BTK Targeted Agents are Potent Against the REC-1 Mantle Cell Lymphoma (MCL) Cell Line with Incomplete Killing



- **Compounds active against BTK reduce cell viability at low doses, but this effect plateaus**

IMiDs are Less Potent Against the REC-1 MCL Cell Line but Demonstrate More Complete Killing

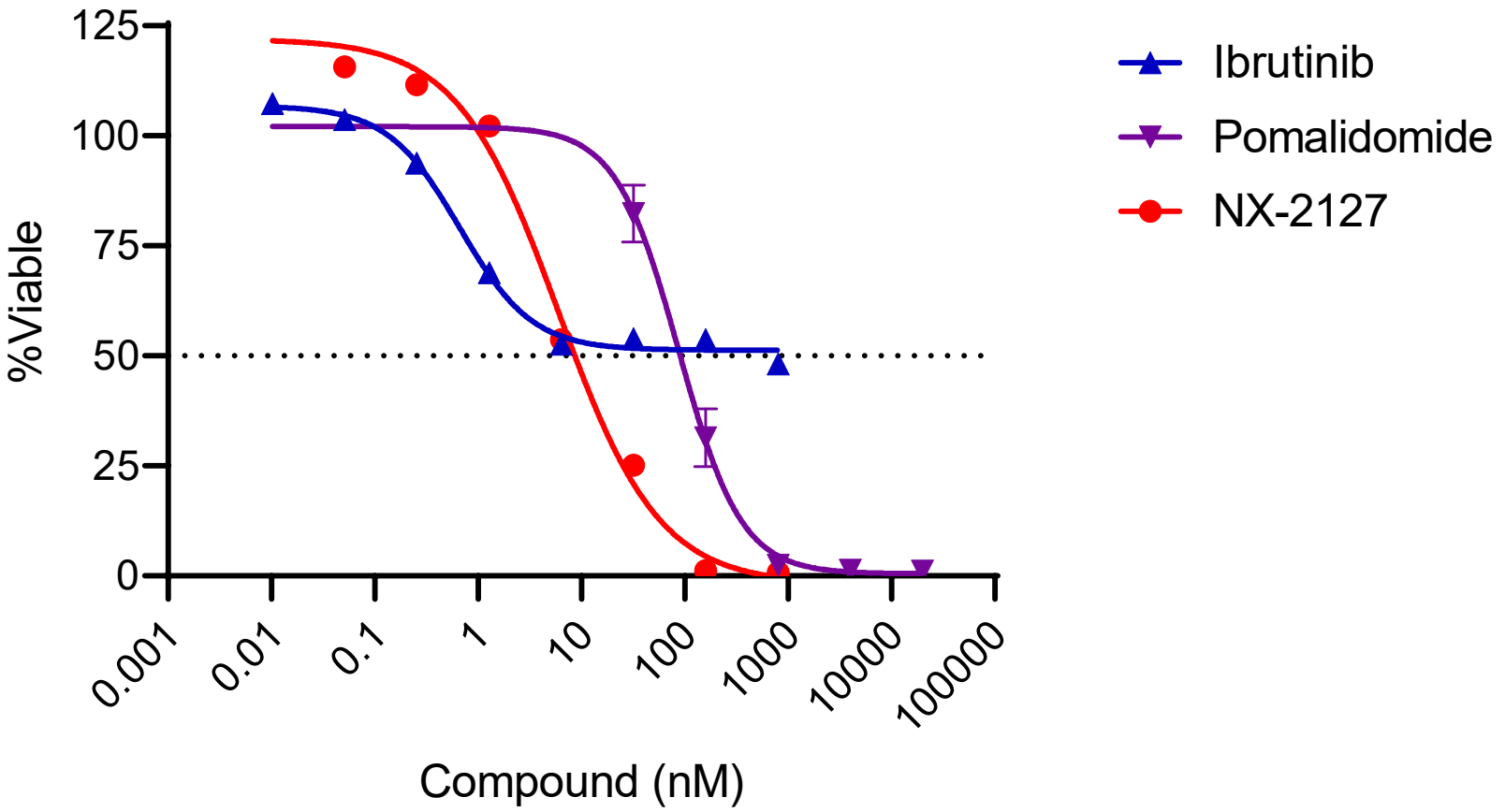
REC-1 (Mantle Cell Lymphoma)



- Compounds active against BTK reduce cell viability at low doses, but this effect plateaus
- **IMiDs promote more complete killing but require higher doses to reduce cell viability**

NX-2127 is Both Potent and Provides Complete Cell Killing in the REC-1 MCL Model

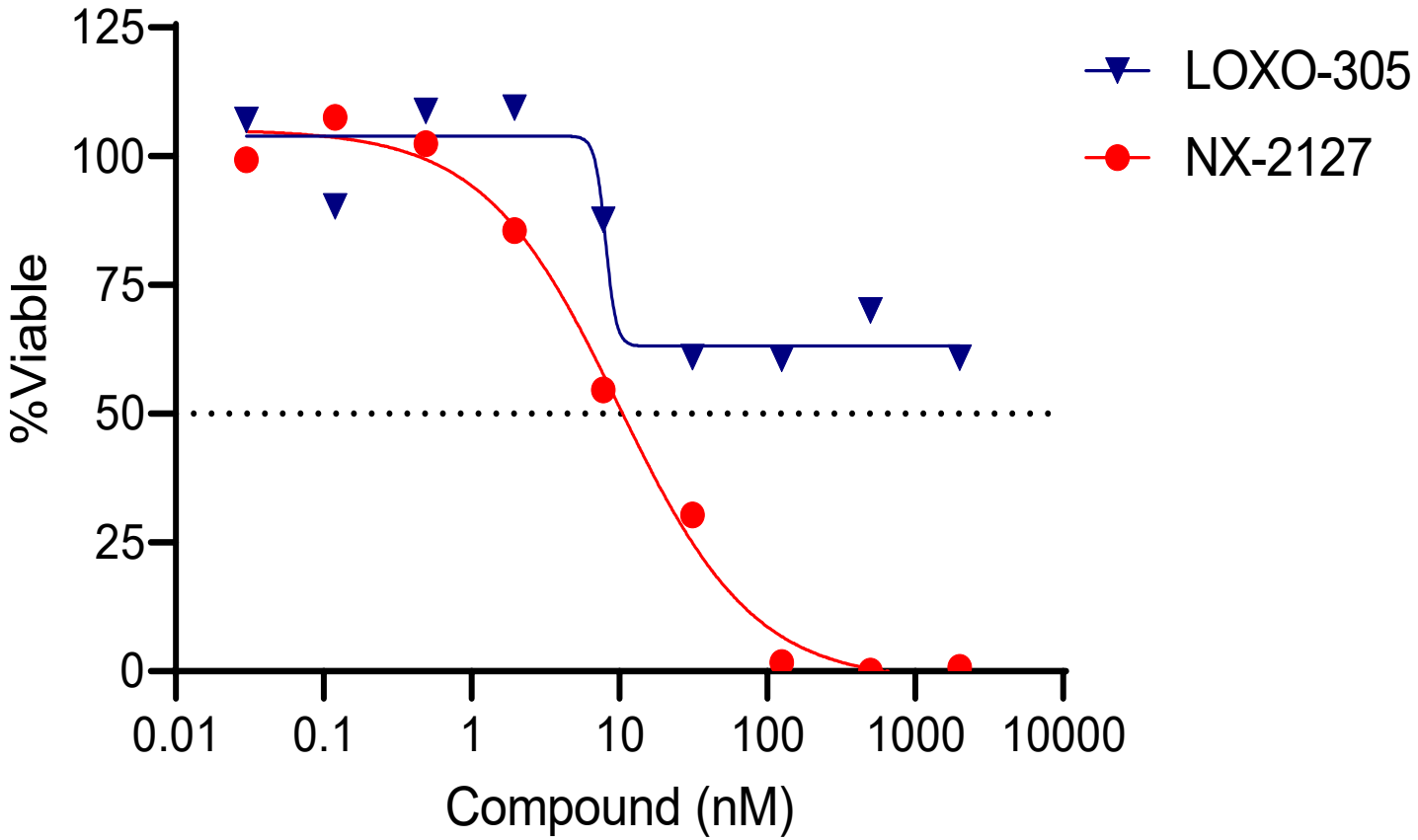
REC-1 (Mantle Cell Lymphoma)



- Compounds active against BTK reduce cell viability at low doses, but this effect plateaus
- IMiDs promote more complete killing but require higher doses to reduce cell viability
- **The combined BTK and IMiD activities of NX-2127 allow it to potently and completely kill REC-1 cells**

NX-2127 Kills REC-1 Cells More Completely than Next-Generation BTK Inhibitor LOXO-305 (pirtobrutinib)

REC-1 (Mantle Cell Lymphoma)



- The next generation non-covalent BTK inhibitor, pirtobrutinib, has an activity curve similar to other BTK inhibitors
- NX-2127 shows similar potency and greater depth of cell killing compared to pirtobrutinib

NX-2127: Phase 1 Clinical Trial Ongoing

Phase 1a - Monotherapy
Dose Escalation
(n= ~24)

Dose L4
Dose L3
Dose L2
Dose L1

Patients: relapsed/refractory B-cell malignancies
- Oral dosing once per day
- 4 to 6 cohorts
- Total projected patients, n = ~24

Phase 1b Monotherapy Expansion
Recommended Phase 2 Dose
(n= ~100)

Chronic Lymphocytic Leukemia (CLL) with C481 mutation (n=~20)

CLL – unselected (n=~20)

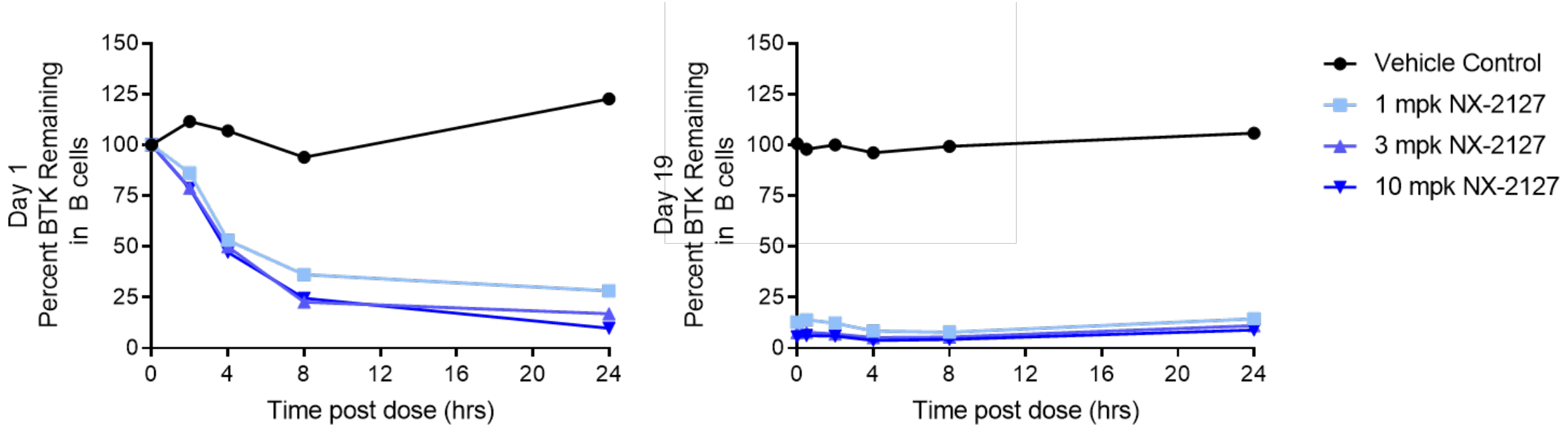
Mantle Cell Lymphoma (MCL), Marginal Zone Lymphoma (MZL), Waldenstrom's Macroglobulinemia (WM) (n=~20)

Follicular Lymphoma (FL) (n=~20)

Diffuse Large B-Cell Lymphoma (DLBCL) (n=~20)

- Establish proof of concept in relapsed and refractory B-cell malignancies including those in which have shown ibrutinib resistance or intolerance
- Planning a two-part Phase 1 monotherapy trial in relapsed or refractory NHL and CLL
  - Phase 1a:
    - Assess safety and tolerability
    - Assess PK: PD via degradation MOA
    - Identify maximum tolerated dose
  - Phase 1b:
    - 5 cohorts of up to 20 patients each
    - Patients with CLL, CLL + C481 mutation, MCL, MZL or WM, FL and DLBCL

Oral Dosing of NX-2127 Degrades BTK in Non-Human Primates



- Significant degradation of BTK in 4 hours and more than 90% degradation through 24 hours post dosing at the highest dose level
- Once daily, oral dosing of NX-2127 maintains suppression of BTK protein levels throughout the 19-day duration of the study (NX-2127 PK $t_{1/2}$ = 5.4 h)

Nurix's Wholly-Owned Targeted Protein Modulation Drug Pipeline: Four Clinical Programs Expected This Year

Drug Candidate	Target / Delivery	Therapeutic Area	Discovery	Lead Optimization	Preclinical	Phase 1	Phase 2	Phase 3
Protein Degradation Chimeric Targeting Molecule (CTM) Portfolio								
NX-2127	BTK + IMiD activity *Oral*	B-cell Malignancies						
NX-5948	BTK *Oral*	B-cell Malignancies and Autoimmune Diseases				Commence in H2 2021*		
KINASE-CTM3	T Cell Kinase	T-cell Malignancies and Autoimmune Diseases						
COVID-CTM	Intracellular SARs COV-2 proteins	Anti-viral						
Ligase Inhibition Portfolio								
NX-1607	CBL-B *Oral*	Immuno-oncology				Commence in H2 2021*		
DeTIL-0255	CBL-B (NX-0255) *ex vivo*	Adoptive Cell Therapy (ACT)				Commence in H2 2021*		
LIGASE-INH2	Undisclosed	Immuno-oncology						

* Expected timing of commencement of Phase 1 clinical trials based on calendar-year periods

Thank you

Nurix Therapeutics