Nurix Therapeutics

Blazing a New Path in Medicine

Targeted Protein Modulation: Harnessing or Inhibiting E3 Ligases to Decrease or Increase Protein Levels

TPD Conference 2020

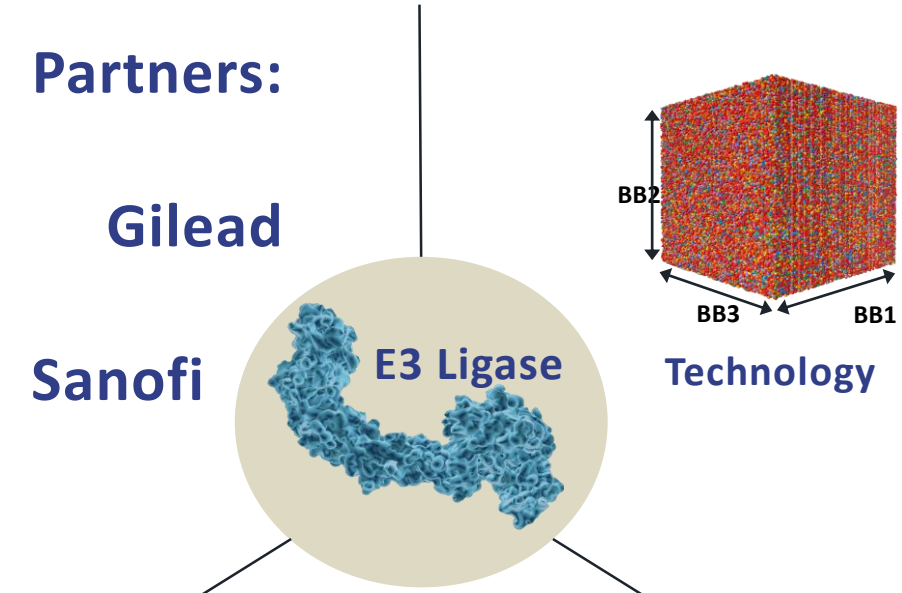
Important Notice and Disclaimers

This presentation contains forward-looking statements and information relating to Nurix Therapeutics, Inc. (the “Company,” “we," "us" or "our"). 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 facts, contained in this presentation are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, 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 product candidates; the timing of our planned IND submissions for our product candidates; the potential advantages of our DELigase™ platform and product candidates, including NX-1607 and NX-0255; the extent animal model data predicts human efficacy; and the success and timing of our development and commercialization of our product 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 product candidates; 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 final prospectus pursuant to Rule 424(b)(4) filed with the Securities and Exchange Commission (the “SEC”) on July 24, 2020 and in our Quarterly Report on Form 10-Q for the quarter ended August 31, 2020, as well as other SEC filings. 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.

Nurix: A Targeted Protein Modulation Company

- Targeting E3 ligases to develop small molecule targeted protein modulation drug candidates that can *increase* or *decrease* protein levels
- Four wholly-owned oncology and immunology drug candidates with first clinical trial expected to commence in H1 2021
- Applying targeted protein modulation to create new adoptive cell therapies for cancer and to discover anti viral drugs
- DELigase™: a versatile drug discovery platform comprised of massive DNA-encoded libraries to screen an expanded universe of E3 ligases
- Revenue generating drug discovery partnerships with Sanofi and Gilead



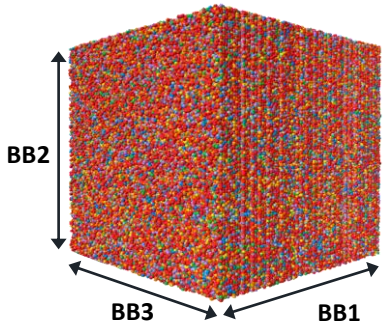
Pipeline

Drug Candidate	Target / Delivery	Therapeutic Area	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		*Late Q4 '20 – Q1 '21			
NX-5948	BTK *Oral*	B-cell Malignancies And GVHD		*H2 '21			
Ligase Inhibition Portfolio							
NX-1607	CBL-B *Oral*	Immuno-oncology		*Q3 '21			
DeTIL-0255	CBL-B *ex vivo*	Adoptive Cell Therapy (ACT)		*H2 '21			

*Expected IND submission timing based on calendar year quarters

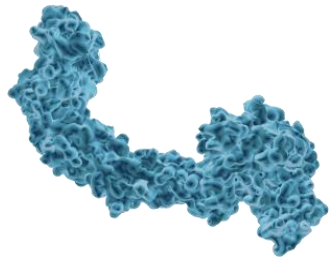
DELigase™: Platform Enables Two Complementary Protein Modulation Approaches for Drug Discovery

1



Proprietary DNA-Encoded Libraries, >10^9 compounds

2



Expanded universe of E3 ligases, >30 ligases currently in discovery

Protein Modulation Platform

Inhibitors *of* E3 Ligases

Harnesses *of* E3 Ligases

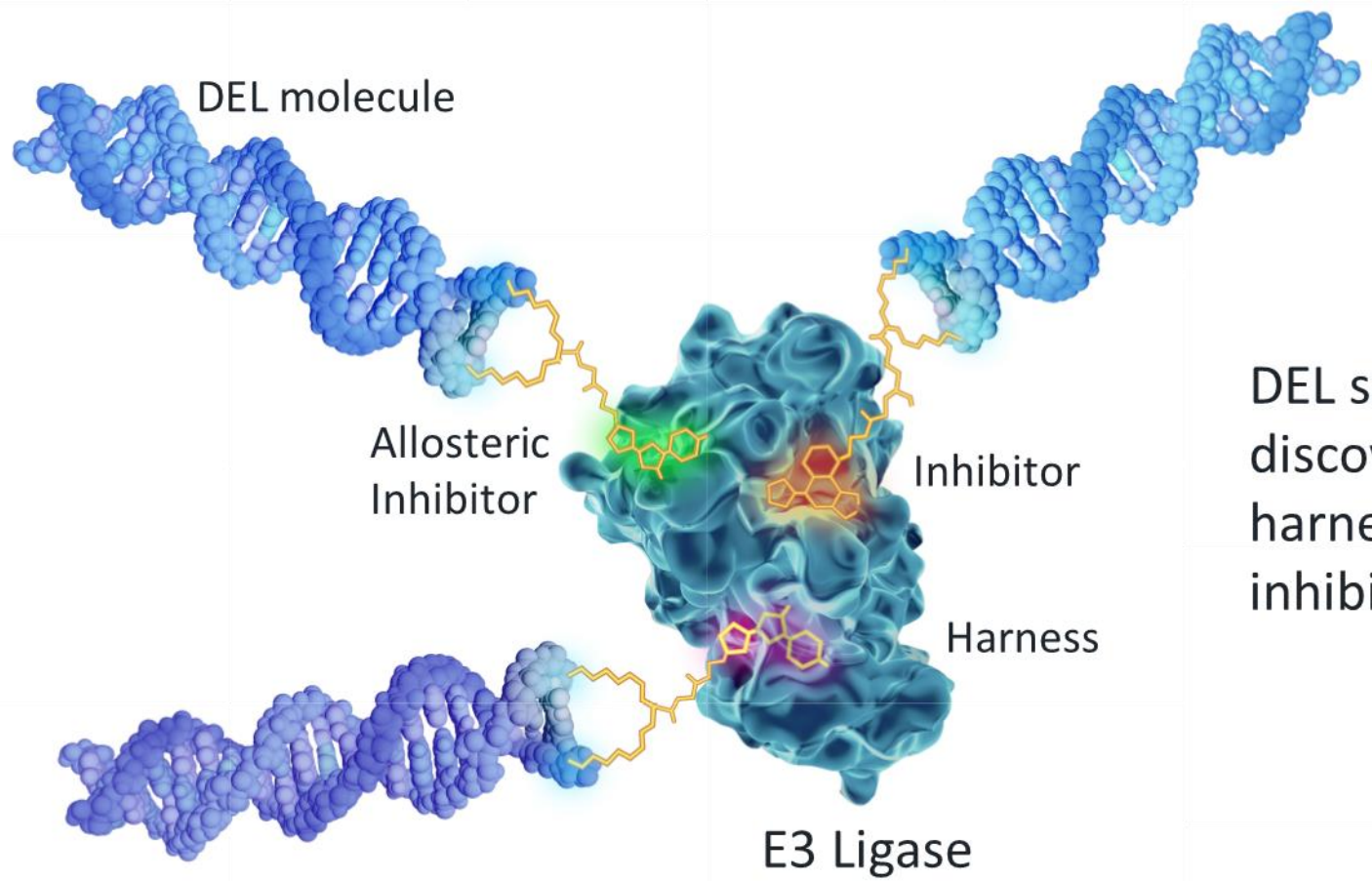
Ligase Inhibitors *Increase* specific protein levels

3 Ability to push protein levels in either direction

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

Drug Development

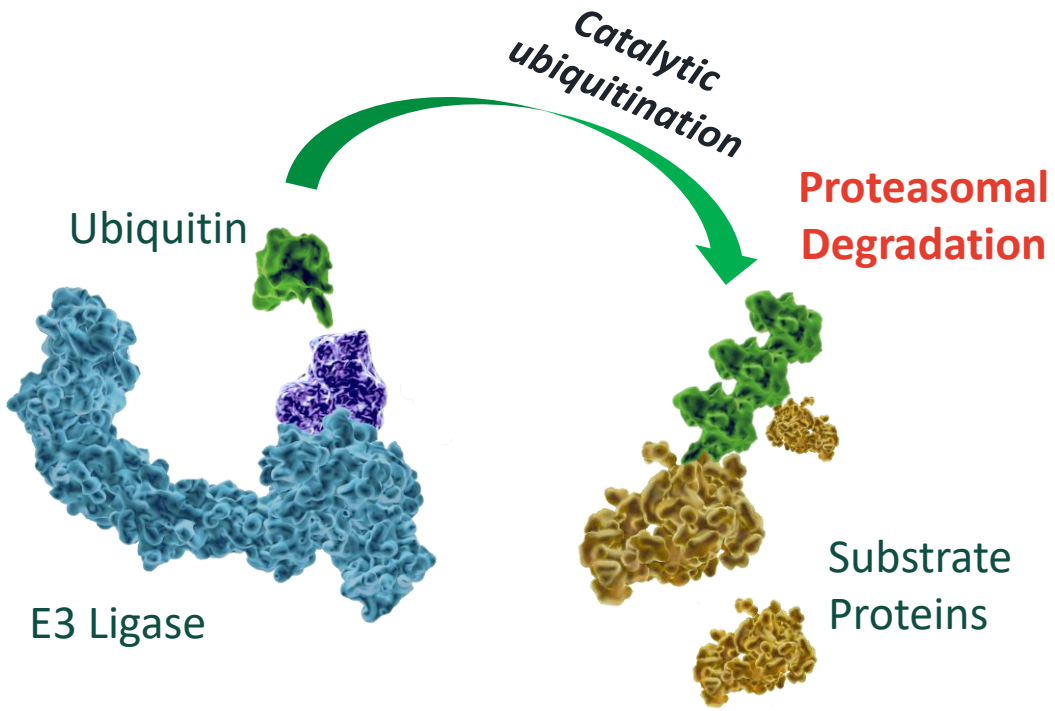
DELigase™ Identifies a Spectrum of Binders Across the Ligase Surface



DEL screening enables discovery of both harnesses and inhibitors of E3 ligases

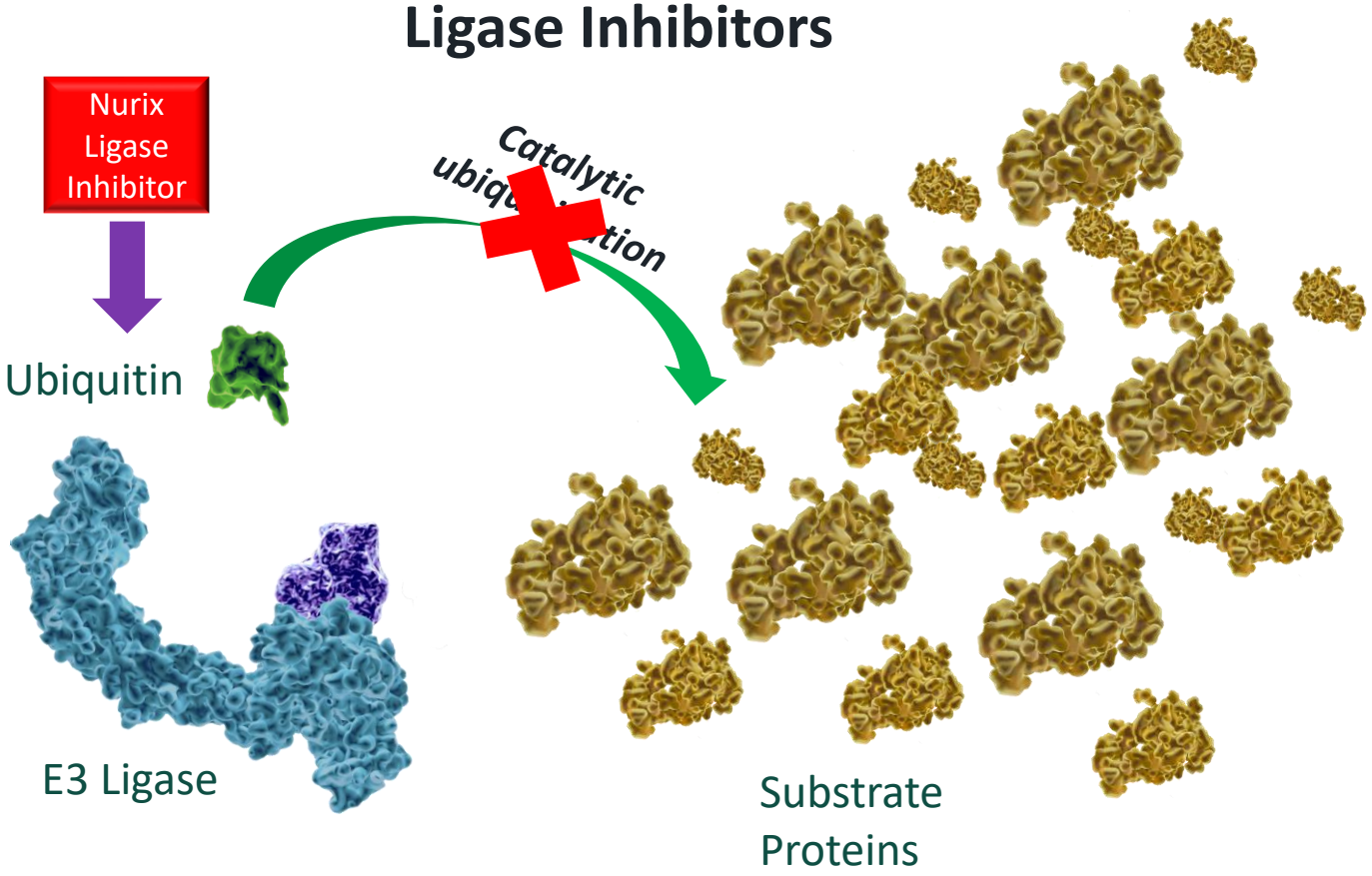
Ligase Inhibitors Can *Increase* Levels of Specific Substrate Proteins

Natural E3 Ligase-Mediated Proteasomal Degradation



E3 Ligase-mediated proteasomal degradation can be highly specific to decrease substrate proteins

Ligase Inhibitors



Substrate protein levels increase

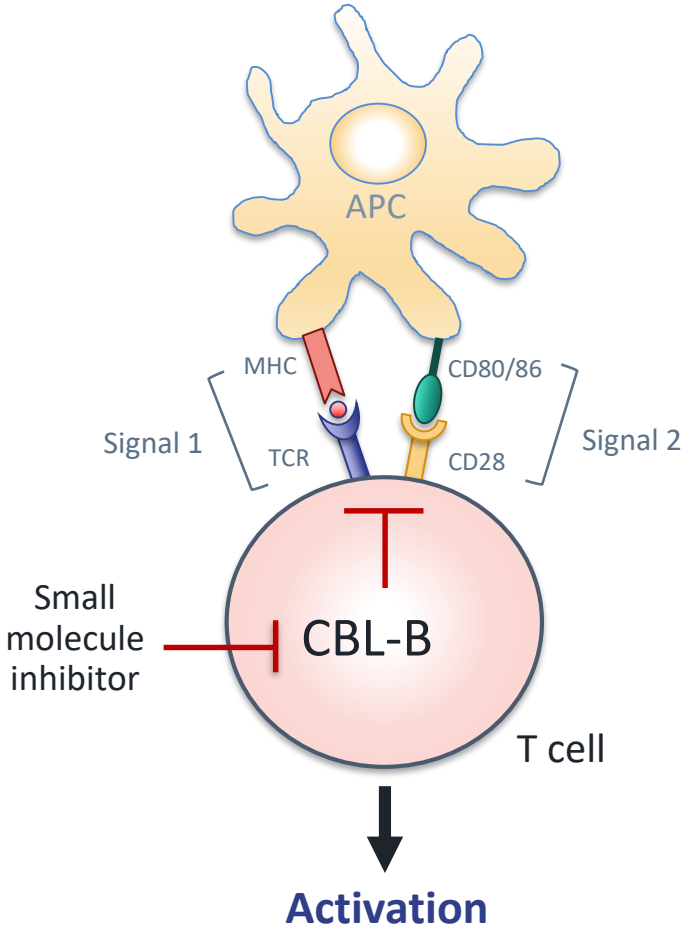
Nurix's Wholly-Owned Targeted Protein Modulation Drug Pipeline: Multiple Clinical Programs Expected Next Year

Drug Candidate	Target / Delivery	Therapeutic Area	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	***Late Q4 '20 – Q1 '21**				
NX-5948	BTK *Oral*	B-cell Malignancies And GVHD	***H2 '21**				
Ligase Inhibition Portfolio							
NX-1607	CBL-B *Oral*	Immuno-oncology	***Q3 '21**				
DeTIL-0255	CBL-B *ex vivo*	Adoptive Cell Therapy (ACT)	***H2 '21**				

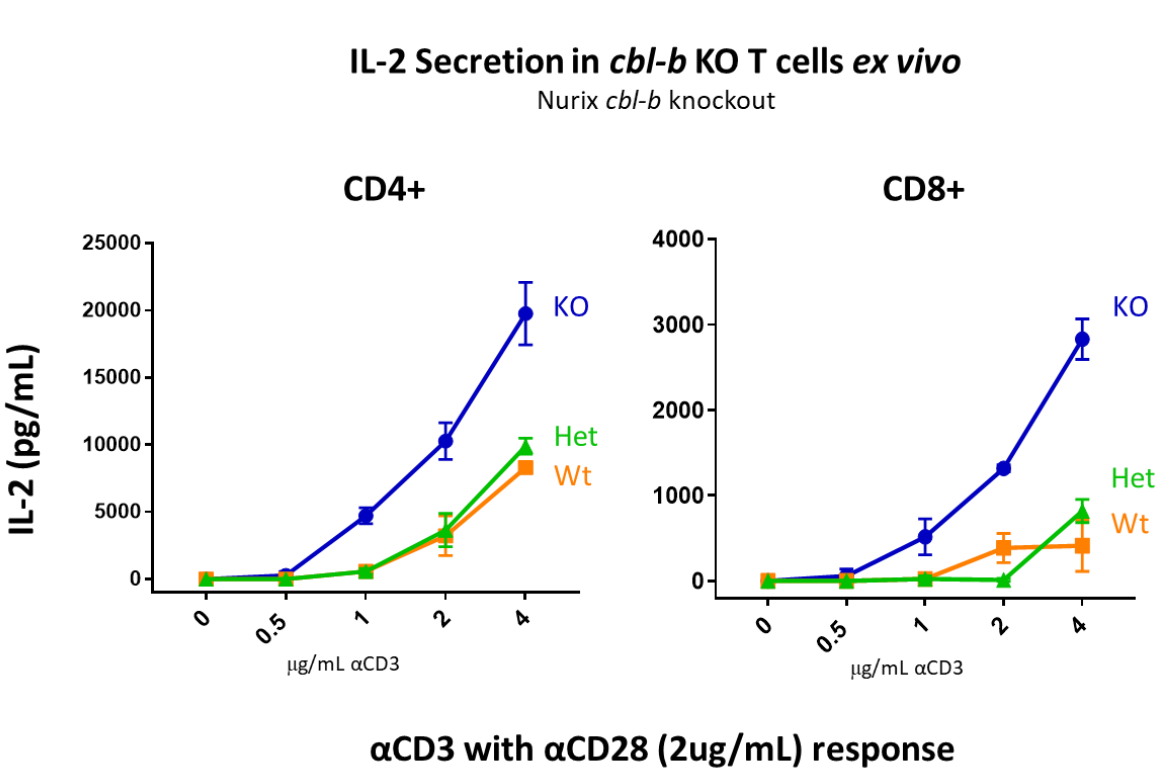
*Expected IND submission timing based on calendar year quarters

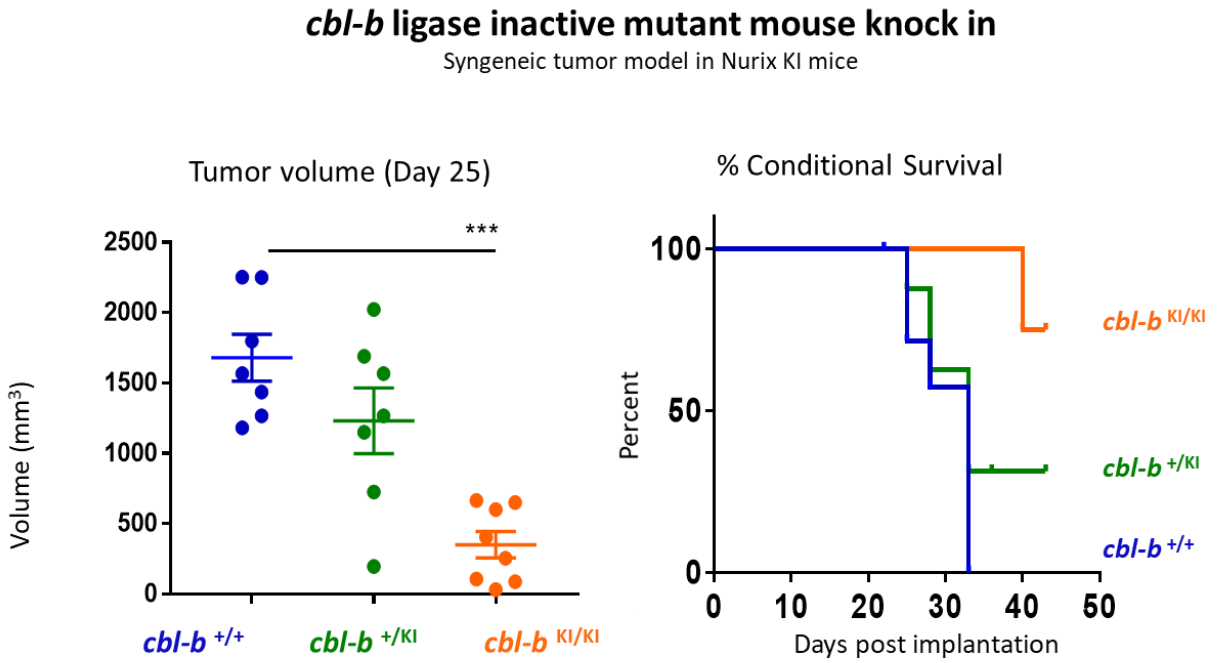
CBL-B: A Modulator of T Cell Activation for Tumor Immunotherapy

- CBL-B is an E3 ligase that regulates the immune system by specifically degrading proteins involved in shutting off T-cell signaling
- Blocking CBL-B removes a brake on the immune system
- CBL-B function is supported by mouse and human genetics
- CBL-B inhibitors have remarkable effects on T cells
  - CBL-B inhibitors induce immune cells to secrete IL-2
  - Skewing T cells to a central memory phenotype
  - *Ex vivo* and *in vivo* administration of CBL-B inhibitors demonstrate anti-tumor effects in animal models of cancer

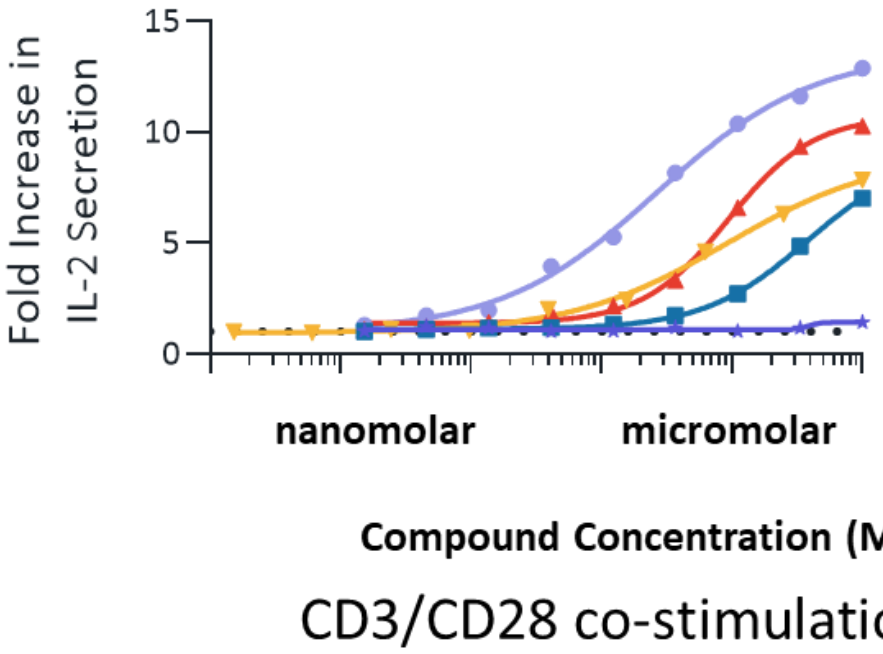


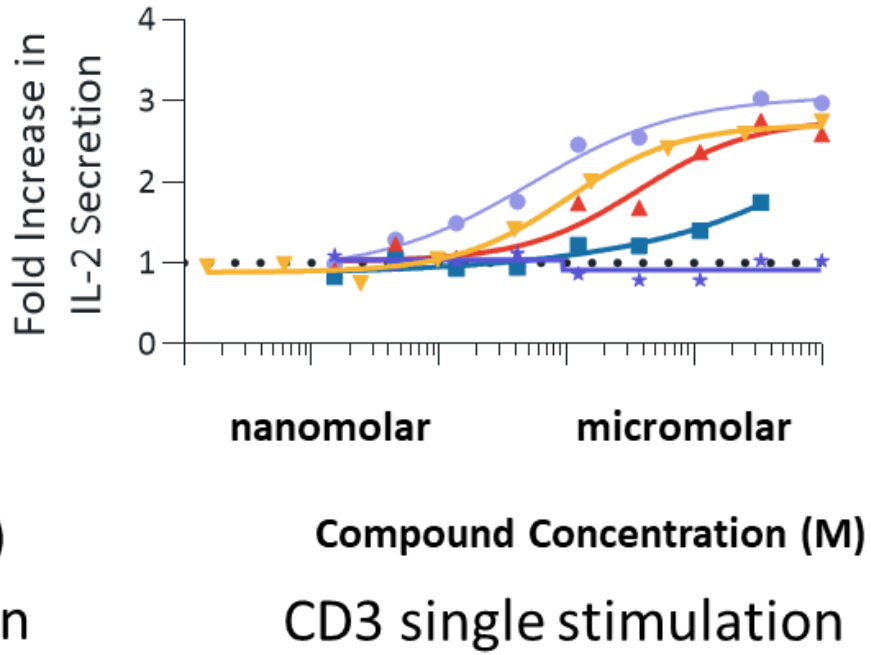
CBL-B Knockout Validation: Enhanced IL-2 Secretion, Tumor Growth Inhibition, and Survival





Nurix CBL-B Inhibitors Elevate IL-2 Levels *ex vivo* in Human Donor T Cells





Biochemical Activity

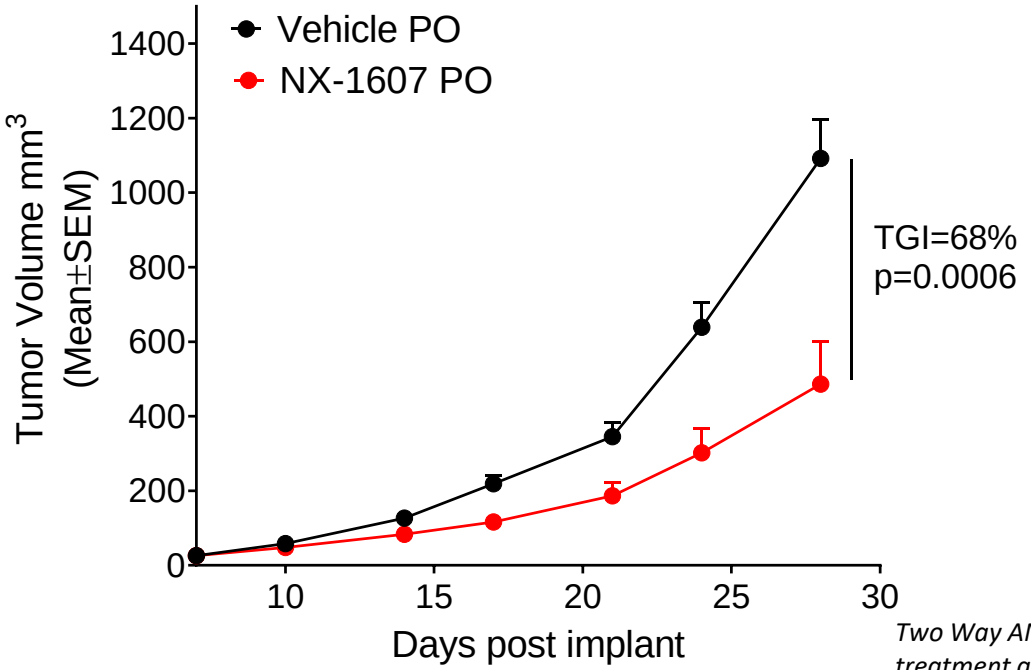
Compound	IC_{50} nM
NRX-5	5
NRX-4	15
NRX-3	26
NRX-2	112
NRX-1 (inactive enantiomer of NRX-4)	1,191

T cell activity ranks orders with biochemical activity

- Several fold increase in IL-2 production corresponds with increasing biochemical activity of CBL-B inhibitors
- CBL inhibition results in increased T cell activation in the absence of co-stimulation with CD3 and CD28, a potential advantage in a suppressive tumor microenvironment

Once Daily Oral Dosing of NX-1607 Recapitulates Anti-Tumor Effects of CBL-B, Ligase Inactive, Knock-in Mouse Model

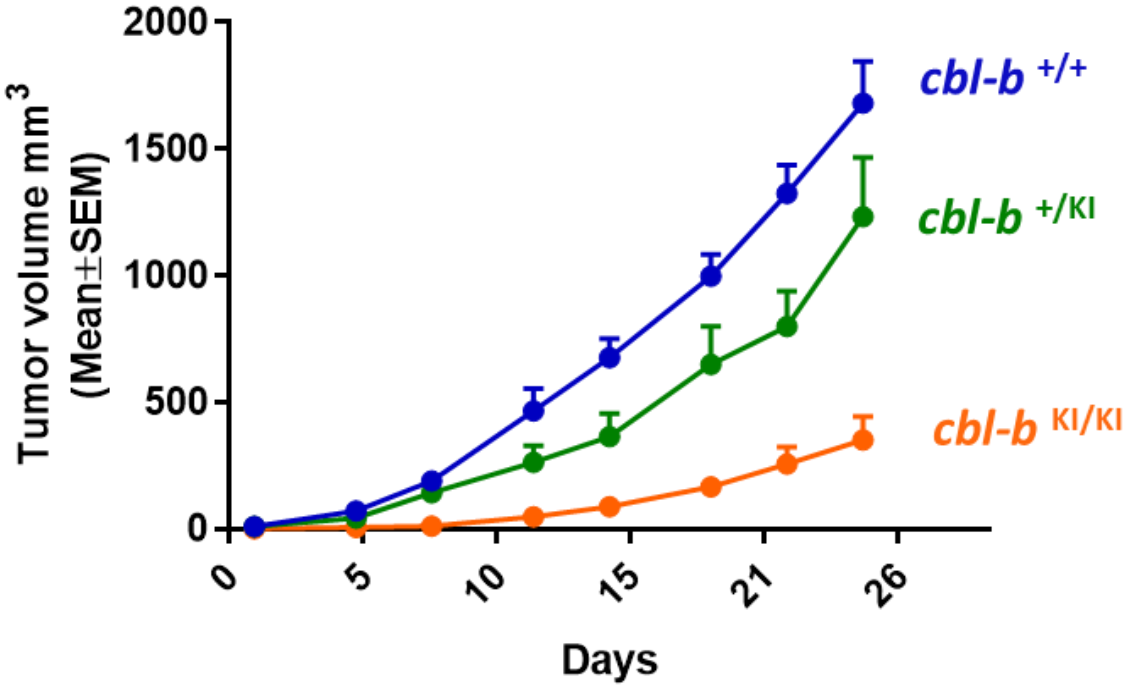
Oral daily dosing of NX-1607



Two Way ANOVA of treatment group vs vehicle control
Average tumor volumes from both flanks are depicted

Tumor growth inhibition (TGI) with NX-1607 treatment; tumors implanted at Day 0; once daily oral dosing of NX-1607 was given from Day 9 to Day 28

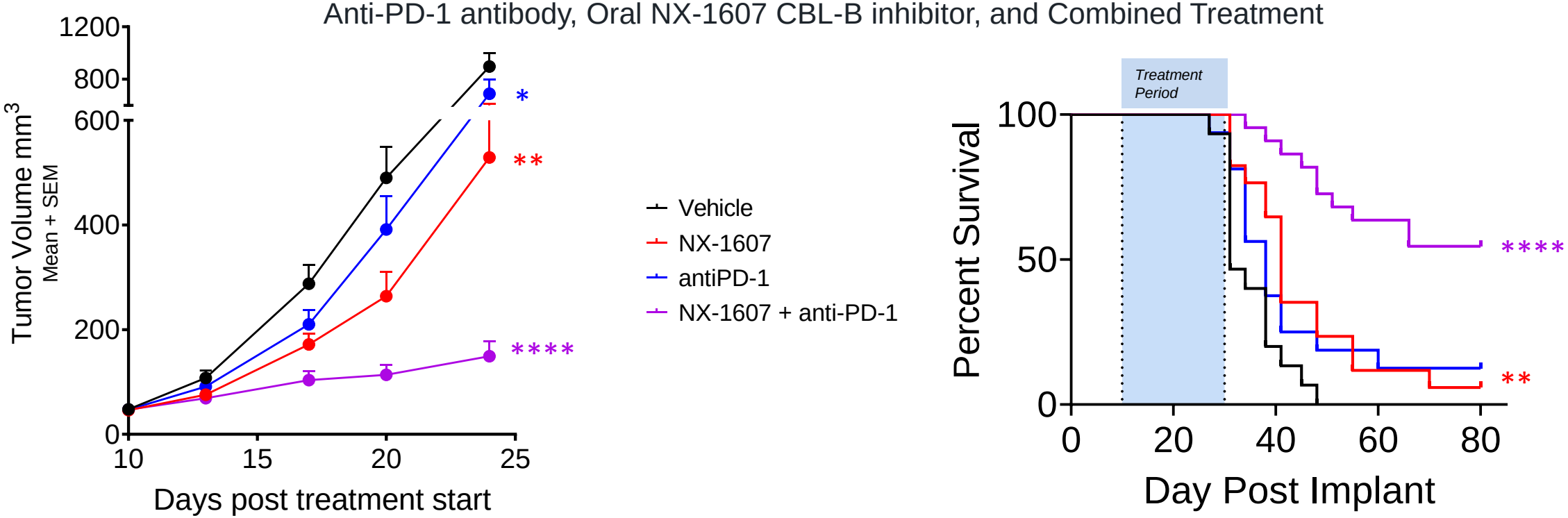
CBL-B ligase-dead, knock-in (KI) model



Anti-tumor effects in ligase-inactive, knock-in (KI) mutation model

NX-1607 and Anti-PD-1 Synergize to Improve Anti-Tumor Effects and Survival of Tumor-bearing Mice

Anti-PD-1 antibody, Oral NX-1607 CBL-B inhibitor, and Combined Treatment



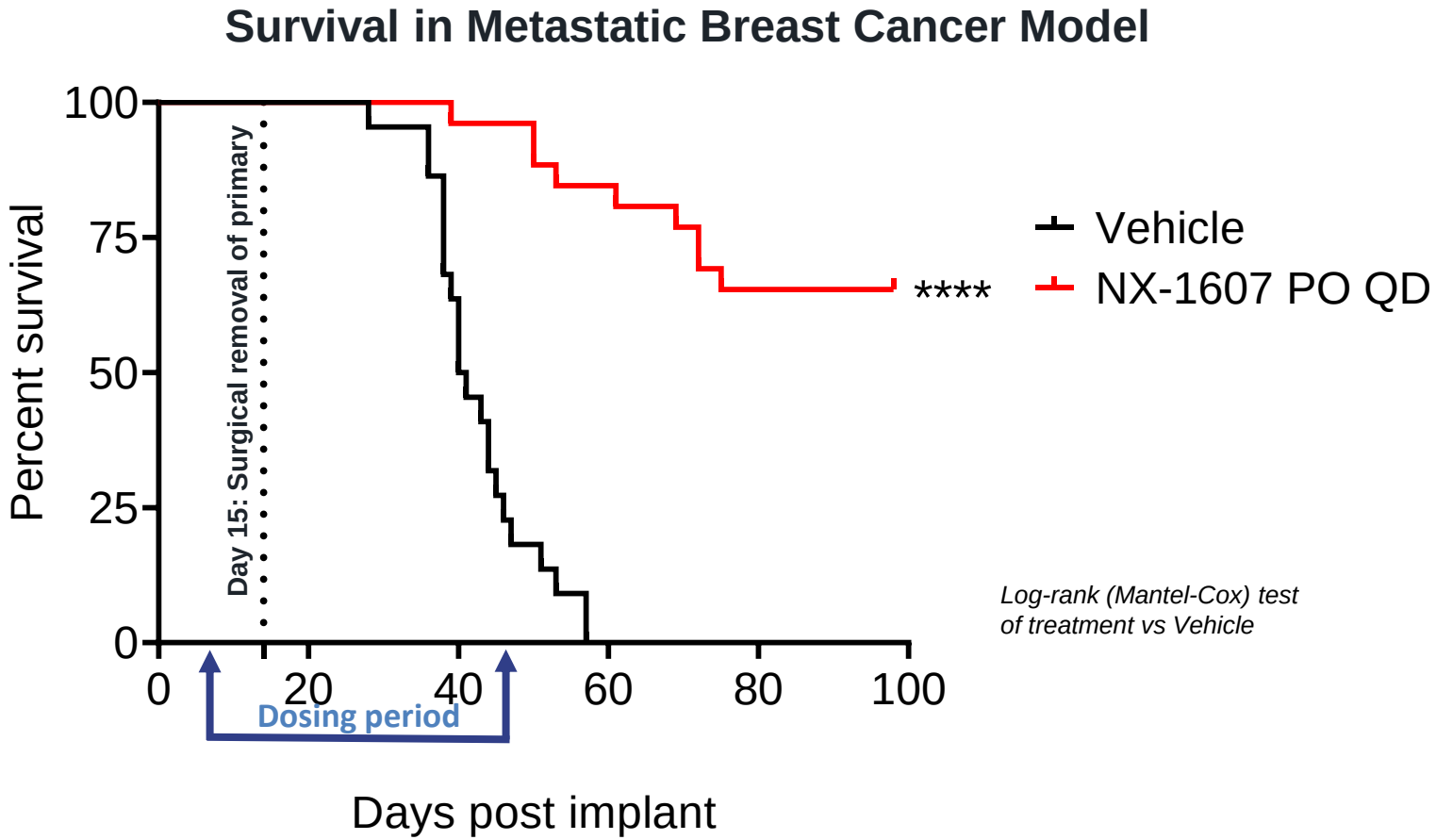
Combination of NX-1607 and anti-PD-1 treatment significantly improves anti-tumor response and survival in mice bearing two tumors relative to vehicle or anti-PD-1 alone

Tumors from both flanks plotted
Two-way ANOVA of treatment group vs vehicle control

Log-rank (Mantel-Cox) test of vehicle vs treatment

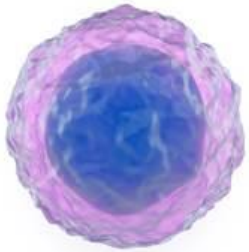
NX-1607 Induces Long Term Survival in Metastatic, Triple Negative, Breast Cancer Model

- Once daily oral dosing of NX-1607
- Tumors implanted at Day 0
- Surgical removal of primary tumor at Day 15
- NX-1607 was given before the surgery from day 7 to day 15 (neo-adjuvant phase) and continued after surgery until day 46.



Triple negative breast carcinoma cells metastasize from subcutaneous space to distant sites

Introducing Pharmacologic Control of Adoptive Cell Therapy with Targeted Protein Modulation



Adoptive Cell Therapy

Convergence

Small molecule targeted protein modulation:
CBL-B Inhibitors

DeCART™

Drug-**E**nhanced
Chimeric **A**ntigen **R**eceptor **T** Cell Therapy

NxACT™

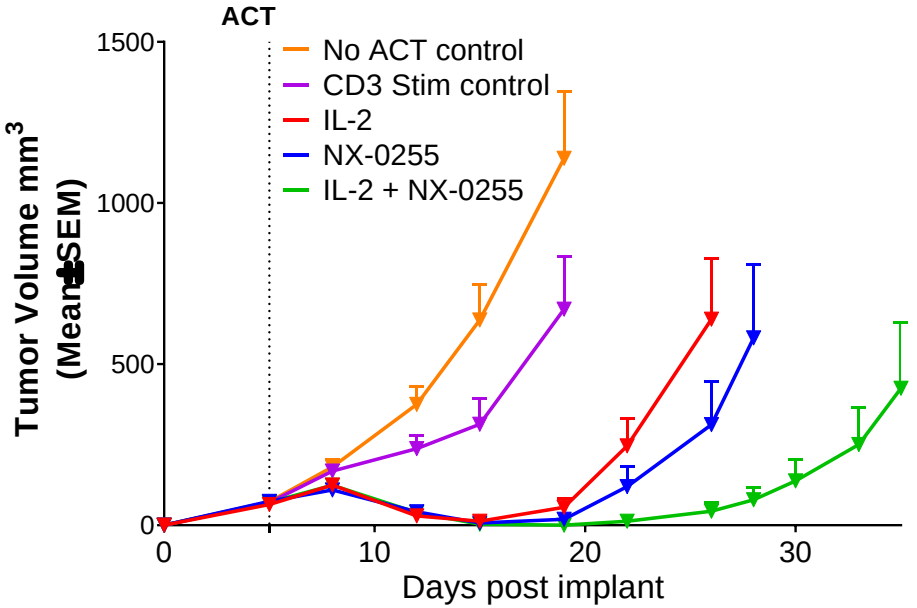
Nurix **A**doptive **C**ell **T**herapy Program

DeTIL™

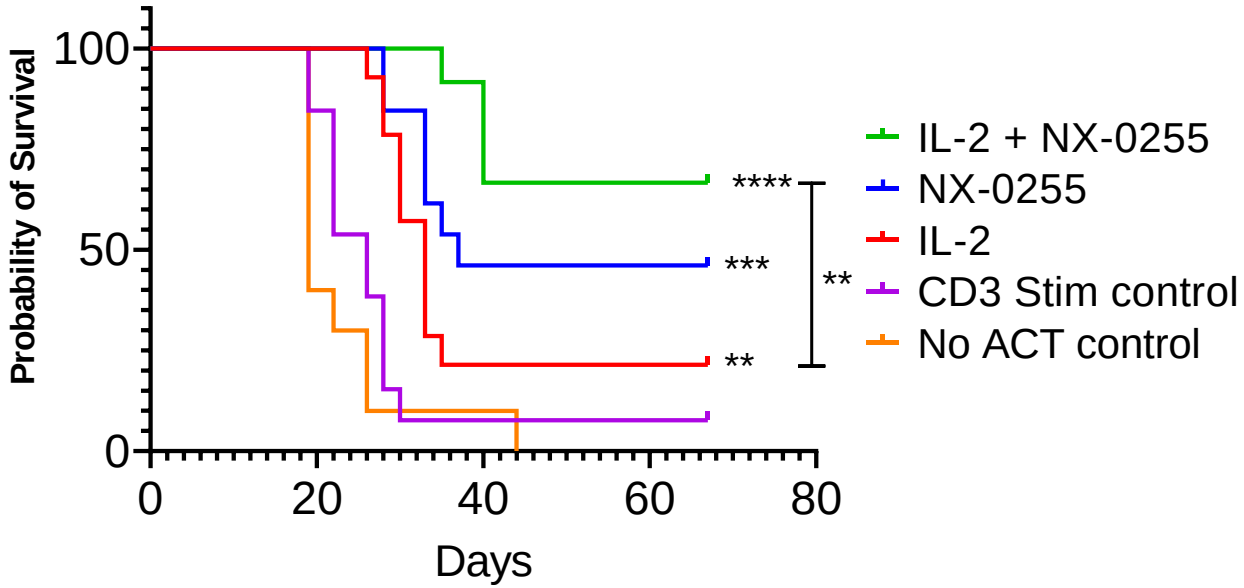
Drug-**E**nhanced
Tumor **I**nfiltrating **L**ymphocytes

NX-0255 *ex vivo* Treatment Provides Robust Anti-Tumor Activity in Mouse Model

Reduction in Tumor Growth in Mouse ACT Tumor Model



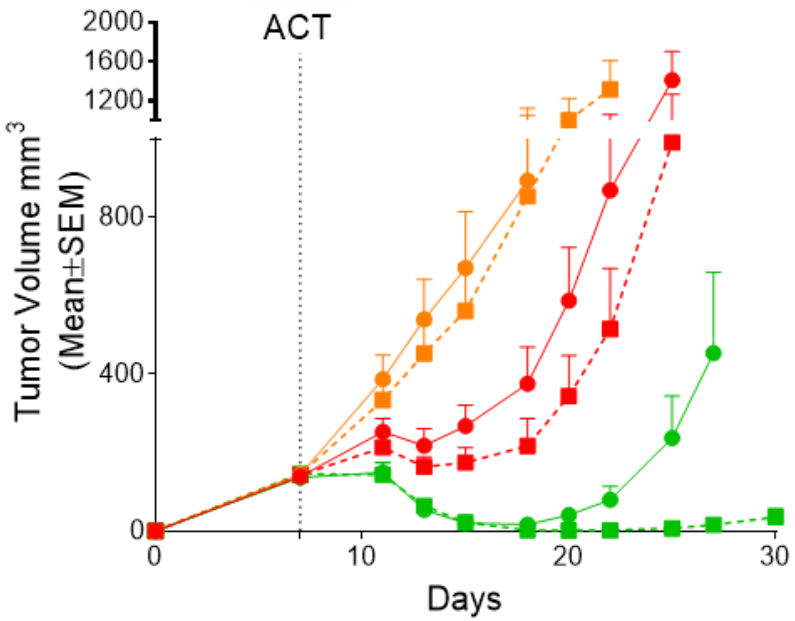
Improvement in Conditional Survival in Mouse ACT Tumor Model



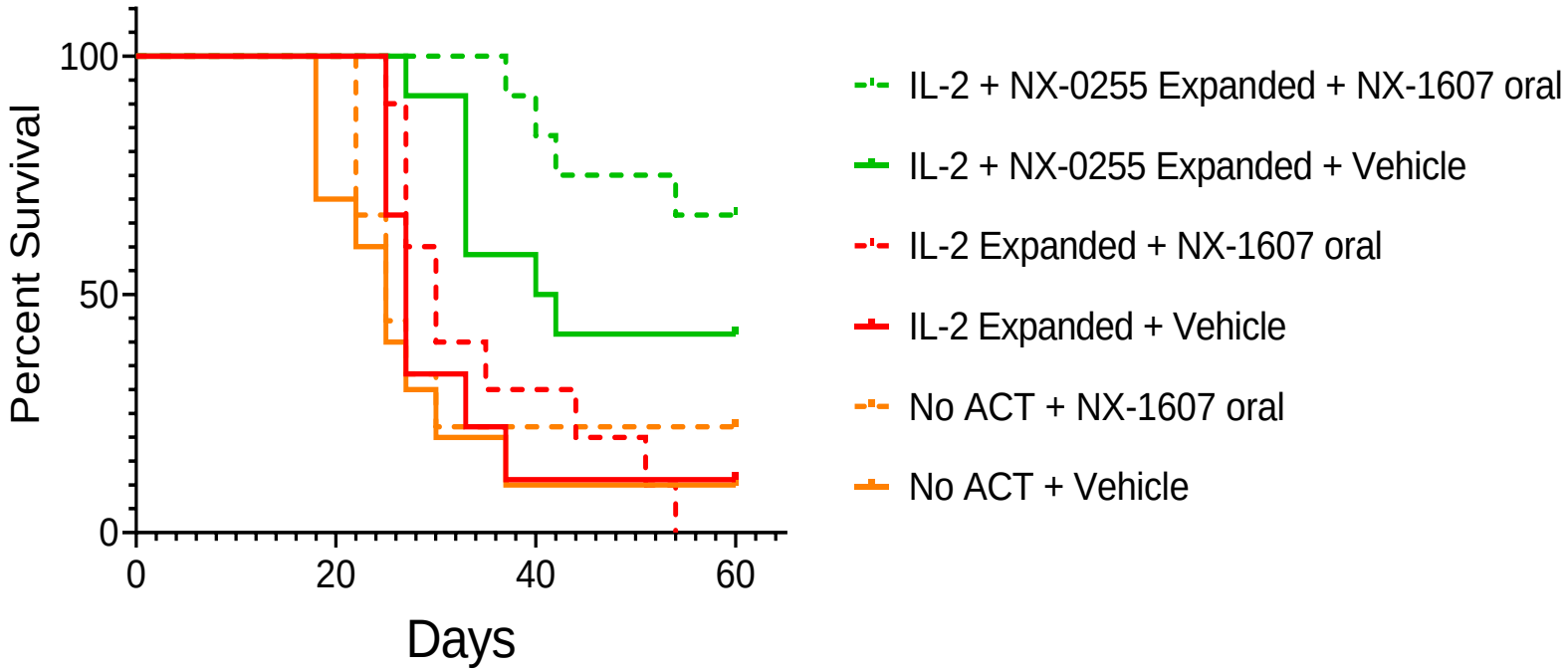
- CD8+ cells exposed to NX-0255 alone *ex vivo* resulted in superior conditional survival compared to using IL-2 alone
- CD8+ cells exposed to NX-0255 and IL-2 combined *ex vivo* exert a deeper anti-tumor response
- NX-0255 *ex vivo* exposure period is only three days, anti-tumor effects persist for over a month after engraftment
- Animals that rejected tumor were rechallenged 80 days post ACT. All animals rejected tumor, demonstrating immunological memory

Oral NX-1607 Augments Anti-Tumor Activity Observed with *ex vivo* NX-0255 Combination in ACT Mouse Model

Reduction in Tumor Growth in Mouse ACT Tumor Model



Improvement in Conditional Survival in Mouse ACT Tumor Model

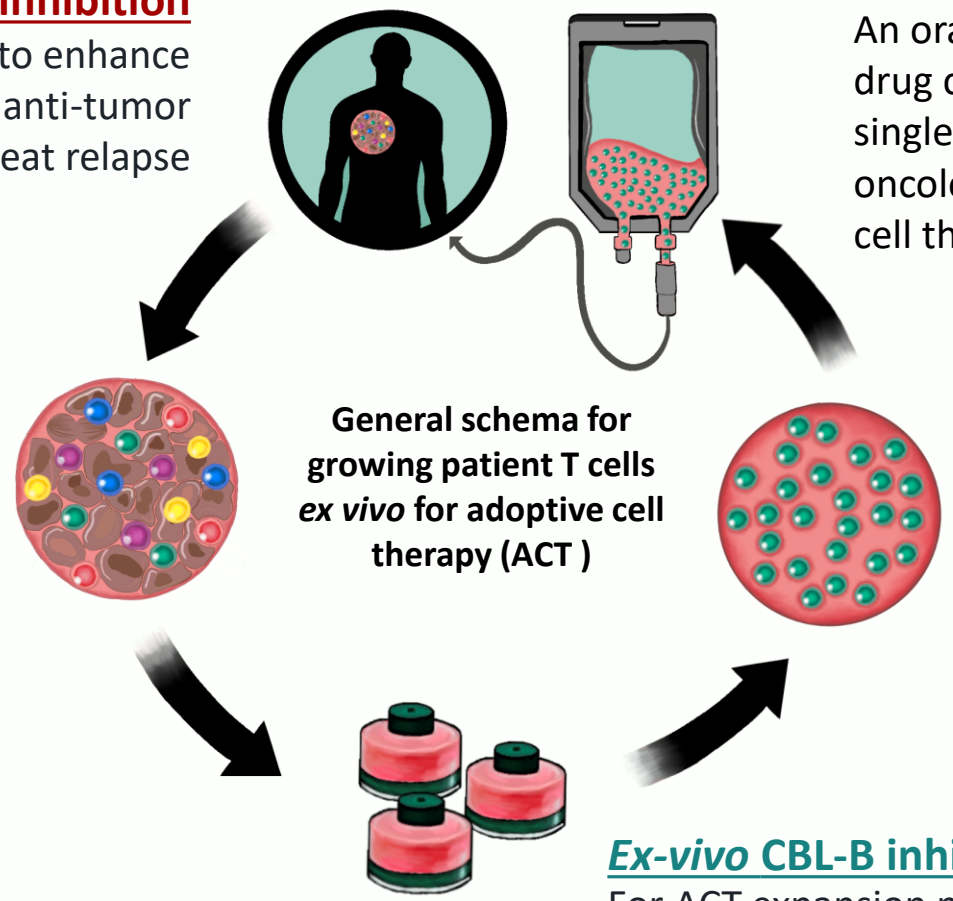


- Oral NX-1607 treatment once daily further enhances conditional survival and anti-tumor activity of T cells expanded for three days with recombinant IL-2 plus NX-0255 *ex vivo* in adoptive cell therapy mouse model

CBL-B Inhibitors to Enhance Adoptive Cell Therapy: DeTIL™ and DeCART™

Oral CBL-B inhibition
For co-administration to enhance engraftment to improve anti-tumor activity or to treat relapse

Oral NX-1607
An oral small molecule immunotherapy drug candidate in development as a single agent or in combination with other oncology therapies including adoptive cell therapy



General schema for growing patient T cells *ex vivo* for adoptive cell therapy (ACT)

***Ex-vivo* CBL-B inhibition**
For enhanced isolation of T cells for TIL or CAR-T therapy

***Ex vivo* NX-0255**
DeTIL and DeCART created by *ex vivo* CBL inhibition with small molecule NX-0255 producing a TIL and CAR-T cell therapy products with enhanced characteristics

***Ex-vivo* CBL-B inhibition**
For ACT expansion phase to enhance cellular phenotype

Matching the Right Business Strategy with Each NxACT Opportunity

DeTIL

Drug-**E**nhanced

Tumor **I**nfiltrating **L**ymphocytes

TIL research and development being built out in Pittsburgh and Philadelphia by industry leading cell therapy experts

Key recruits bring significant cell therapy experience

Michael T. Lotze, M.D.
Chief Cellular Therapy Officer
- *Formerly CSO at Iovance*

Robert J. Brown, M.D.
Vice President of Clinical Development
- *Formerly Allogene and Iovance*

DeCART

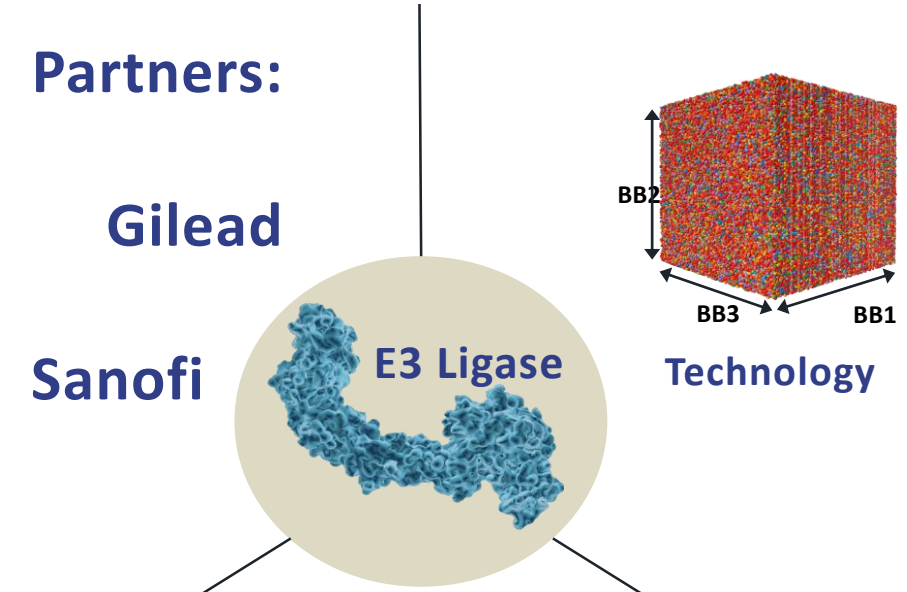
Drug-**E**nhanced

Chimeric **A**ntigen **R**eceptor **T** Cell Therapy

- Wholly owned subsidiary seeded with $3M and a license to three Nurix compounds for combination use with CAR-T to enable independent investment
- Industry leader and DeCART founder **Dr. Carl June** to lead Scientific Advisory Board
- Chief Operating Officer, **Dana Hammill**, former director of strategy and business development at the Center for Cellular Immunotherapies University of Pennsylvania where she co-managed Penn-Novartis alliance for commercialization of CART19

Summary

- DELigase has produced highly potent hits to ligases
- Specific ligase inhibitors can result in pathway-specific changes in ubiquitination status associated with potent biologic effects
- CBL-B inhibitors activate T cells and demonstrate single agent and combination anti-tumor activity in syngeneic models
- CBL-B inhibitors enable drug-enhanced adoptive cell therapy with both DeTIL and DeCART



Pipeline

Drug Candidate	Target / Delivery	Therapeutic Area	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	*Late Q4 '20 – Q1 '21				
NX-5948	BTK *Oral*	B-cell Malignancies And GVHD	*H2 '21				
Ligase Inhibition Portfolio							
NX-1607	CBL-B *Oral*	Immuno-oncology	*Q3 '21				
DeTIL-0255	CBL-B *ex vivo*	Adoptive Cell Therapy (ACT)	*H2 '21				

*Expected IND submission timing based on calendar year quarters

Thank you

Nurix Therapeutics