

### Forward Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are subject to a number of risks, uncertainties and assumptions. Risks regarding our business are described in detail in our Securities and Exchange Commission filings, including in our Annual Report on Form 10-K for the year ended December 31, 2022. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements contained in this presentation reflect our current views with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law.

This presentation includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.



# Landos Biopharma is Singularly Focused on Advancing NX-13 Clinical Development in UC

#### NX-13

# Potentially transformative oral, once-daily therapy for moderate to severe ulcerative colitis (UC)

- Immunometabolism addresses multiple causes of UC through novel, bimodal MOA targeting NLRX1
- Promising safety profile and early signals of clinical improvement in Phase 1b study
- NEXUS Phase 2 proof of concept trial initiated Q2 2023; Top-line results planned Q4 2024



Experienced management team with significant gastroenterology, immunology and drug development expertise



Strong IP position

Significant optionality portfolio-wide for partnerships, development & investment



Capital efficient with sufficient cash to fund planned operations into mid-2025



### Landos Pipeline Focused on Novel, Immunometabolic Targets

| CANDIDATE      | INDICATION                     | Pre-IND | PHASEI            | PHASE II  | PHASE III |  |  |
|----------------|--------------------------------|---------|-------------------|-----------|-----------|--|--|
| NLRX1 Pathway  |                                |         |                   |           |           |  |  |
| NX-13          | Ulcerative Colitis             |         | Phase 2 Topline D | Data 4Q24 |           |  |  |
|                | Crohn's Disease                |         | Phase 2 Ready     |           |           |  |  |
| LABP-66        | Multiple Sclerosis             |         |                   |           |           |  |  |
|                | Neurodegenerative<br>Disorders |         |                   |           |           |  |  |
| LABP-73        | Asthma                         |         |                   |           |           |  |  |
|                | Eosinophilic<br>Disorders      |         |                   |           |           |  |  |
| PLXDC2 Pathway |                                |         |                   |           |           |  |  |
| LABP-69        | Rheumatoid Arthritis           |         |                   |           |           |  |  |
|                | Ulcerative Colitis             |         |                   |           |           |  |  |
|                | Crohn's Disease                |         |                   |           |           |  |  |

Significant **optionality** portfolio-wide for additional *indications*, *partnerships*, *development* & *future investment* 



### Therapeutic Challenges Present Large Unmet Need for UC Patients

#### **Ulcerative Colitis**

Chronic colonic inflammation with rectal bleeding and diarrhea Patients experience relapsing (flares) and remitting episodes of disease severity



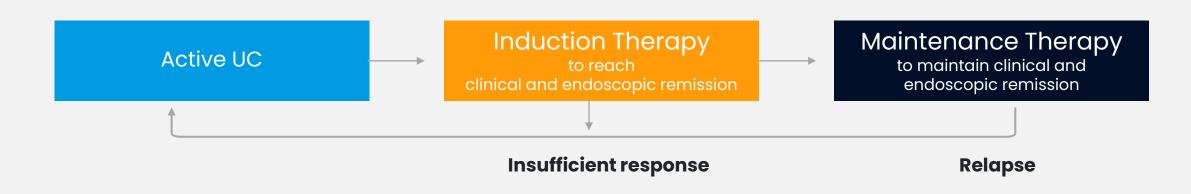
#### **Therapeutic Goals**

Induce and maintain steroid-free symptom relief Healing of colon lining Improved quality of life

#### Therapeutic Challenges

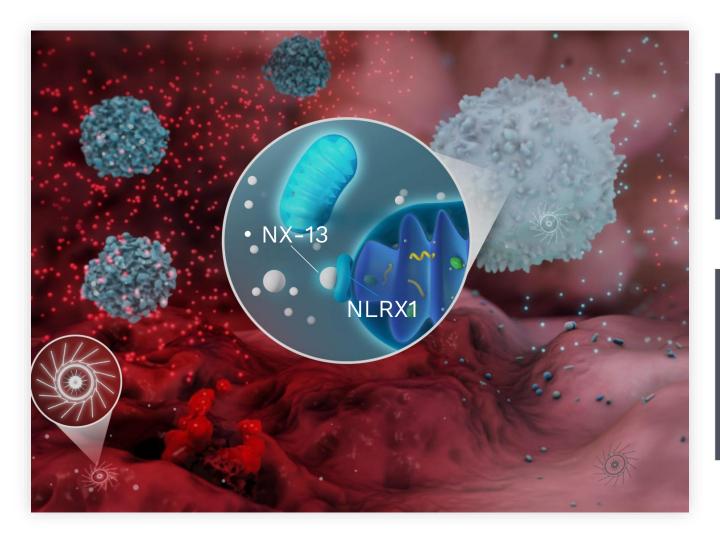
Limited Efficacy: many patients do not respond or lose response to treatment

Safety Risks: infections, cancer, blood clots or cardiac events





# NX-13 Unique Bimodal MOA Activates NLRX1 Pathway for Treatment of Ulcerative Colitis (UC)



NLRX1: the NEXUS of Immunometabolism

Mitochondrial-associated anti-inflammatory NOD-like receptor (NLR)

- Direct metabolic role in mitochondria
- Direct anti-inflammatory role as NLR

NX-13 is an oral, once-daily therapy being developed for moderate-to-severe UC

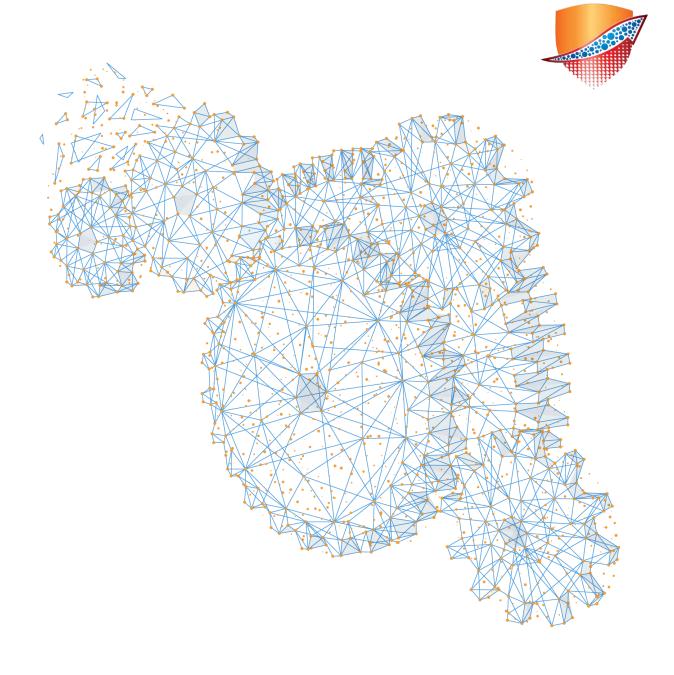
Novel NLRX1 agonist

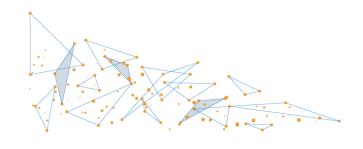
Bimodal MOA aims to reduce reactive oxygen species **intracellularly** and inflammatory pathways **extracellularly** to reduce UC symptoms and flares



Leber et al. *J Immunology* 2019

# Mechanism of Action





# Immunometabolism May Play a Critical Role in Breaking the Therapeutic Ceiling of Current Treatments

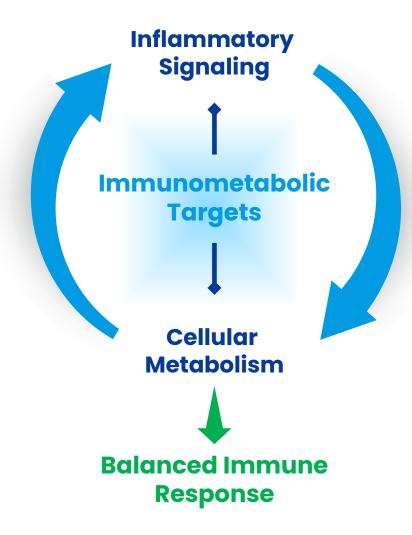
#### **Immunometabolism**

- Cellular metabolism is a central regulator of the activation and function of immune cells
- Dual effects to control both the intracellular metabolic environment and extracellular inflammatory response
  - Addresses the intracellular energy source and requirements of an immune response to shift how a cell responds to extracellular signals
  - Directly affects extracellular inflammatory signals

#### Immunometabolic targets

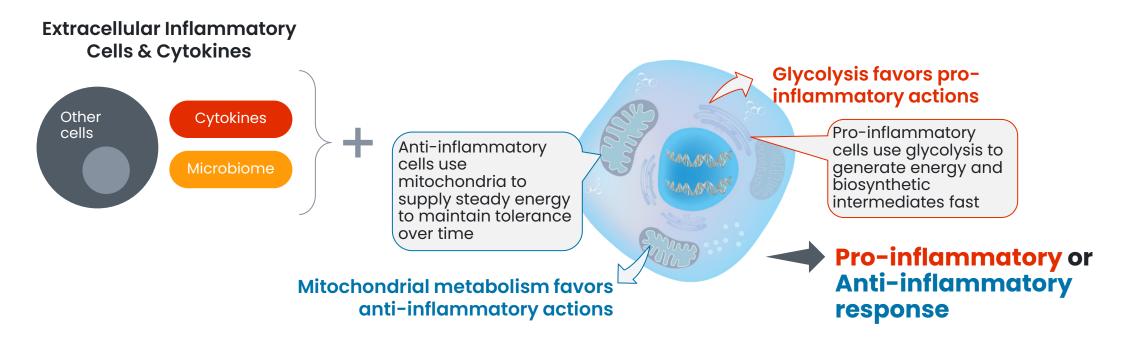
work to restrict entry into the inflammatory cascade and inflammation cycle to maintain (restore) balance

#### **Inflammatory Response**





# Immune Function is Intimately Tied to the Intracellular Environment of Processing & Using Energy



- The intracellular immunometabolic state (the processing & using of energy through glycolysis or mitochondrial metabolism) provides a baseline, and can affect cellular response as pro- or anti-inflammatory
- Many proteins, molecules & substrates have dual action on cellular metabolism AND immune function
- The underlying intracellular (internal) immunometabolic environment can affect the response of multiple cells involved in UC and gut homeostasis (including T cells, antigen presenting cells, and epithelial cells)



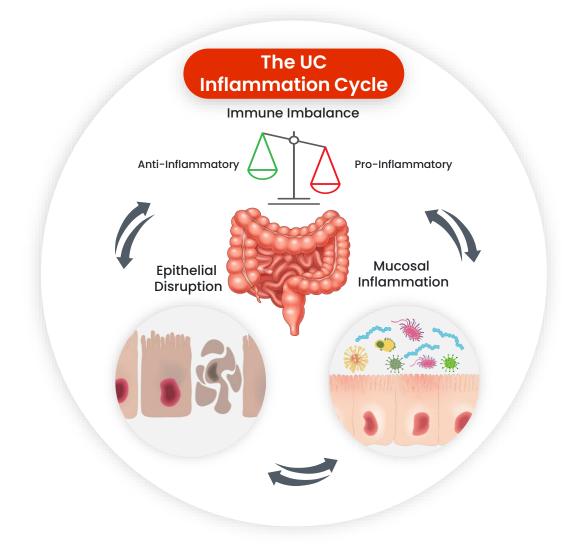
### The Role of Immunometabolism in Immunology & UC

### Immunometabolic response in inflammatory diseases in the immunology universe & UC:

- Abnormal or imbalanced immune activation of the response resulting in over abundance of proinflammatory cells & cytokines with lack of antiinflammatory control.
- In UC, Pathogens cross the damaged epithelial barrier, activating immune response
- Immune activation is energetically costly, requiring the cell to use fast & inefficient glycolytic metabolism.

#### Multiple Factors contribute to the UC Inflammation Cycle:

- Low grade Mucosal Inflammation and microbiome dysbiosis
- Epithelial Cell Damage and barrier disruption
- Broad Immune Activation favoring pro-inflammatory cells and cytokines



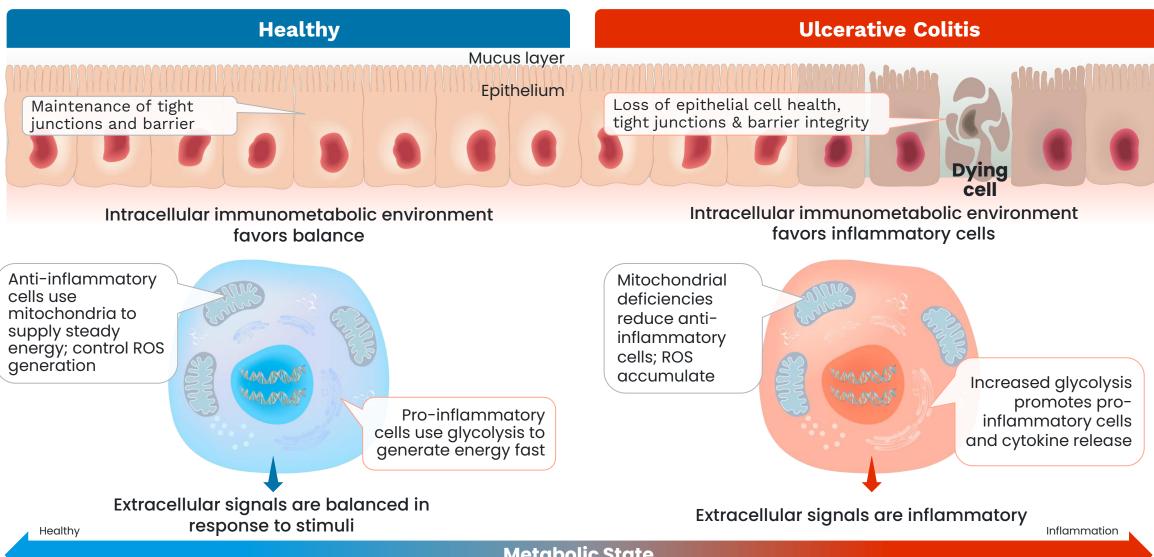


# Current Therapies Focus Exclusively on Extracellular Actions or Signals Falling Short of Effectively Treating a Multifactorial Disease Like UC

| Drug Classes                               | MOA  | Extracellular (External) |                | Intracellular<br>(Internal) |  |
|--|--|--------------------------|----------------|-----------------------------|--|
| Drug Classes                               | MOA  | Cytokines                | Specific Cells | Environment                 |  |
| NX-13 Bimodal targeting (Immunometabolism) | Reduce intracellular reactive oxygen species (ROS) & extracellular immune response | <b>√</b>                 | <b>✓</b>       | <b>✓</b>                    |  |
| Anti-Inflammatory /<br>Immunosuppressants  | Reduce entire immune response  | X                        | X              |                             |  |
| Anti-TNFs, Anti-ILs                        | Block cytokine binding to immune cells   | X                        |                |                             |  |
| Anti-integrins                             | Inhibit entrance of immune cells to the gut tissue from the circulation            |                          | X              |                             |  |
| S1PR modulators                            | Inhibit exit of immune cells from immune organs to circulation & gut               |                          | X              |                             |  |
| JAK Inhibitors                             | Block cytokine signaling (TNF, IL-17, IFN, etc)                                    | X                        | X              |                             |  |



# Bimodal Targeting of the Intracellular Environment & Extracellular Inflammatory Response Aims to Control Multiple Factors in the UC Inflammation Cycle



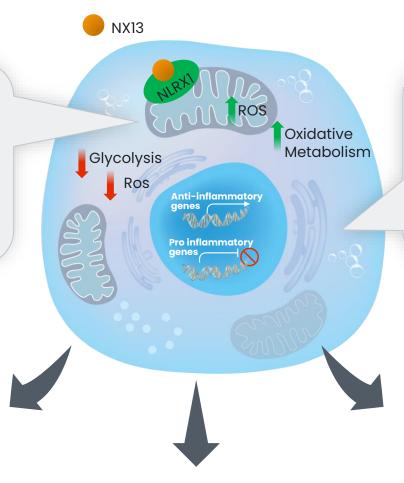


# NX-13 Bimodal MOA Addresses Both Extracellular Signals and Intracellular Environment to Reduce UC Inflammation Cycle

# NX-13 is designed to shift the underlying intracellular immunometabolic environment of immune cells:

- Increases mitochondrial metabolism
- Upregulates antioxidant enzymes
- Decrease ROS
- Decreases Inflammasome activation

Broad immune balance disfavors proinflammatory cells and cytokines with enhanced anti-inflammatory control



Improved epithelial barrier integrity to reduce exposure to inflammatory microbes

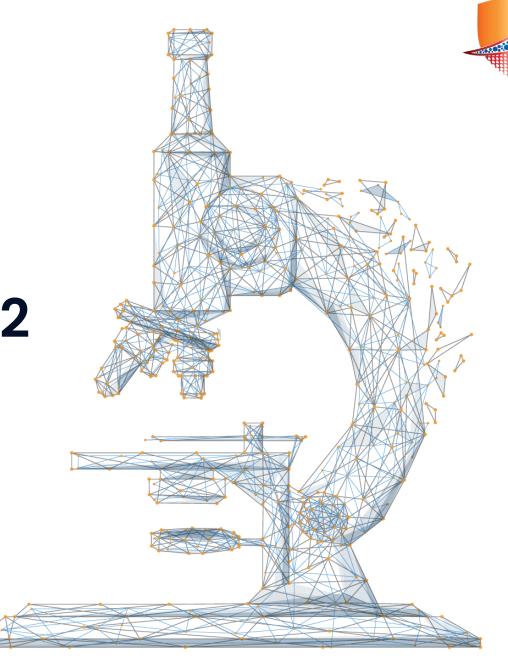
### NX-13 is designed to modulate the extracellular response:

- Reduces inflammatory cell differentiation
- Reduces TNFα, IFNγ, IL-17, IL-1.
- Increases anti-inflammatory activation

Decreased low grade mucosal inflammation and microbiome dysbiosis



# NX-13 Pre-Clinical / Clinical Data & Phase 2 Trial Design

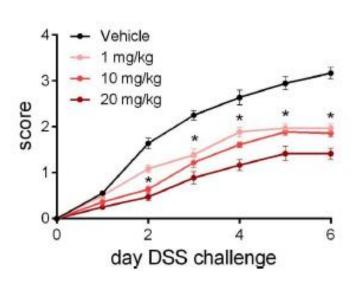


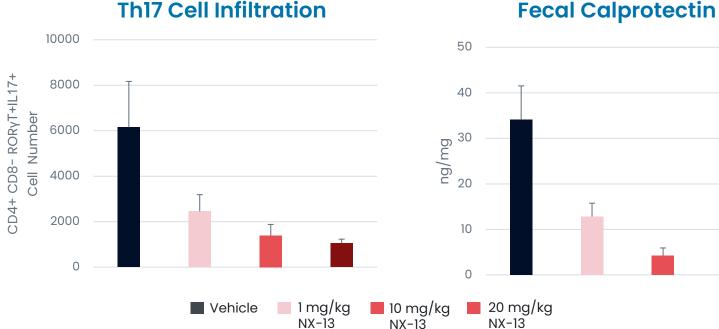
### Pre-Clinical Data Suggests NX-13 Potential to Broadly Reprogram **Immune Response**

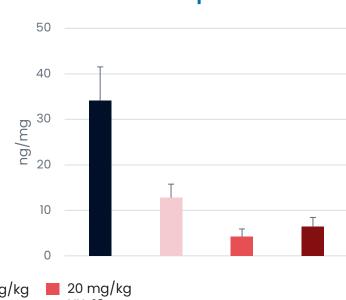
Reduced disease activity driven by robust anti-inflammatory immunometabolic mechanism\*

- Reduced overall Disease Activity in DSS colitis model across dose range
- Reduced Th17 cell infiltration as well as Th1 cells and neutrophils in the lamina propria
- Reduced Fecal Calprotectin and improved cytokine profile with reductions in array of inflammatory cytokines including IL-1, IL-17, IFNy, IL-4, IL-15, TNFa
- Results validated in pig model of acute colitis & human PBMC from UC patients

#### **Disease Activity Challenge**

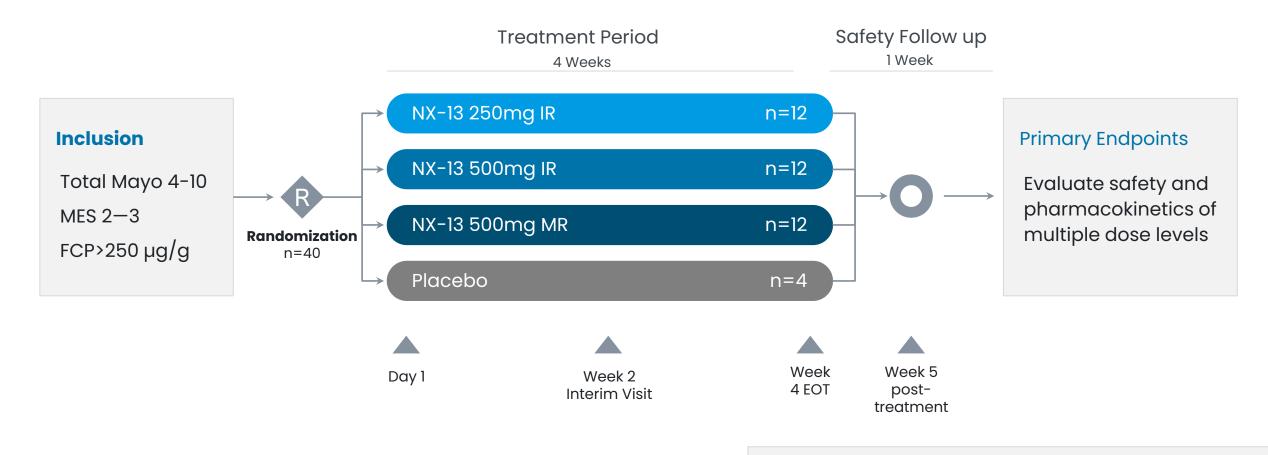








### Phase 1b Study Design of NX-13 in Active UC



#### **Additional Information**

<u>landosbiopharma.com/events-presentations</u> (NX-13 Phase 1b Topline Data Presentation)



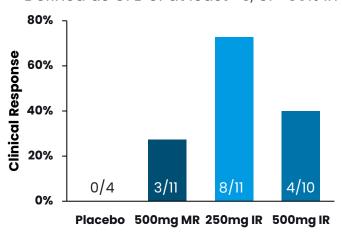
# Phase 1b Results: NX-13 Demonstrated Favorable Endoscopic and Histologic Responses with Reductions in Multiple Clinical Measures After 4 Weeks

Patients receiving NX-13 IR doses responded best:

- Drug activity with IR formulation; study not designed for dose selection
- 72% of 250mg group achieved clinical response; 40% of 500mg IR group achieved clinical response
- 36-40% endoscopic response after just 4 weeks treatment across IR dosage groups
- 36-40% of patients receiving IR achieved histologic remission after 4 weeks of treatment

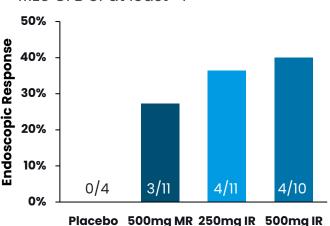
#### **Clinical Response**

Defined as CFB of at least -3, or -30% in Mayo Score



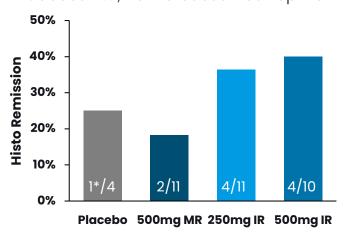
#### **Endoscopic Response**

MES CFB of at least -1



#### **Histologic Remission**

Geboes <3.1, no increased neutrophils in the LP



\*Placebo patient started trial with Geboes <3.1

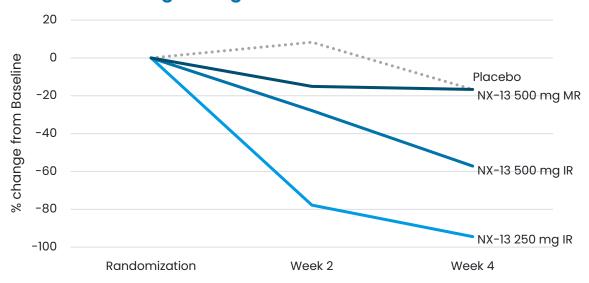


# Phase 1b Results: Fast Onset of Action for NX-13 Supported Symptomatic Remission in Rectal Bleeding & Stool Frequency

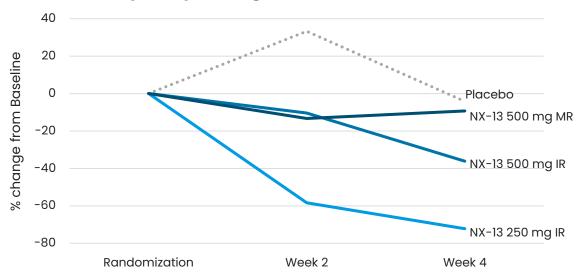
250mg group had greatest reduction of Rectal Bleeding and Stool Frequency at 2 weeks, with further reduction at 4 weeks

Majority of patients treated once daily with 250mg NX-13, saw complete resolution of BOTH rectal bleeding and stool frequency after 4 weeks of treatment

#### **Rectal Bleeding Change from Baseline**



#### Stool Frequency Change from Baseline





# Phase 1b Results: NX-13 Was Well-Tolerated & Shows Promising Signs of Clinical Improvement in Active UC

### Safety



#### Generally well tolerated, consistent with non-clinical, Phase la data

No Serious Adverse Events

#### Pharmacokinetics



## NX-13 was gut-selective with low systemic exposure

- IR dosing peaks ~1 hour post-dose
- No signs of NX-13 accumulation

### Efficacy



NX-13 induced early signs of clinical improvement in patient's symptoms by 2 weeks and endoscopy at 4 weeks:

 Positive signals of target engagement and downstream immunometabolic effects



### **NEXUS Phase 2 Proof of Concept Trial**



Goal

Evaluate safety, efficacy and pharmacokinetics of NX-13 in moderate to severe UC patients in 12-week induction trial



**Timing** 

Initiated in Q2 2023; Planning to report topline results in Q4 2024



Additional Phase 2 Learnings

Dose-Exposure-Response and PK/PD relationships (including site and MOA)



**Dosing** 

Oral, once daily treatment with either: 250 mg IR dose of NX-13 | 750 mg IR dose of NX-13 | Placebo

Key Design Principles



Blinded

Powered



Placebo Controlled



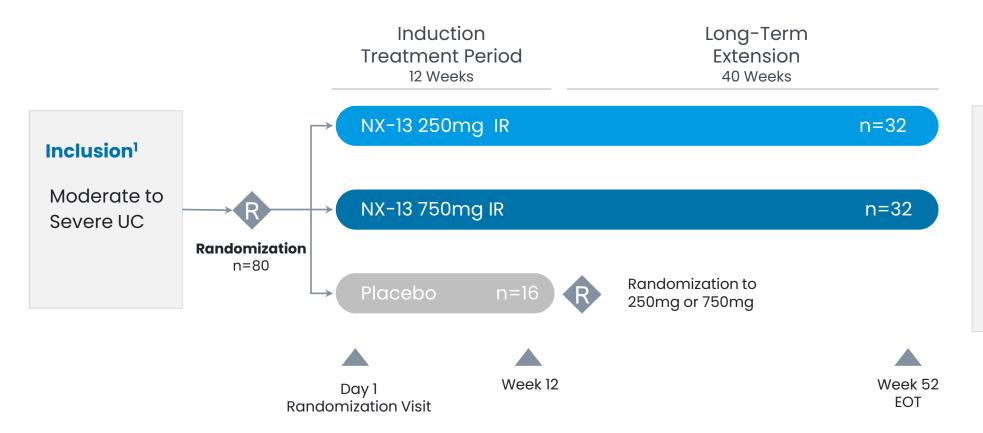
Dose-Ranging





ClinicalTrials.gov Identifier: NCT05785715

## NEXUS Phase 2 Proof of Concept Study Design: NX-13 in Moderate to Severe UC



#### **Primary Objective**

Evaluate the clinical efficacy, safety and pharmacokinetics of oral NX-13 in moderate to severe UC patients in 12-week induction trial

**Additional Information** 

clinicalTrials.gov: NCT05785715





# Market & NX-13 Positioning





### **Attractive & Growing Market Opportunity in UC**

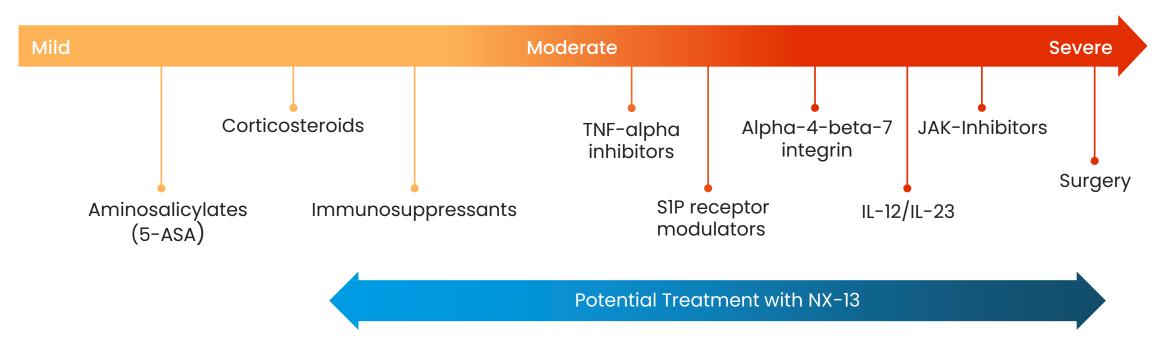
Largest market opportunity is Global UC Diagnosed Patients<sup>1</sup> Global UC Sales<sup>1</sup> in moderate to severe<sup>2</sup> patients 2,450 \$10 \$8.6 2,400 Number of Patient s (thousands) \$8 \$6.9 2,350 Moderate to Mild to \$6 US \$ (Billions) Severe Moderate 63% 2,300 37% \$4 2,250 \$2 2,200 \$0 2023 2024 2025 2026 2028 2022 2027 2029 2030 2031 ~89% of sales<sup>2</sup> are in moderate to 2022 2031 severe category



### NX-13 Poised for Broad Utilization in Both Early & Late-Stage Disease

#### Potential benefits may help transform the current treatment paradigm:

- Gut selective allowing target engagement with the GI tract
- Novel, first-in-class MOA with convenient, oral, once-daily dosing
- MOA may allow for improved efficacy, greater mucosal healing, and safety for long-term use
- No on-target toxicities associated with NLRX1, with adverse event incidence in Phase 1a & 1b similar to placebo





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### Landos Pipeline Focused on Novel, Immunometabolic Targets

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| NLRX1 Pathway  |                                |         |                   |           |           |  |  |
| NX-13          | Ulcerative Colitis             |         | Phase 2 Topline D | Data 4Q24 |           |  |  |
|                | Crohn's Disease                |         | Phase 2 Ready     |           |           |  |  |
| LABP-66        | Multiple Sclerosis             |         |                   |           |           |  |  |
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|                | Ulcerative Colitis             |         |                   |           |           |  |  |
|                | Crohn's Disease                |         |                   |           |           |  |  |

Significant **optionality** portfolio-wide for additional *indications*, *partnerships*, *development* & *future investment* 



# Future NLRX1 & PLXDC2 Indications & Programs Provide Compelling Growth Potential Beyond NX-13 in UC

|  | Ulcerative<br>Colitis  | Crohn's<br>Disease | Asthma <sup>1</sup>      | Multiple<br>Sclerosis <sup>2</sup> | Rheumatoid<br>Arthritis     |
|--|------------------------|--------------------|--------------------------|------------------------------------|-----------------------------|
| <b>WW Annual Sales</b> <sup>3</sup> 2022→ 2031 (in billions) | ~\$6.9 <b>→</b> ~\$8.6 | ~\$18.2 → ~\$19.1  | ~\$15.6 <b>→</b> ~\$20.8 | ~\$17.2 <b>→</b> ~\$21.7           | ~\$33.5 <b>&gt;</b> ~\$33.1 |
| <b>US Diagnosed Population</b> <sup>3</sup> (in millions)    | ~1.0                   | ~.91               | ~3.9                     | ~.48                               | ~3.6                        |
| Landos Asset NX-13   |                        | LABP-73            | LABP-66                  | LABP-69                            |                             |
| Target Pathway   | NLRX1                  |                    |                          |                                    | PLXDC2                      |

Potential Areas of Future Development Include Eosinophilic Esophagitis, Dermatology & Neuroscience



### **Experienced Management Team in Immunology & Drug Development**



**GREGORY OAKES President & Chief Executive Officer** 









**DAWN LOURO** Vice President, Clinical Operations







**FABIO CATALDI, MD Executive Vice President & Chief Medical Officer** 







**REBECCA MOSIG, PHD** Vice President, Corporate Development







**JENN CREEL** Interim Chief Financial Officer







**DAVID PEREIRA, PHD** Vice President, CMC









**CLAUDIA LOPEZ, DVM** Vice President, Clinical Development







**AMY PLACE, PHD** 

Vice President, Project Leadership & Site Engagement









### **Top-Tier Advisory Teams**

#### **Board of Directors**

#### **Scientific & Steering Committee**

**GREGORY OAKES** 

President & Chief Executive Officer

**CHRIS GARABEDIAN** 

Chairman

Xontogeny, Perceptive Advisors

**ROGER ADSETT** 

Chief Operating Officer of Insmed, Inc.

ALKA BATYCKY, PH.D.

Director

FRED CALLORI

Xontogeny, Perceptive Advisors

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University Hospitals Leuven, KU Leuven

ANDRES YARUR, MD

Cedars Sinai Medical Center



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Capital efficient with sufficient cash to fund planned operations into mid-2025





Thank you



#### **Contact:**

IR@landosbiopharma.com

### **Appendix: Key Publications**

- (11/23) The Safety, Tolerability, Pharmacokinetics and Clinical Efficacy of the NLRX1 agonist **NX-13** in Active Ulcerative Colitis: Results of a Phase 1b Study. Journal of Crohn's and Colitis, e-published ahead of print
- (10/23) The Nucleotide-Binding Oligomerization Domain, Leucine Rich Repeat Containing X1 (NLRX1) Agonist NX-13 Demonstrates Rapid Symptomatic and Biomarkers Improvement in Ulcerative Colitis: Results In a Phase 1b Study. <u>UEG Week Journal Abstracts 2023; Poster Presentations United European Gastroenterology Journal (11) S8 (Publication OP078 / p76)</u>
- (10/23) Symptomatic Relief Is Correlated with Early Endoscopic Response to the Nucleotide-Binding Oligomerization Domain, Leucine Rich Repeat Containing X1 (NLRX1) Agonist NX-13 In Ulcerative Colitis: Results in a Phase Ib Study. <a href="UEG Week Journal Abstracts">UEG Week Journal Abstracts 2023; Poster Presentations United European Gastroenterology Journal (11) S8 (Publication OP104 / p103)</a>
- (10/23) Target Engagement And Pharmacodynamic Molecular Mechanism Evaluation In A Phase 1b Study of the Nucleotide-binding Oligomerization Domain, Leucine Rich Repeat Containing X1 (NLRX1) Agonist NX-13 in Ulcerative Colitis. UEG Week Journal Abstracts 2023; Poster Presentations - United European Gastroenterology Journal (11) S8 (Publication PP785 / p975)
- (2/23) A Phase 1b Study to Evaluate Safety, Tolerability, Pharmacokinetics and Clinical Efficacy of the Nucleotide-binding oligomerization domain, Leucine rich Repeat containing X1 (NLRX1) agonist **NX-13** in Ulcerative Colitis. Journal of Crohn's and Colitis, Volume 17, Issue Supplement 1 (Publication P577)
- (10/21) Safety and Tolerability of NX-13 in a Randomized, Double-Blind Placebo Controlled Phase I Study in Normal Healthy Volunteers. <u>UEG Week 2021 Poster Presentations United European Gastroenterology Journal (9) S8 (Publication P0480)</u>
- (11/19) Activation of NLRX1 by **NX-13** Alleviates Inflammatory Bowel Disease through Immunometabolic Mechanisms in CD4+ T Cells. The Journal of Immunology (November 6, 2019)
- (6/19) Exploratory studies with **NX-13**: oral toxicity and pharmacokinetics in rodents of an orally active, gut-restricted first-in-class therapeutic for IBD that targets NLRX1. <u>Drug and Chemical Toxicology (June 10, 2019)</u>
- (5/19) Preclinical Efficacy and Safety of NX-13: A Novel NIrxl-Targeting Immunometabolic Therapeutic for Crohn's Disease and Ulcerative Colitis. AGA
   <u>Journals (May 2019)</u>
- (2/18) NLRX1 Modulates Immunometabolic Mechanisms Controlling the Host-Gut Microbiota Interactions during Inflammatory Bowel Disease. Front Immunol (February 2018)
- (3/17) NLRX1 Regulates Effector and Metabolic Functions of CD4+ T Cells. J Immunol (March 2017)
- (5/21) PLXDC2 activation by PX-69 ameliorates rheumatoid arthritis through activation of novel immunometabolic mechanisms. J Immunol (May 1, 2021)

