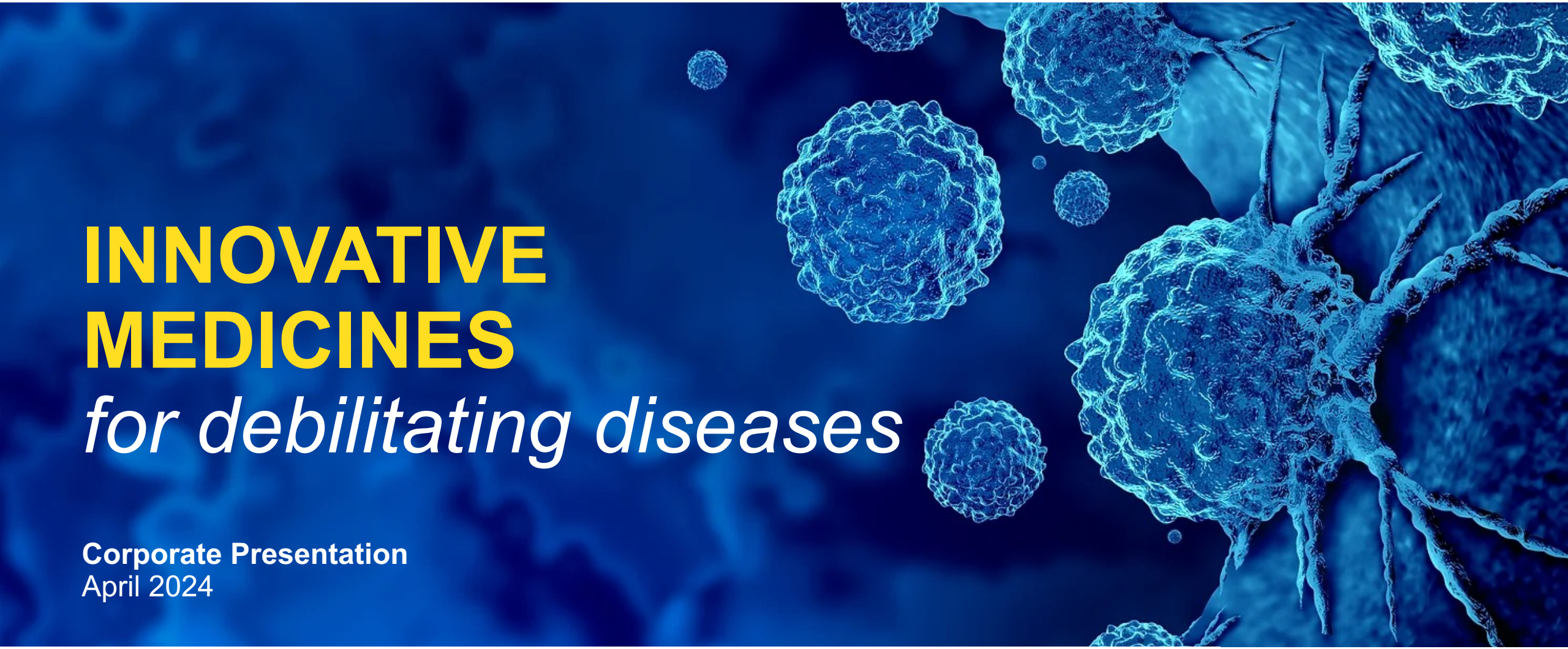
Lirum THERAPEUTICS



# INNOVATIVE MEDICINES

*for debilitating diseases*

**Corporate Presentation**
April 2024

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This presentation and the accompanying oral presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities in any state or jurisdiction where such offer, solicitation or sale would be unlawful, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction. Recipients of this presentation should carefully review the Company's Registration Statement on Form S-1, including the risk factors contained therein, before making any investment decision.

# Forward Looking Statements

Some of the statements we use in this presentation contain certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. You can identify some of these forward-looking statements by words or phrases, such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "target," "will," "would" or other similar expressions. We have based these forward-looking statements largely on our current expectations and projections about future events that we believe may affect our financial condition, results of operations, business strategy and financial needs.

These forward-looking statements include statements relating to the timing, progress and results of preclinical studies and clinical trials for our product candidates, including our product development plans and strategies; the timing, scope and likelihood of regulatory filings and approvals, including opportunities to use expedited regulatory pathways and final regulatory approval of our product candidates; the potential benefits and market opportunity for our product candidates; expectations regarding the size, scope and design of clinical trials; our plans and strategy with respect to our drug development efforts; our manufacturing, commercialization, and marketing plans and strategies; our plans to hire additional personnel and our ability to attract and retain such personnel; our estimates of the number of patients who suffer from the diseases we are targeting and potential growth in our target markets; our expectations regarding the approval and use of our product candidates; our competitive position and the development and impact of competing therapies that are or may become available; expectations and strategies for entering into potential collaborations and additional licensing agreements; our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering product candidates we may develop, including the extensions of existing patent terms where available, the validity of intellectual property rights held by third parties, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights; the rate and degree of market acceptance and clinical utility of product candidates we may develop; our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; our future financial performance; the period over which we estimate our existing cash on hand will be sufficient to fund our future operating expenses and capital expenditure requirements; the impact of laws and regulations; pandemics, epidemics, and other major world crises; and our anticipated use of the net proceeds from our initial public offering, as well as other factors included in the "Risk Factors" in our Registration Statement on Form S-1 filed with the SEC, which is available at https://www.sec.gov.

The forward-looking statements made in this presentation relate only to events or information as of the date on which the statements are made. Except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise, after the date on which the statements are made or to reflect the occurrence of unanticipated events

This presentation also contains market data related to our business and industry, including projections that are based on a number of assumptions. If these assumptions turn out to be incorrect, our actual results may differ materially from the projections based on these assumptions. As a result, the market for our product candidates may not grow at the rates projected by these data, or at all.

# Investment Highlights

*Clinical Stage Biopharmaceutical Company Focused on Treatment of Debilitating Diseases*

## Veteran team with proven track record

- ✓ Experienced leaders with history of shareholder value creation
- ✓ Multiple approvals and commercial launches

## Innovative technology with differentiated MOA

- ✓ Clinical-stage, novel targeted therapy directed to IGF-1R (LX-101)
- ✓ Positive clinical experience in Phase 1a trial

## Tremendous commercial opportunity

- ✓ Multiple cancers with well-established IGF-1R pathway involvement
- ✓ Commercially validated in thyroid eye disease (TED) (>$3.5 billion market)

## Next Steps/Catalysts

- ➢ **Advance LX-101 in IGF-1R-driven pediatric and adult cancers and TED**
- ➢ **Data presentations at major conferences**
- ➢ **Opportunistically expand pipeline**

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# Lirum Team: Track Record of Approvals & Launches

**Ivan Bergstein, MD**
Chairman

**Ken Hoberman**
Director

**Peter McDonald**
Chief Executive Officer

- ✓ **Veteran leadership team**
- ✓ **Founders and management of Stemline (formerly NASDAQ: STML; now Menarini Stemline via acquisition)**
- ✓ **Proven track record of shareholder value creation**
- ✓ **IPOs, multiple drug approvals and launches**

ELZONRIS® (tagraxofusp-erzs) Injection — Stemline®

✓ Commercial; oncology; US and EU

ORSERDU™ elacestrant — MENARINI group — Stemline® A Menarini Group Company

✓ Commercial; oncology; US and EU

briumvi™ ublituximab-xiiy 150 mg/6 mL injection for IV — TG Therapeutics

✓ Commercial; neurodegenerative; US & EU

Auryxia® (ferric citrate) tablets — KERYX BIOPHARMACEUTICALS, INC

✓ Commercial; renal; US

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# LX-101: Novel IGF-1R Targeted Therapy

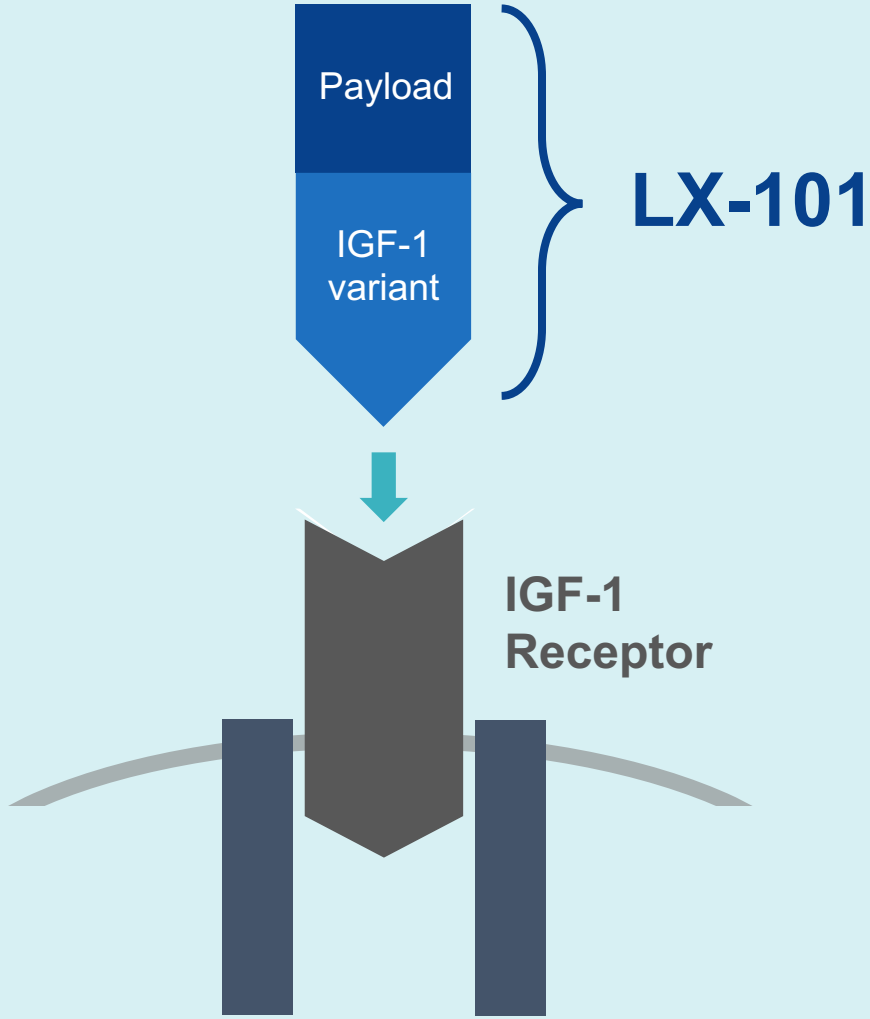
**Precision targeting:** Optimized IGF-1 variant enabling precise payload delivery to IGF-1R+ cells

**Rational payload:** Delivers methotrexate (MTX), a drug used to treat cancer and autoimmune disease (including TED), directly to diseased cells

**Novel and differentiated:** Differentiated mechanism of action (MOA) compared to past and present IGF-1R targeting agents

**Positive Clinical Experience:** Well-tolerated with single agent activity in Phase 1a trials of advanced, pretreated cancer patients

**Large market opportunity:** Wide range of oncologic and autoimmune indications

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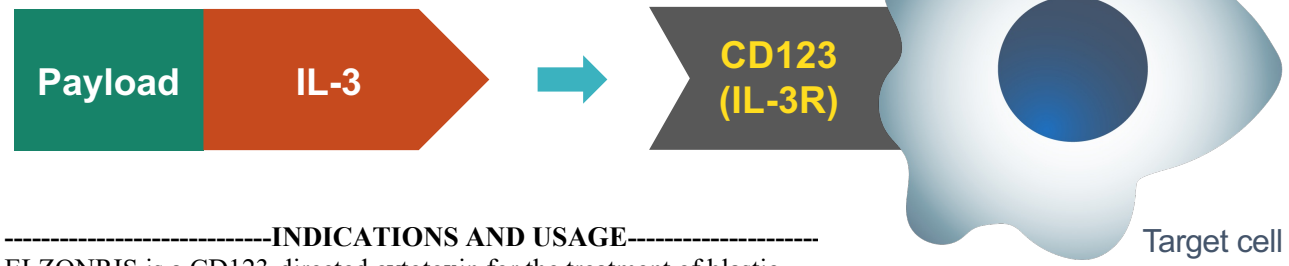
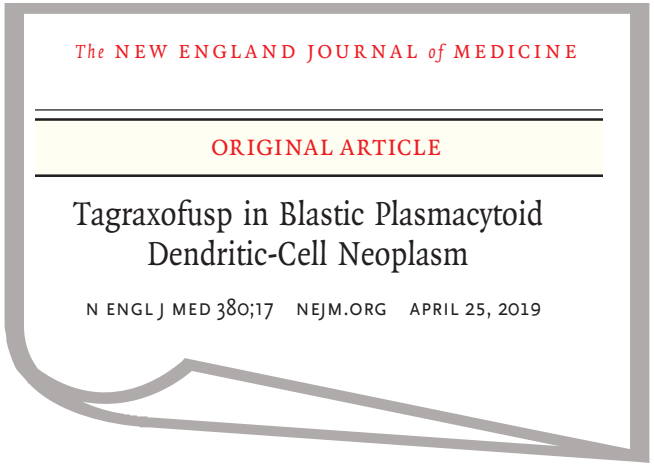
# LX-101: Similar, in many ways, to ELZONRIS


**ELZONRIS**
(tagraxofusp)

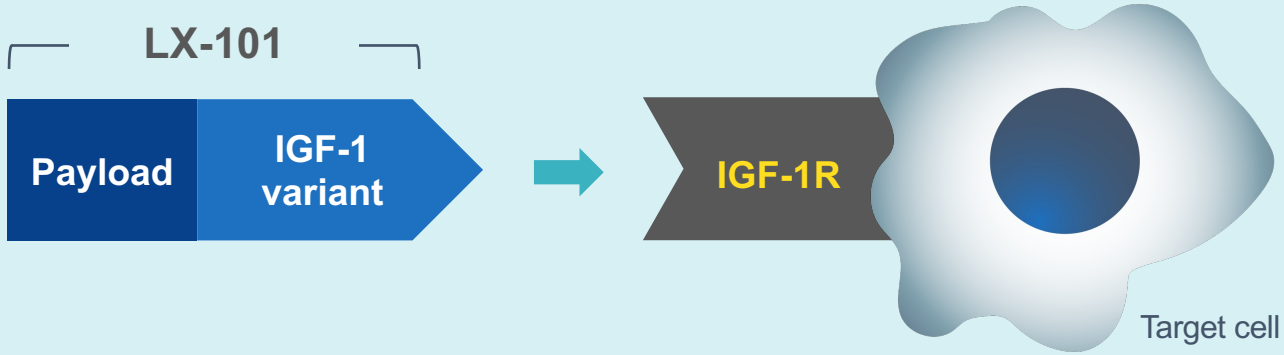



----------**INDICATIONS AND USAGE**----------
ELZONRIS is a CD123-directed cytotoxin for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older. (1)

- ✓ Breakthrough Therapy Designation
- ✓ US and EU approvals in BPDCN
- ✓ Commercial in US and EU

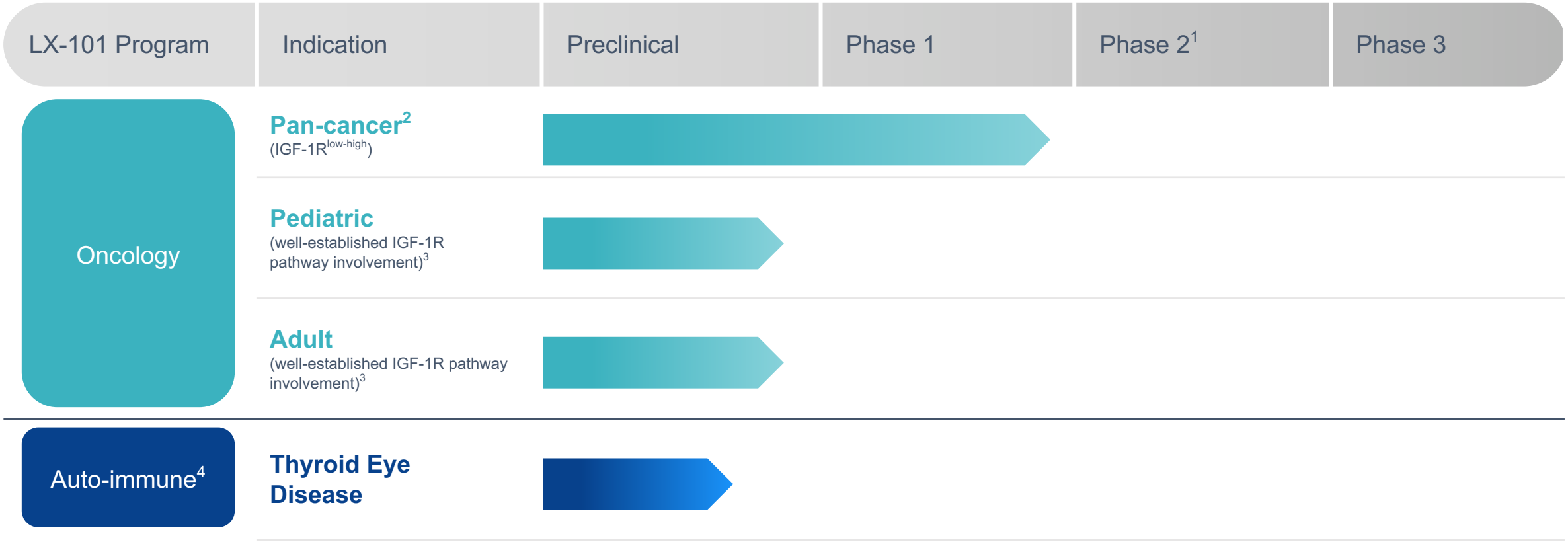



**LX-101**




*Note: FDA approvals for related drugs may not be indicative of what may be required for approval of LX-101*

# Lirum Pipeline




[1]Some indications by virtue of certain factors (e.g., unmet medical need, etc.) could lend themselves to the possibility of pivotal phase 2 studies or other expedited development pathways, although we cannot be assured that LX-101 or any future products will qualify.
[2]This trial, conducted by the licensor with 765IGF-MTX, the former name of LX-101, enrolled patients with multiple cancer types including colorectal, endometrial, pancreatic, breast, basal cell carcinoma, Hodgkin's lymphoma, and others. IGF-1R expression was assessed on patient tumors via immunohistochemical staining and scored based on the proportion of cells that were positive (PS=proportion score; range 0%-100%) and Q score (range 0-7), which is the combination of PS and intensity score (IS).
[3]Cancers with "well-established IGF-1/IGF-1R pathway involvement" include those tumor types with genetic alterations relating to the pathway and/or elevated IGF-1R expression.
[4]Reviewing opportunities in other autoimmune diseases including rheumatoid arthritis, Graves' disease, Cushing's syndrome, lupus, Crohn's disease, and others.

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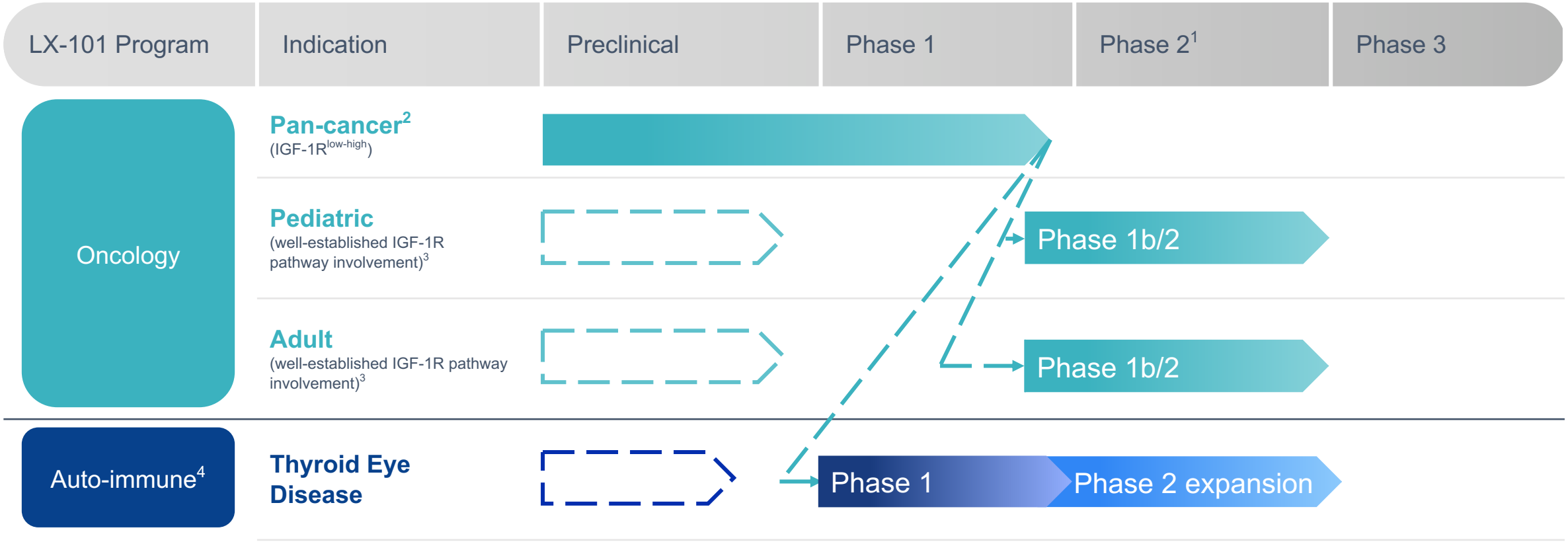
# Lirum Pipeline

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# LX-101

## Oncology

# IGF-1 / IGF-1R in Cancer

## IGF-1 / IGF-1R pathway involvement is well-established in a wide variety of cancers

- Past IGF-1R targeting approaches had evidence of clinical activity, but fell short of approval
  - Consisted of naked mAbs and small molecules (i.e., non-payload bearing)
  - Cancer cells may utilize many **escape mechanisms**, including redundant pathways, to *work-around* blockade of IGF-1R signaling

**LX-101 is designed to address these issues by:**

✓ **Delivering a cytotoxic payload to overcome redundant signaling**

✓ **Focusing on cancer types with well-established ties to the IGF-1 / IGF-1R pathway**

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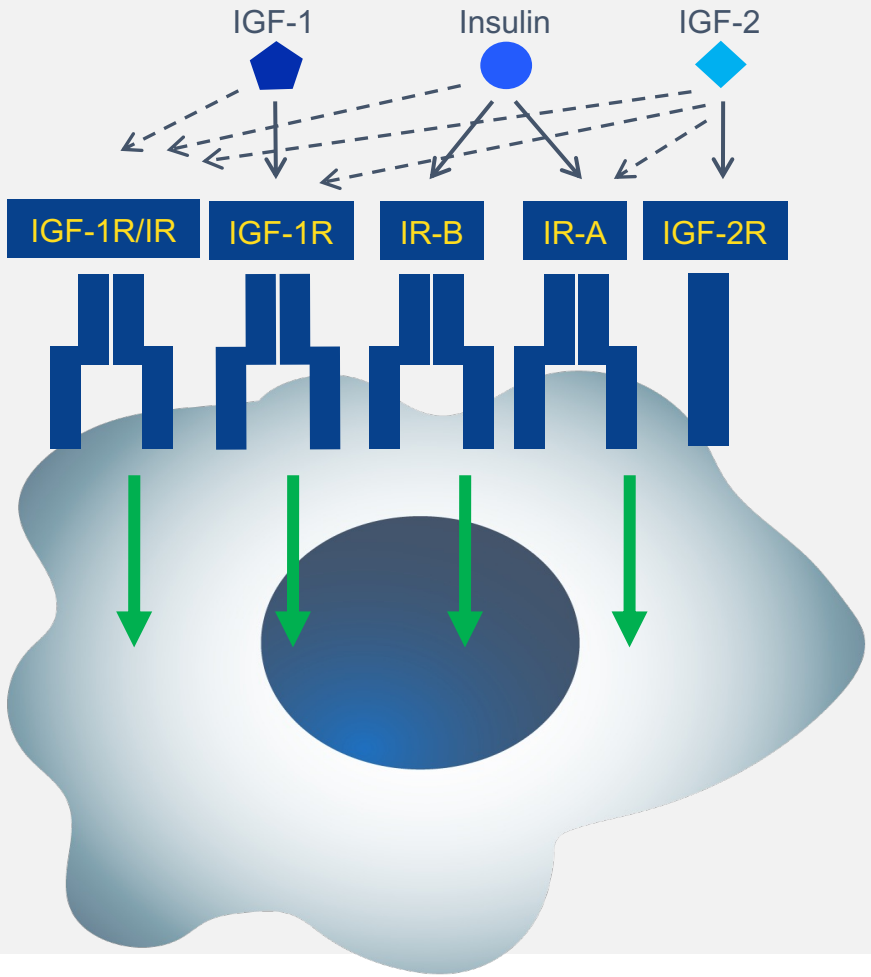
# IGF Signaling in Cancer – Redundant Pathways

## IGF Signaling




## Tumor promotion

↑ Survival

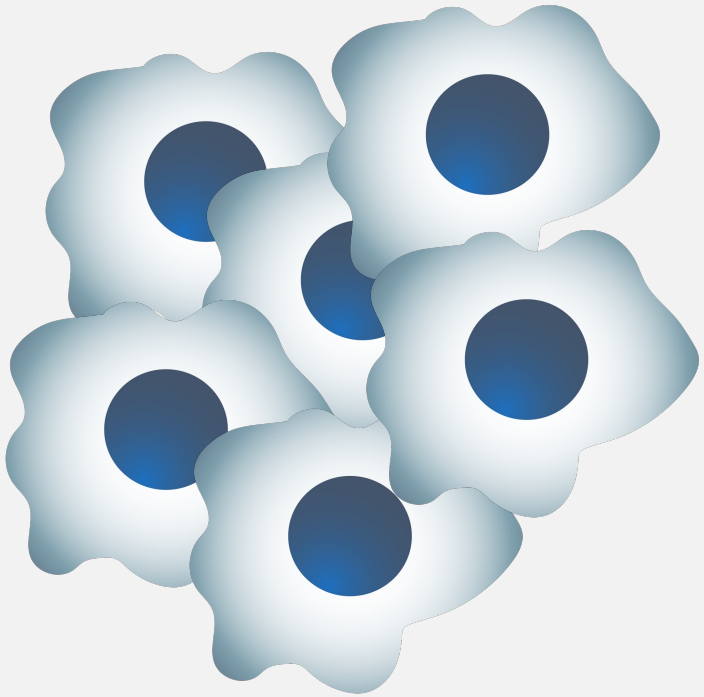
↑ Proliferation

↑ Migration

↑ Invasion

↑ Metastasis

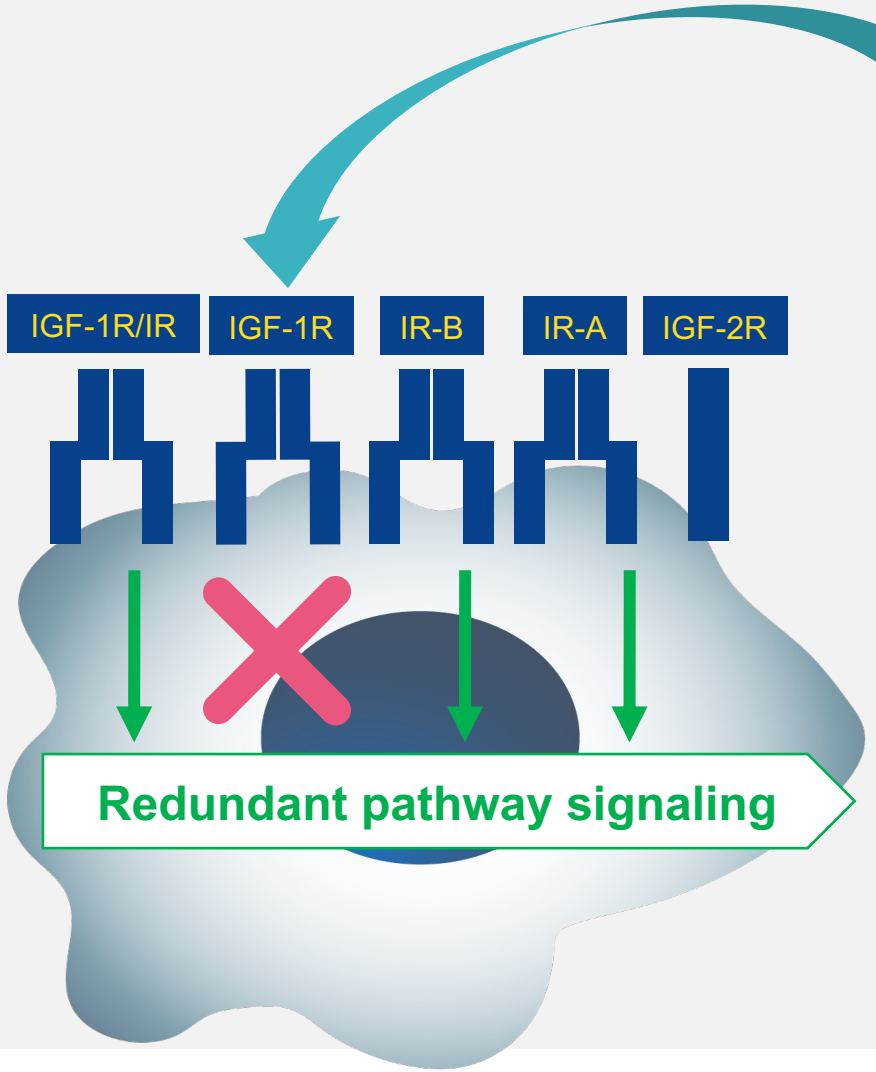
## Clinical manifestation



Malignancy

*Adapted from Scotlandi, ASCO 2012*

# IGF-1R Directed Therapy: Historical Approach




**Historical approach**

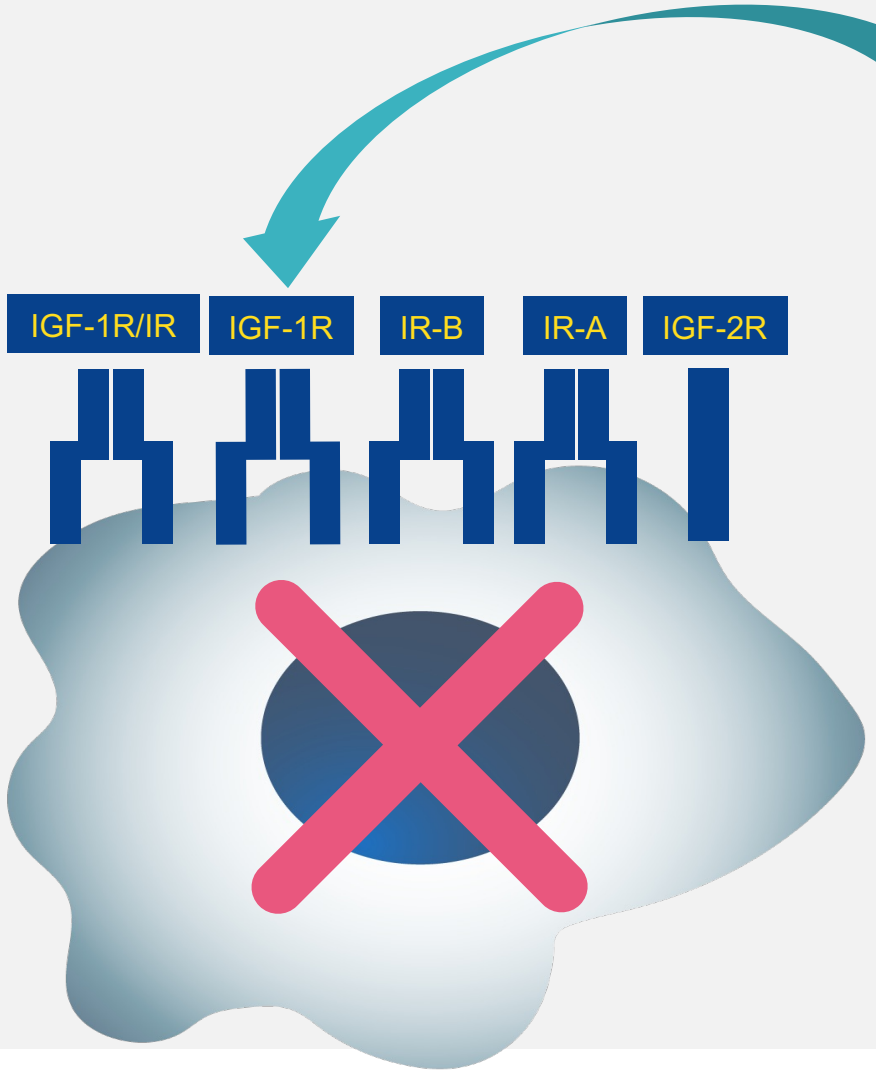
- Blockade/Inhibition of IGF-1R
- But redundant pathways may continue to signal, enable cell escape, and act as disease effectors

➢ Leaves room for improvement

**Cell escape**

*Adapted from Scotlandi, ASCO 2012*

# IGF-1R Directed Therapy: Lirum Approach




**Lirum approach**

- LX-101 delivers payload directed to IGF-1R+ cells
- Cytotoxicity prevents redundant pathway escape mechanisms

➢ More definitive approach

**No escape**

*Adapted from Scotlandi, ASCO 2012*

# LX-101: Positive Clinical Experience

## Clinically tested

- 19 patients with advanced, pre-treated cancers in Phase 1a trials
- Some IGF-1R expression[1] (IGF-1R$^{low-high}$)

## Favorable safety experience

- Well tolerated
  - Most common adverse events (AE): chills/rigors, hypoglycemia, nausea and vomiting
    - Including, grade 2: peripheral neuropathy (n=1); grade 3: abdominal pain (n=6), back pain (n=1), bradycardia (n=1), hypoglycemia (n=1), hypertension (n=1), lymphopenia (n=1), anemia (n=1); grade 4: hypotension (n=1)
  - Low rate of treatment-related hyperglycemia (a known class side effect of IGF-1R inhibition that is potentially treatment-limiting)
- No DLT or MTD reached → Further dose escalation and schedule optimization

## Clinical activity

- 1 PR (at highest dose tested)
- 1 bone marrow CR, 4 stable diseases (including 1 pathologic CR) (at lower doses)

## IGF-1R Expression

- All enrolled and evaluated patients (n=17/19) had some degree of IGF-1R expression (IGF-1R$^{low-high}$)[1]
  - 4/17 (24%) were “High IGF-1R Expressers” (IGF-1R$^{high}$)[2]; 3/4 evaluable for disease control
  - 2/3 (67%) achieved disease control, including 1/1 (100%) at highest dose tested

[1]IGF-1R expression ≥ 10% IGF-1R by IHC or ≥ 0.1% by flow cytometry. [2]We considered “high IGF-1R expressers” (IGF-1R$^{high}$) as patients whose tumors had both a very high Q score (>=6) and very high PS (>90%). DLT = dose limiting toxicity; MTD = maximum tolerated dose; PR = partial response; CR = complete response. Venepalli et al., Am J Clin Oncol, 2019; Alkhateeb et al., Anticancer Res, 2020; Investigator Brochure, April 25, 2017

# LX-101: Trend Toward Dose/Benefit

| Dose (uEq/kg) | n (evaluable) | Disease Control |
|---|---|---|
| 2.5 | - | |
| 1.6 | - | |
| 0.80 | 7 (4) | • PR |
| 0.40 | 3 (3) | • SD |
| 0.20 | 9 (7) | • BMCR<br>• SD (with pathologic CR)<br>• SD<br>• SD |
| 0.1 | 1 (1) | |
| 0.05 | 1 (1) | |


PR = partial response; BMCR = bone marrow complete response; SD = stable disease

# IGF-1R$^{high}$ Tumors Are Sensitive to LX-101

| Dose (uEq/kg) | n (evaluable) | Disease Control | High IGF-1R Expressers[1] (n=3 evaluable) |
|---|---|---|---|
| 2.5 | - | | |
| 1.6 | - | | |
| 0.80 | 7 (4) | • PR | + |
| 0.40 | 3 (3) | • SD | |
| 0.20 | 9 (7) | • BMCR<br>• SD (with pathologic CR)<br>• SD<br>• SD | + |
| 0.1 | 1 (1) | | |
| 0.05 | 1 (1) | | |

**100%** (1/1)

Disease Control Rate at highest dose tested

**67%** (2/3)

Disease Control Rate at all evaluable doses tested

[1]IGF-1R expression was assessed on patient tumors via immunohistochemical staining and scored as intensity score (IS, 0 = no stain, 1 = weak stain, 2 = intermediate stain, 3 = strong stain) and proportion score based on % of cells with IGF-1R positivity (PS, 0% - 9% = 0, 10% - 24% = 1, 25% - 49% = 2, 50% - 74% = 3, 75% - 100% = 4) combined to create a Q score (range 0-7). We considered "high IGF-1R expressers" (IGF-1R$^{high}$) as patients whose tumors had a very high Q score (≥ 6) with IGF-1R expression ≥ 90%.
Venepalli et al., Am J Clin Oncol, 2019; Alkhateeb et al., Anticancer Res, 2020; Investigator Brochure, April 25, 2017

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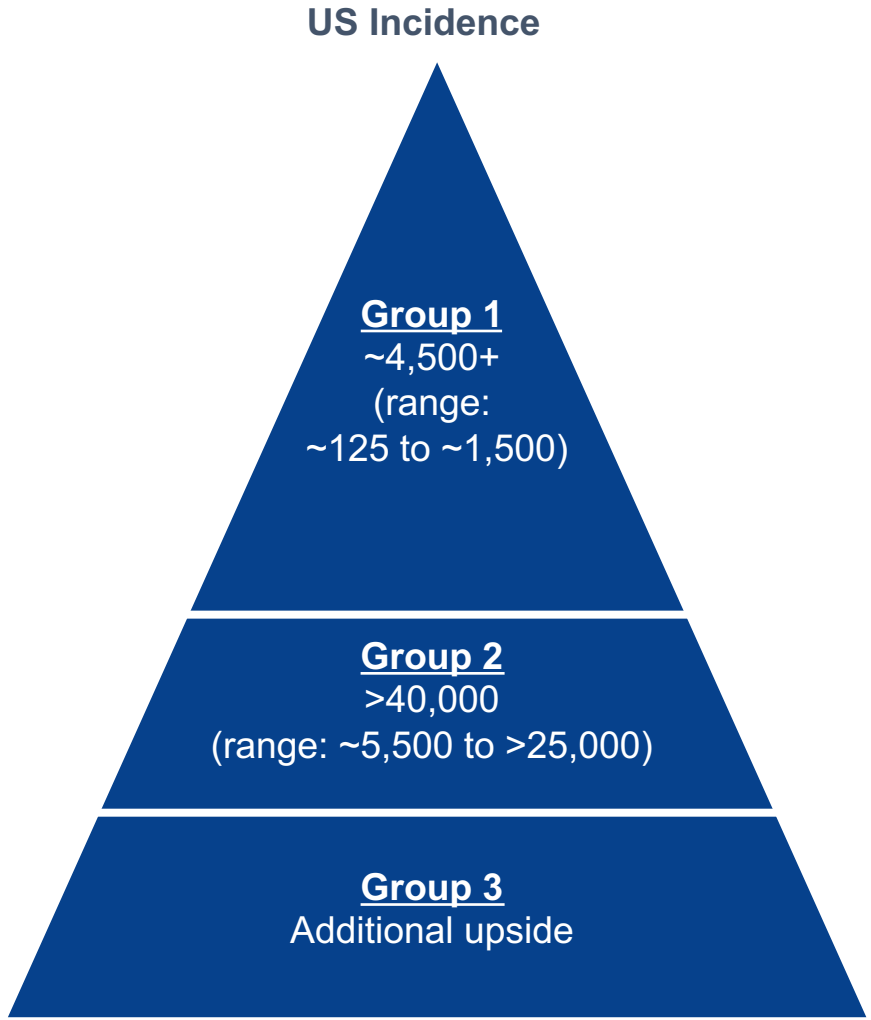
# Select Cancers with Well-Established Ties to IGF-1/IGF-1R Pathway

***✓Strong Scientific Rationale ✓Potential for expedited regulatory pathways ✓Compelling commercial opportunities***

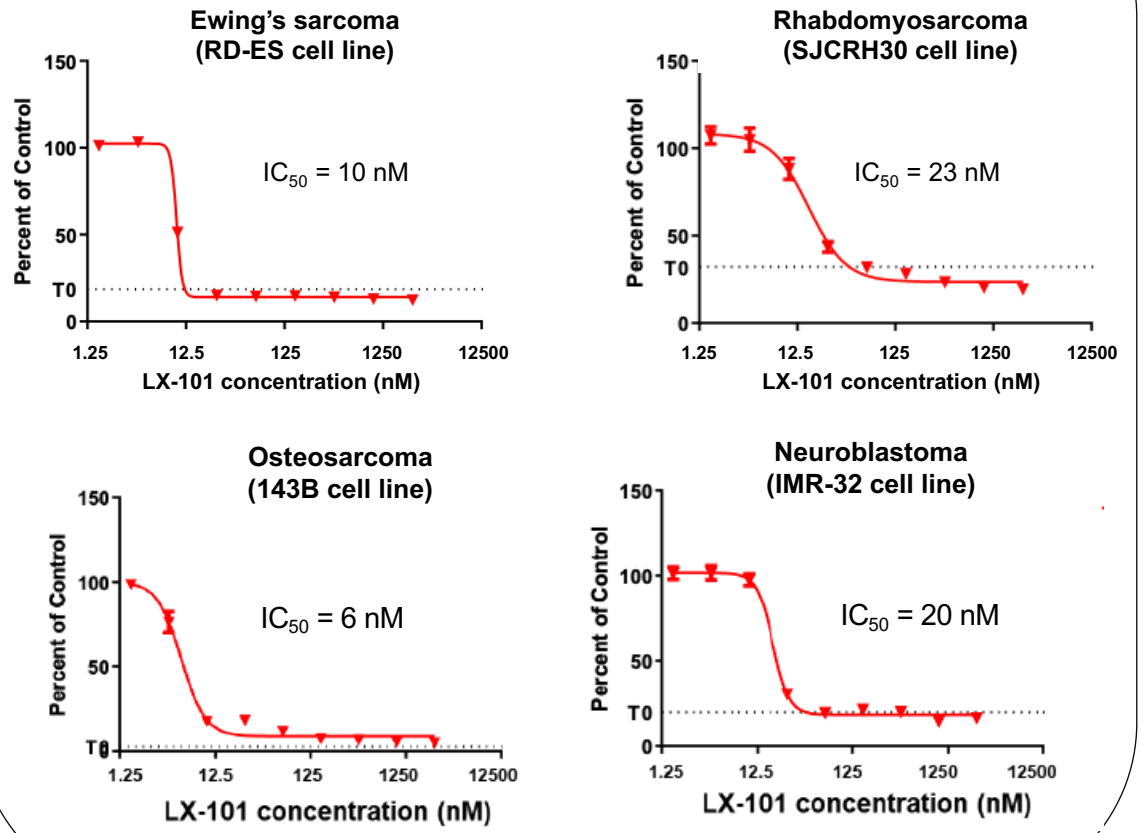
| Cancer Type | Epigenetic and Genetic Alterations | |
|---|---|---|
| Ewing's sarcoma | IGF-1R and poor outcomes | EWSR1-FLI1 |
| Rhabdomyosarcoma | IGF-1R and short survival | PAX3/7-FKHR/FOXO1 |
| GIST | High IGF-1R in peds (WT) | NBF1-IGF1R |
| Synovial Sarcoma | IGF-1R and more aggressive | SYT-SSX1/2 |
| Neuroblastoma | IGF-1R and poor outcome | |
| Osteosarcoma | IGF-1R and poor prognosis | |
| Wilms Tumor | IGF-1R and poor outcome | IGF-1R gene amplification |
| DSRCT | IGF-1R and upregulation | EWSR1-WT1 |
| Adrenocortical carcinoma | IGF-2 overexpression | |
| Adenoid cystic carcinoma | IGF-2 overexpression | MYB-NF1B |
| H&N cancer, HPV(-) | IGF-1R and poor outcome | |
| Bladder cancer, invasive | IGF-1R and higher mortality | |
| Breast cancer, triple negative | IGF-1R and short survival | |
| Many cancer type subsets, including lung, breast, colorectal, prostate, ovarian, gastric, esophageal, etc. | IGF-1R and over-expression and poor outcome features | |




GIST – Gastrointestinal stromal tumor; DSRCT – Desmoplastic small round cell tumor; H&N cancer HPV(-) – head and neck cancer not associated with human papillomavirus

# LX-101: Broad Activity in IGF-1 / IGF-1R Prominent *Pediatric* Tumor Types

## LX-101: Activity in Select Pediatric Cancers

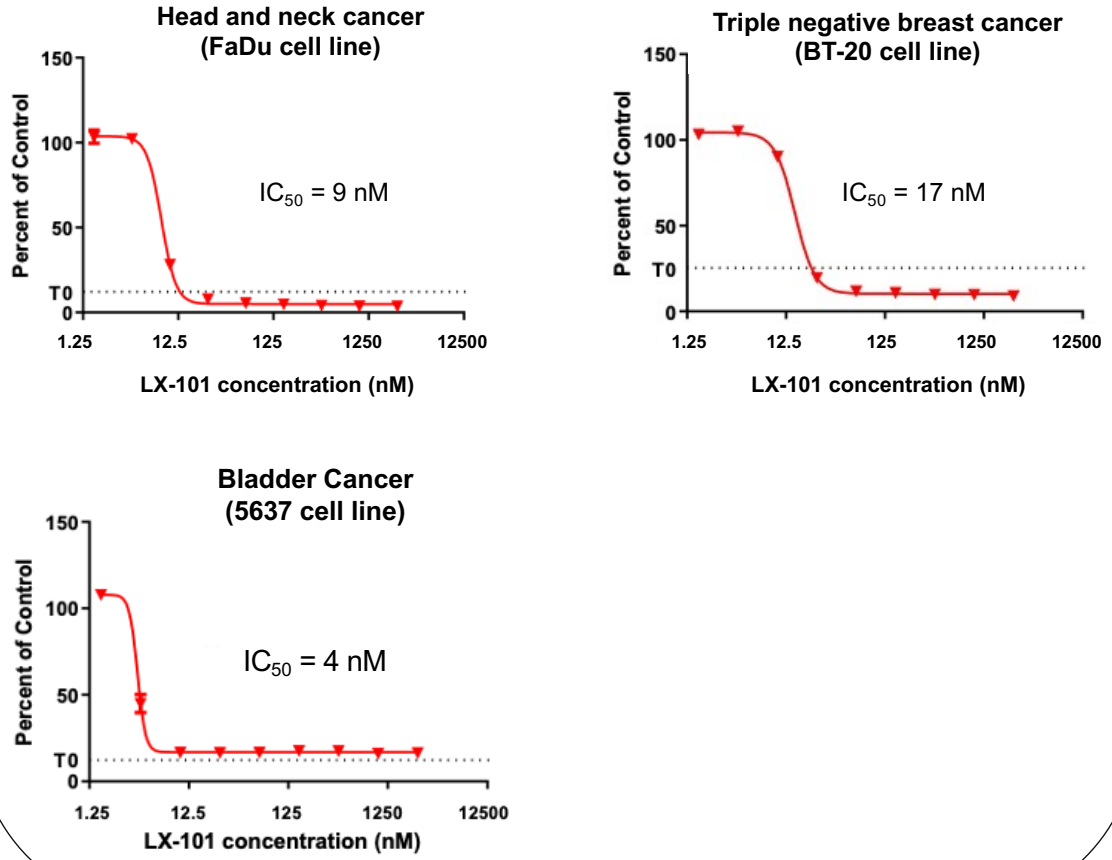



| Population | Indication | Cell lines | Absolute $IC_{50}$ (nM IGF)[2] |
|---|---|---|---|
| Reference | Breast | MCF7 | 35 |
| Pediatric | Ewing's sarcoma | RD-ES<br>CADO-ES1<br>A673<br>SK-ES-1 | 10<br>14<br>14<br>29 |
| | Adrenocortical carcinoma | SW-13<br>NCI-H295R | 9<br>>2500 |
| | Rhabdomyosarcoma | SJCRH30 (alveolar)<br>TE 441.T (embryonal) | 23<br>>2500 |
| | Osteosarcoma | 143B<br>HOS<br>U2OS<br>Saos-2 | 6<br>7<br>32<br>>2500 |
| | Synovial sarcoma | SW-982 | >2500 |
| | Neuroblastoma | SK-N-AS<br>IMR-32<br>SH-SY5Y | 16<br>20<br>30 |

*Source: Presentation CTOS 2023 Annual Meeting; Lirum data on file*

# LX-101: Broad Activity in IGF-1 / IGF-1R Prominent *Adult* Tumor Types

## LX-101: Activity in Select Adult Cancers




| Population | Indication | Cell lines | Absolute $IC_{50}$ (nM IGF)[2] |
|---|---|---|---|
| Reference | Breast | MCF7 | 35 |
| Adult | Head and neck cancer (HPV-) | FaDu (pharyngeal)<br>SCC25 (tongue) | 9<br>>2500 |
| | Triple negative breast cancer | BT-20<br>HCC1143 | 17<br>>2500 |
| | Bladder cancer | 5637<br>T24 | 4<br>61 |

*Source: Presentation 7th Cancer World Conf; Lirum data on file*

# LX-101: Highlights in Oncology

## Summary/Key Points

- ✓ Next generation IGF-1R-targeted therapy
- ✓ Leverage positive clinical experience
- ✓ Identified novel indications with attractive regulatory paths and commercial opportunities

## Key Value-Creating Milestones for Oncology in the Next 12-18 Months

**Initiate Phase 1b/2 trials in IGF-1R prominent pediatric and adult cancers**

**Demonstrate value-creating data in one or more indications**

**Generate and present data updates at major medical conferences**

**Registration-directed expansion cohorts in one or more indications**

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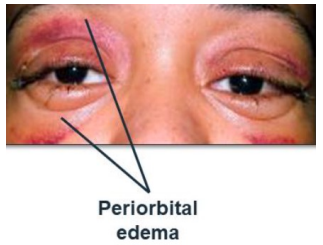
# LX-101

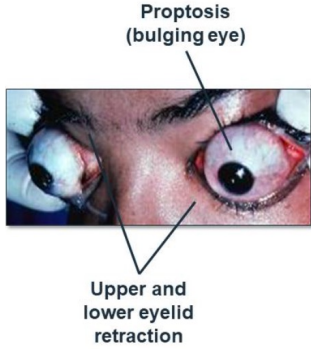
## Thyroid Eye Disease

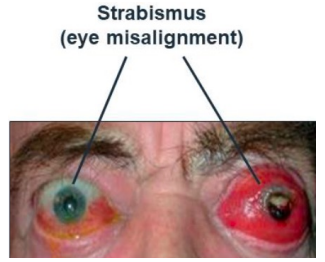
# Thyroid Eye Disease (TED): Overview

## The Condition

- TED is an autoimmune disease characterized by progressive inflammation and damage to tissues around the eyes
- Acute/active (1-3 years) and chronic (>3 years) phases
- Symptoms range from mild to severe (including possible vision loss), and repeated exacerbations can occur




## The Opportunity

### Incidence / Prevalence

- Acute phase: ~20-25K/year U.S. incidence
- Chronic phase: >70K/year U.S. prevalence

### Large Market

- Tepezza®, FDA approved naked mAb to IGF-1R
- ~$2B in sales in ‘22 (3rd year on market)
- Over $3.5B estimated global market

### Novel Approach

- Numerous opportunities for a novel, differentiated approach to penetrate this expanding and segmented market

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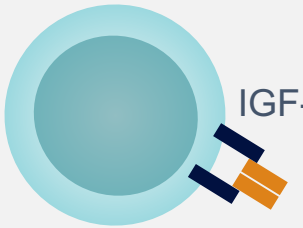
Mohyi et al., J Mol Endocrinol, 2018; Verity et al., Eye (Lond), 2013; McAlinden Eye Vis (Lond), 2014; Horizon Therapeutics earnings releases and company reports.

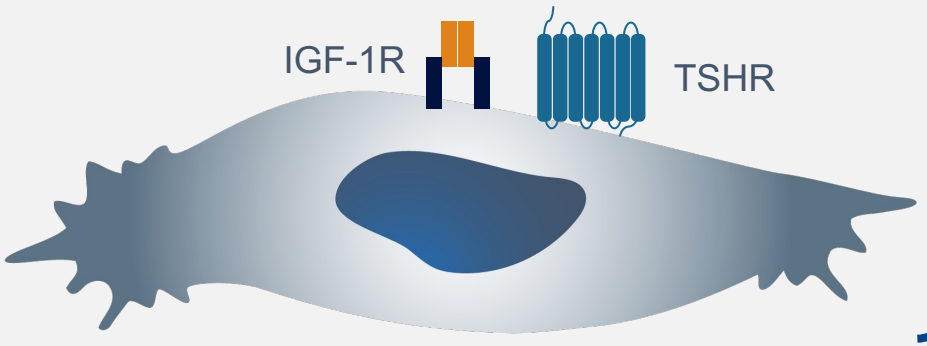
# TED Pathogenesis

## Autoimmune process

T cell



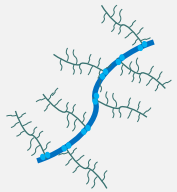

B cell


Orbital fibroblast

## Overproduction of molecular and cellular factors

Hyaluronan synthesis

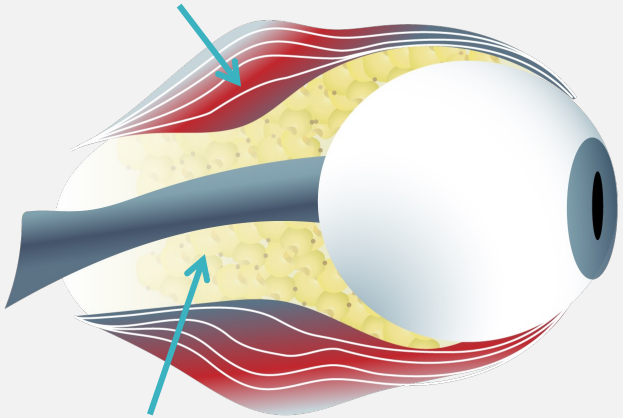


Differentiation
(adipocytes, myofibroblasts)

Inflammatory cytokines

## Extraocular muscle enlargement and orbital expansion

**Enlarged Muscle**



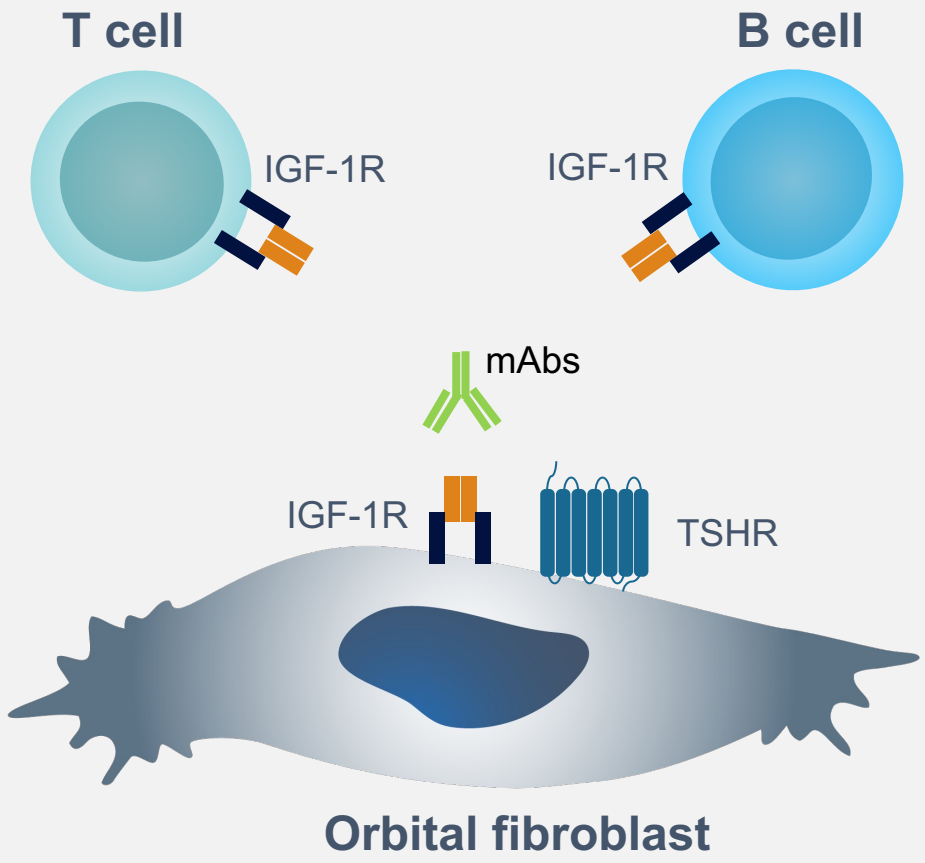
**Expanded Orbital Tissue and Fat**

**Proptosis**, increased orbital pressure, congestion, periorbital edema, and other, sometimes sight-threatening, symptoms

TSHR = thyroid-stimulating hormone receptor

Ugradar et al., Eye (Lond), 2021; Iyer et al., Best Pract Res Clin Endocrinol Metab, 2012, Krieger et al., Pharmacol Ther, 2020

# TED Treatment: Historical and Current Approaches




**Historical and Current Approaches include**

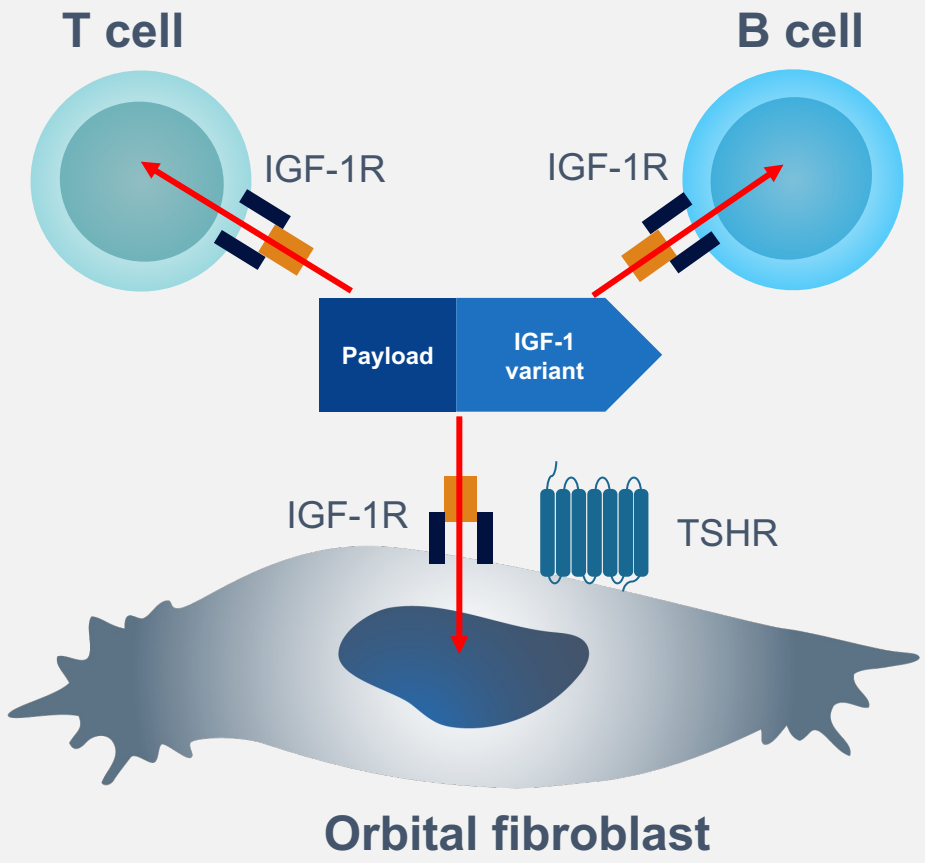
- Blockade/Inhibition of IGF-1R
- Effective, but may lack potency and other redundant pathways may continue to signal and act as disease effectors

➢ Thus, this approach may have limitations and leave room for improvement

TSHR = thyroid-stimulating hormone receptor

Ugradar et al., Eye (Lond), 2021; Iyer et al., Best Pract Res Clin Endocrinol Metab, 2012, Krieger et al., Pharmacol Ther, 2020

# TED Treatment: Lirum Approach




**Lirum Approach**

- LX-101 delivers a payload directly to IGF-1R+ cells,
- Payload designed to add potency to signal blockade, while also eliminating escape via pathway redundancy

➢This differentiated MOA may provide a more definitive and/or complementary approach to treating various segments of acute and chronic TED

TSHR = thyroid-stimulating hormone receptor

Ugradar et al., Eye (Lond), 2021; Iyer et al., Best Pract Res Clin Endocrinol Metab, 2012, Krieger et al., Pharmacol Ther, 2020

# Horizon: Acquired by Amgen for $27.8B

✓ **Tepezza®, approved for TED, key growth driver for Horizon**

✓ **TED represents a multi-billion dollar market opportunity with significant growth potential**

- HZNP acquired by Amgen for $27.8 billion
- Tepezza® annual sales
  - 2021: $1.7B
  - 2022: ~$2.0B
- Significant and growing global market for TED is estimated to be greater than $3.5B
- TED market is segmented and includes acute, chronic, recurrent, residual, refractory, less severe, tolerability issues

➢ ***Offers multiple opportunities for market entry and expedited development for new entrants, and especially ones with differentiated MOAs like LX-101 which may also complement and/or offer advantages over current approaches***

Lirum THERAPEUTICS

*Source: Horizon SEC filings and analyst estimates*

# LX-101: Highlights in TED

**Summary/Key Points**

- **Novel and differentiated approach to commercially validated target**
- **Clinical experience with well-tolerated safety profile**
- **Commercially attractive market opportunity**
  - >$3.5B globally
  - Segmented with multiple entry opportunities for LX-101

## Key Value-Creating Milestones for TED in the Next 12-18 Months

**Initiate clinical trials in multiple TED segments**

**Generate and present data at major medical conferences**

**Demonstrate value-creating data in one or more segments**

**Advance to registration-directed stage in one or more areas of TED**

Lirum THERAPEUTICS

# Key Take Aways

## Lead by a veteran team with strong track record of success

- ✓ History of shareholder value creation
- ✓ Multiple approvals and commercial launches

## Innovative technology with differentiated MOA

- ✓ Positive clinical experience
- ✓ Differentiated profile compared to other IGF-1R targeted approaches
- ✓ Tremendous commercial opportunity in oncology and autoimmune diseases

## Next Steps

- ➢ Advance LX-101 into IGF-1R-driven pediatric and adult cancers and TED
- ➢ Continue to opportunistically expand pipeline

## Multiple Near Term Key Value-Creating Milestones in the Next 12-18 Months

- **Initiate clinical trials focused on cancer types of high interest**
- **Initiate clinical trials in multiple TED segments**

→

- **Demonstrate value-creating data in oncology and TED**
- **Present updates at major medical conferences**

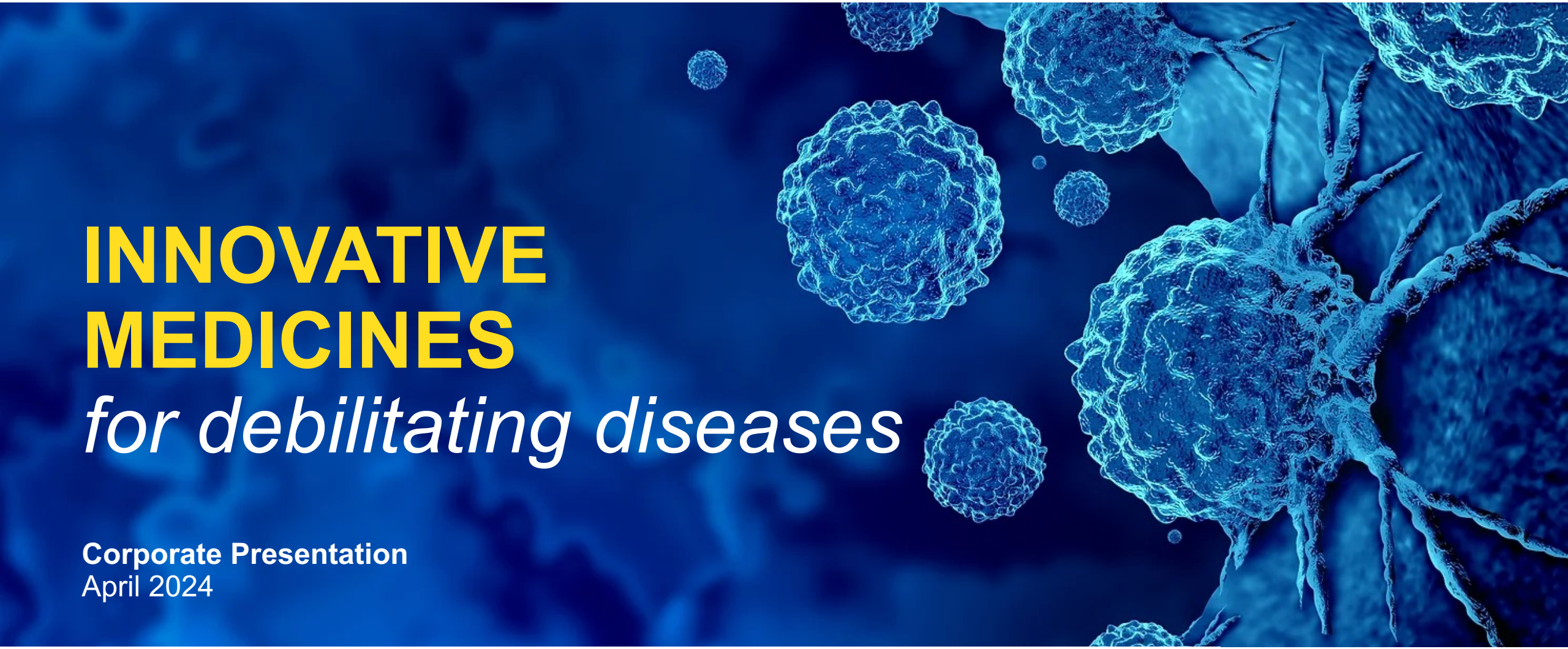
→

**Advance to registration-directed efforts**

- **In one or more oncology indications**
- **In one or more TED patient segments**

Lirum THERAPEUTICS

Lirum THERAPEUTICS



# INNOVATIVE MEDICINES

*for debilitating diseases*

**Corporate Presentation**
April 2024