

## **CORPORATE PRESENTATION**

## DECEMBER 2023

Making Smart Chemical Changes to Create Improved Novel Therapeutics

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## LB PHARMACEUTICALS INVESTMENT HIGHLIGHTS

CNS-focused biotech building a pipeline of potential best-in-class therapies for the US market



## LB PHARMACEUTICALS BUSINESS STRATEGY

- CNS-focused development stage company intent on building a pipeline of improved versions of effective drugs that are commercially unavailable in the US
- Lead asset LB-102 is a methylated version of amisulpride, one of the leading antipsychotics in use worldwide for the treatment of schizophrenia
  - LB-102 was designed to be effective at lower doses than amisulpride, which could improve safety and tolerability
  - LB-102 is a novel chemical structure with composition of matter patents issued in the US and abroad
  - Even if clinically equivalent to amisulpride, LB-102 would be one of the most effective antipsychotics on the US market with IP until at least 2037 and potential to yield \$1 billion in annual sales based on ex-US market data\*
- First-in-class team of executives, board members, and advisors with extensive experience in drug development in the psychiatric arena

## **MANAGEMENT TEAM**

#### Zachary Prensky, Chief Executive Officer & Co-Founder

- Managed family office from 1997-2015
- Portfolio responsibilities included oversight of all biotechnology investments

#### Anna Eramo, M.D., Chief Medical Officer

- Former Clinical and Medical Affairs head at Lundbeck
- Has 18 years of global CNS experience; oversaw US development of brexpiprazole
- Trained clinical psychiatrist

#### Andrew Vaino, Ph.D., Chief Science Officer

- Chemistry PhD from Queen's University with two decades experience in biotech
- MBA from UC Irvine
- Inventor of two molecules studied clinically

#### Marc Panoff, Chief Financial Officer

- Previously CFO of Retrophin raised \$150 million in equity and debt financings and uplisted company to Nasdaq Global Market
- Previously CFO of Neurologix and Nephros

## **SCHIZOPHRENIA**

- Schizophrenia (SCZ) is a chronic and debilitating disease affecting approximately 1% of the US population<sup>1</sup>
  - 100,000 new SCZ patients diagnosed per year<sup>2</sup>
  - SCZ patients have profoundly diminished quality of life
    - Fewer than 20% hold full-time employment;<sup>3</sup> increased odds of arrest<sup>1</sup>
  - Life expectancy of SCZ patients is reduced by 10-20 years compared to the general population<sup>4</sup>
    - Approximately 5% SCZ patients die of suicide<sup>5</sup>
  - Disease defined by three major groups of symptoms
    - Positive symptoms: delusions, hallucinations, agitation
    - Negative symptoms: lack of social engagement, depression
    - Cognitive symptoms: memory deficits, impaired executive functions

<sup>1</sup> About Schizophrenia - Schizophrenia & Psychosis Action Alliance (sczaction.org)

<sup>2</sup> Schizophrenia Symptoms, Patterns and Statistics and Patterns (mentalhelp.net)

<sup>3</sup> The Atlantic, "Job Hunting with Schizophrenia", Maria Hengeveld, July 28, 2015

<sup>4</sup> Moradi et al. 2018

## US ANTIPSYCHOTIC MARKET LANDSCAPE<sup>(1)</sup>



- Branded antipsychotic drugs generate ~\$11 billion in sales annually in the US
- Despite limited efficacy, and a crowded generic market, new branded antipsychotics such as Latuda, Vraylar, and Rexulti are approaching or have achieved > \$1 billion each in annual sales in the US

## SCHIZOPHRENIA – UNMET MEDICAL NEED

- Despite 20+ FDA approved drugs, SCZ patients don't get adequate help
  - An estimated 50% of patients with SCZ do not take their prescribed medications as directed<sup>1</sup>
  - Up to 75% of SCZ patients cycle through multiple drugs within 18 months, with up to 60% failing to find an effective therapy<sup>2</sup>

Standard of care treatments do not adequately treat a heterogeneous patient population; alternative novel treatments are badly needed



### Branded Rx growing

TRx Branded APs (Latuda, Vraylar, Rexulti, Caplyta,

Phase 2 data price catalyst<sup>3</sup>

Share Price Pre/Post P2 SCZ Data					
	Phase 2	<b>PANNS</b> $\Delta$	Share Price	Mkt Cap	
Company	Announcement	From BL	Increase	Increase (\$B)	
KRTX	11/18/19	-17.4	5.5x	2	
CERE	6/29/21	-19.5*	<b>2.4</b> x	2.2	

\* 30 mg QD

1 About Schizophrenia - Schizophrenia & Psychosis Action Alliance (sczaction.org)

2 Lieberman JA, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med. 2005;353:1209–1223.

3 Shows percentage change of closing share price and market capitalization for two companies upon annoucement of successful Phase 2 clinical studies for schizophrenia during 2019-2021. Source: NASDAQ.

## AMISULPRIDE BACKGROUND

- Amisulpride is a benzamide indicated for the treatment of schizophrenia in Europe since 1986
  - Patented and developed by Synthélabo (acquired by Sanofi)
  - Selective  $D_2 (K_i = 2.8 \text{ nM})/D_3 (K_i = 3.2 \text{ nM})$  and  $5HT_7 (K_i = 31 \text{ nM})$  antagonist
  - In July 2000 Sanofi announced it would discontinue development of amisulpride in the US based on IP
- Amisulpride has generated over 2.5 million prescriptions annually for the past three years in Europe
- 35 years of clinical use demonstrates an excellent efficacy/safety profile

## AMISULPRIDE COMPARATIVE EFFICACY/SAFETY

Meta-Analysis of 32 Schizophrenia (SCZ) Drugs<sup>(1)</sup> (n = 53,500)

### **Antipsychotic Efficacy**



### Amisulpride is one of the most effective antipsychotics in the world

EUFEST Study<sup>(2)</sup> (Clinical Trial of 5 SCZ Drugs in First Episode) (n = 498)

#### **All-Cause Discontinuation**



#### Amisulpride is one of the best tolerated antipsychotics

### **AMISULPRIDE COMPARATIVE SAFETY**



• All cause discontinuation combines efficacy and tolerability. When reported separately, more patients dropped out due to inefficacy (40%) than due to adverse events (20%)

# LB-102 OVERVIEW

LB-102 is a methylated version of amisulpride



- Novel chemical structure with chemical properties designed to improve amisulpride's efficacy and safety
- Safe and well-tolerated in two (n = 80) Phase 1 clinical studies
- More than 20 issued patents worldwide including composition of matter covering LB-102 extending to at least 2037
- CNS receptor binding profile similar to amisulpride: high selectivity for D<sub>2/3</sub> and 5HT<sub>7</sub>
- LB-102 same as/better than amisulpride in preclinical animal models of SCZ

## LB-102 AND AMISULPRIDE RECEPTOR SPECIFICITY

LB-102 is a selective  $D_2/D_3/5HT_7$  antagonist with minimal off-target activity



### LB-102: ENHANCING AMISULPRIDE'S PRODUCT PROFILE

- Of 30 psychiatric medications tested amisulpride was least able to passively diffuse across model BBB<sup>(1)</sup>
- Improving BBB permeability could improve efficacy/decrease adverse events
- Methylation has been shown to improve membrane permeability without changing receptor binding activity, for example desipramine to impramine and nortriptyline to amitriptyline



 In a PET study, using <sup>11</sup>C raclopride, directly measuring dopamine RO in mice the same dose of LB-102 showed LB-102 bound D<sub>2/3</sub> receptors ~2X as strongly as amisulpride (K<sub>i</sub>s are similar)



PET scans taken 140 min after dosing either 100 mg/kg amisulpride or LB-102

## LB-102 PHASE 1 CLINICAL TRIAL OVERVIEW

- Dosing: 5 single ascending dose (SAD) cohorts/3 multiple ascending dose (MAD, 1 week, BID dosing) cohorts
- Endpoints: Safety and pharmacokinetics
- Single Site: Medpace in Cincinnati, OH



## LB-102 PHASE 1 PHARMACOKINETICS (SAD)

LB-102 exhibits favorable PK properties, with a half-life of 12+ hours and Tmax of 2-3 hours

Dose LB-102 (mg)	Cmax (ng/mL)	AUCinf (h*ng/mL)	Tmax (h)	T <sub>1/2</sub> (h)
10	24	253	3	13.7
50	176	1600	3	12.3
100	349	2823	2.8	14.7
150	596.5	4650	3.2	12.6
200	976	7001	2	12.8

Healthy volunteers single ascending doses of LB-102



## PLASMA EXPOSURE OF LB-102 > AMISULPRIDE

Rosenzweig<sup>(1)</sup> reported PK data on 18 healthy volunteers exposed to a single dose 50 mg amisulpride



### Observed LB-102 plasma exposure is ~ 2.5x that of amisulpride<sup>(2)</sup>

# LB-102 PHASE 1 ADVERSE EVENTS

Single ascending dose					Multiple ascending dose				
Adverse event	Placebo	10 mg	50 mg	100 mg	150 mg	200 mg	50 mg BID	75 mg BID	100 mg BID
n	16	6	6	6	6	6	6	6	6
Elevated prolactin		2	3	1	1	1	2	2	1
Diarrhea			1						
Upper respiratory infection			1	1					
Abdominal pain	1	1		1					
Nausea						1		1	1
Urticaria				1					
Acute dystonia						1		1	2
QT prolongation						1			
Insomnia						1		1	
Gastroesophageal reflux						1			
Headache	1					1			
Oropharyngeal pain						1			
Heart palpitations						1			
Vomiting									1
Dry mouth									1
Somnolence								1	1
Dizziness								1	
Migraine								1	
Back pain	1							1	
Bug bite	1								
Total AEs	4	3	5	4	1	9	2	9	7

- Prolactin elevation (PRL), which was reversible and unassociated with clinical consequences, was observed at all doses, a consequence of dopamine receptor binding
- Dosing in 200 mg/d MAD cohort was stopped after 3 days due to two occurrences of EPS (acute dystonia)
  - EPS associated with excess D<sub>2/3</sub> RO, suggesting need to tamp down dose < 200 mg/d</li>

### DOPAMINE RO DIRECTLY LINKED TO IMPROVEMENTS IN SCZ PATIENTS



Dopamine RO a good predictor of PANSS improvement<sup>(1)</sup>

## LB-102 PHASE 1b PET IMAGING STUDY (NCT04588129)

- **Dosing:** Adaptive design with 4 cohorts of 4 healthy volunteers each
  - Multiple PET scans per subject using <sup>11</sup>C raclopride as tracer
- Study Objectives: To confirm  $D_2/D_3$  target engagement and inform Phase 2 dosing



## PHASE 1b - COHORTS 1 - 3, SINGLE DOSE



- Subjects in Cohorts 1 (100 mg) and 2 (50 mg) were scanned at 2.5, 7.5, and 23.5 hrs post-dose
- Subjects in Cohort 3 (75 mg) were scanned at 2.5, 23.5, and 47.5 hrs post-dose
- Desired dopamine RO between 60% and 75%
- Data suggests that LB-102 can be dosed once a day

### PHASE 1b - COHORT 4, STEADY STATE, 100 MG (N=2); 50 MG (N=2)



- Subjects scanned 2.5, 7.5, and 23.5 hrs after 4 days QD dosing
  - Dopamine RO observed at 50 mg was in the desired range for an effective schizophrenia drug
  - 50 mg LB-102 afforded same dopamine RO as 400+ mg amisulpride per day

## PHASE 1b - KEY TAKEAWAYS

- No reported SAEs or EPS
- Dopamine receptor occupancy in desired range at 50 mg to 100 mg dose
- Confirms hypothesis from Phase 1 study
- Planned dosing for Phase 2 study: 50 mg, 75 mg, and 100mg once per day
  - FDA guided LB-102 could be dosed up to 200 mg/d in SCZ patients
  - Therapeutic doses expected to be well within the margin of safety

# **LB-102 KEY DIFFERENTIATORS**

 Superior efficacy than most recently launched antipsychotics and other compounds in development

	Avg PANSS $\Delta$ from BL <sup>1</sup>
Caplyta	-14.1
Rexulti, 4 mg	-19.9
Vraylar, 3 mg	-22.4
Amisulpride	-28.9

- Minimal off-receptor binding (D<sub>2</sub>, D<sub>3</sub>, 5HT<sub>7</sub>) potentially leading to low incidence of AEs
- Potential use in patients with predominantly negative symptoms, bipolar depression, depression, and Alzheimer's psychosis
  - Amisulpride one of two drugs to show statistically significant improvement in negative symptoms (SANS  $\Delta$  12 points vs. placebo)<sup>2</sup>
  - Equivalent to Prozac in clinical study of depression<sup>3</sup>
  - ATLAS study showed amisulpride effective in treating psychosis in elderly<sup>4</sup>
- Weakly metabolized, low risk of drug/drug interactions
- LB-102's low expected therapeutic doses (50 mg LB-102 = same dopamine RO as 400 mg amisulpride) could be amenable to LAI formulation

## **LB-102 US MARKET OPPORTUNITY**

- Amisulpride/LB-102 differentiated by robust efficacy for both positive and negative symptoms of the disease and a clean AE profile
  - Prescriptions in the Europe exceed 2.5 million/year<sup>1</sup> despite a lack of sales/marketing support for 15 years
- Branded antipsychotic drugs generate ~\$11 billion in sales annually in US



### LB-102 combines de-risked efficacy/safety of amisulpride with IP of a NCE



## THANK YOU