

# INVESTOR PRESENTATION

# JULY 2022

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

## **BOARD OF DIRECTORS**

### Zachary Prensky, CEO and Co-Founder

### Robert Ruffolo, Ph.D., D.Sc. (h), D.Eng. (h), F.C.P.P.

- Former President of R&D, Wyeth Pharmaceuticals
- Previously SVP and Director, Biological Sciences, Worldwide, SmithKline Beecham Pharmaceuticals (now GlaxoSmithKline)

#### **Piero Poli**

 Owner and CEO of Rivopharm SA, a Swiss company that has developed over 25 molecules and registered generic products throughout Europe, including amisulpride

#### Vincent Grattan, R.Ph

- Co-Founder and senior consultant
- PA registered pharmacist currently employed by MHM Services, responsible for all facets of drug utilization management collaborating with a team of 300+ clinicians; 20 years of psychopharmacology experience

#### Edmund Sullivan, Founding Investor

• Formerly at Citigroup and Cowen & Company

## SCIENTIFIC ADVISORS

#### John M. Kane, M.D., Chairman

 Vice President, Behavioral Health Sciences, Northwell Health; Chairman of Psychiatry, Zucker Hillside Institute

### Christoph Correll, M.D.

 Medical Director, Recognition and Prevention Program, The Zucker Hillside Hospital; Professor, Center for Psychiatric Neuroscience, The Feinstein Institute for Medical Research

### Stefan Leucht, M.D.

 Department of Psychiatry and Psychotherapy, Technische Universitat Munchen, Munich, Germany

#### Ira Glick, M.D.

 Professor of Psychiatry and Behavioral Sciences, Stanford University School of Medicine

#### Herbert Meltzer, M.D.

 Professor of Psychiatry & Behavioral Sciences, Pharmacology and Physiology, Northwestern University

# LB PHARMACEUTICALS – FINANCING HISTORY

Financing Round	Date(s)	Gross Amount Raised	Milestones Achieved
Seed Rounds	2015 - '17	\$1.9M	LB-102 Invention and <i>in-vitro</i> studies 3 animal SCZ pre-clinical studies Initial CMC Formulation
Series A	2017 - '18	\$8.4M	Completion of all IND-enabling studies Successful Phase 1 clinical trial in 64 healthy volunteers Successful completion of Phase 1 trial (safety/PK) in 64 healthy volunteers
Convertible Notes	2020	\$10.0M	Successful Phase 1b PET imaging study (dopamine receptor occupancy) in 16 healthy volunteers Successful completion of two long-term toxicity studies in dogs and rats Production of LB-102 tablet for Phase 2 drug product Phase 2 clinical trial preparation; CMO hire, CRO engagement, site selection
Totals		\$20.3M	LB-102 Phase 2 Ready

# **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 2PANNS $\Delta$ Share PriceMkt Cap									
Company	Announcement	From BL	Increase	Increase (\$B)					
KRTX	11/18/19	-17.4	5.5x	2					
CERE	6/29/21	-19.5*	2.4x	2.2					

\* 30 mg QD

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

2 Patel et al. P&T 2014 Sep; 39(9): 638–645.

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
- Three US and four ex-US composition of matter patents covering LB-102 issued 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 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  $(D_2, D_3, 5HT_7)$  potentially leading to low incidence of AEs
- Potential use in patients with predominantly negative symptoms, 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 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	8	8	8	8	8	8	8	8	
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									

- 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 and 75 mg, 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 PHASE 2 CLINICAL PROGRAM

- Trial Size: Expecting to enroll ~300 SCZ patients at ~25 sites
- **Design:** 2 doses LB-102 versus placebo (4 weeks duration, in-patient, double-blind, placebo controlled)
- **Primary Endpoint:** Change in PANSS
- Development plan will follow well-established criteria for FDA approval of a schizophrenia drug (cf. Rexulti, Vraylar, Latuda)
  - LB-102 Phase 2 study designed to potentially be registrational study



Inclusion Criteria • Adults, 18 to 50 years old, with acute schizophrenia diagnosis

# LB-102 CLINICAL DEVELOPMENT PROJECTED TIMELINE

		FY 2020		FY 2021		FY 2022		F	FY 2023		
Study	Size		Q1	Q2	Q3	Q4	1H	2H	1H	2H	
Phase 1a SAD/MAD	n = 64	Completed									
Phase 1b PET	n = 16		(	Completed							
Phase 2	n = 300										,
CARC											
СМС											
			- Indi	cates expec	cted compl	etion of enro	llment				

- Phase 1 and 1b studies completed; End of Phase 1 meeting with FDA took place in 2021
- Start of Phase 2 study dependent on close of Series B financing
- CMC activities to support Phase 2 study to be completed in Q3 2022

# **LB-102 US MARKET OPPORTUNITY**

- Expect LB-102 would be 3<sup>rd</sup> line SCZ treatment initially
- 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 despite a lack of sales/marketing support for 12 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

# **PIPELINE EXPANSION POTENTIAL**

LB-102 has the potential for clinical impact in areas outside of schizophrenia, such as depression

Product Indication	Discovery	Pre-Clinical	Phase 1	Phase 2	Phase 3
LB-102 (schizophrenia)					
LB-104 (depression)					
LB-102 (schizophrenia – negative symptoms)					
LB-102 (schizophrenia - LAI)					

# LB PHARMACEUTICALS INVESTMENT HIGHLIGHTS

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





# THANK YOU