

# CORPORATE PRESENTATION JANUARY 2019

Making Smart Chemical Changes to Create Improved
Novel Therapeutics

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## LB PHARMACEUTICALS INVESTMENT HIGHLIGHTS

- 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 for the treatment of schizophrenia has potential, to yield in excess of \$1 billion in annual sales based on current ex-US market data\*
- Companies in the psychiatric space with comparable (later stage) profiles comparable (but later stage) have generated public market capitalizations of between \$300 million and \$500 million upon successful Phase 2 clinical trials
- First-in-class team of executives, board members and advisors with extensive experience in drug development in the psychiatric arena
  - Rivopharm SA, the world's largest supplier of amisulpride, is LB's largest investor to date and manufacturing advisor
- We expect to complete our IND-enabling studies for LB-102 in Q3 2019 and to initiate Phase 1 clinical study in Q4 2019

### MANAGEMENT TEAM

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

- Experienced biotechnology and pharmaceutical investor
- Managed family office from 1997-2015
- Has 18+ year history of strategic consulting in the biotech industry (Datascope, Caliper, Emisphere, Aldeyra, and others)

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

- Former VP of R&D at Retrophin, Inc.
- Invented and brought drug to treat PKAN (RE-024) from idea to dosing in humans in under 2 years

#### 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**

Chief Executive Officer and Co-Founder, LB Pharmaceuticals, Inc.

#### Isaac Blech

- Biotechnology investor and entrepreneur
- Co-Founder, Celgene Corporation, Genetic Systems Corporation, Icos Corporation, Nacuity Pharmaceuticals,
   Inc., Nova Pharmaceuticals Corporation, etc., combined value > \$100 billion

#### Piero Poli

- Investor, LB Pharmaceuticals, Inc.
- Chief Executive Officer and Owner, Rivopharm SA, a Swiss company that has developed over 25 molecules and registered generic products throughout Europe, including amisulpride

#### **Edmund Sullivan**

- Managing Partner, Remsen Investors, LP; Angel Investor in LB Pharmaceuticals, Inc.
- Formerly at Citigroup and Cowen & Company

#### Vincent Grattan, R.Ph

- Co-Founder and senior consultant, LB Pharmaceuticals, Inc.
- 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 experience in psychopharmacology

## **SCIENTIFIC ADVISORY BOARD**

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

- Vice President, Behavioral Health Sciences, Northwell Health
- Chairman of Psychiatry, Zucker Hillside Institue

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

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

#### 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

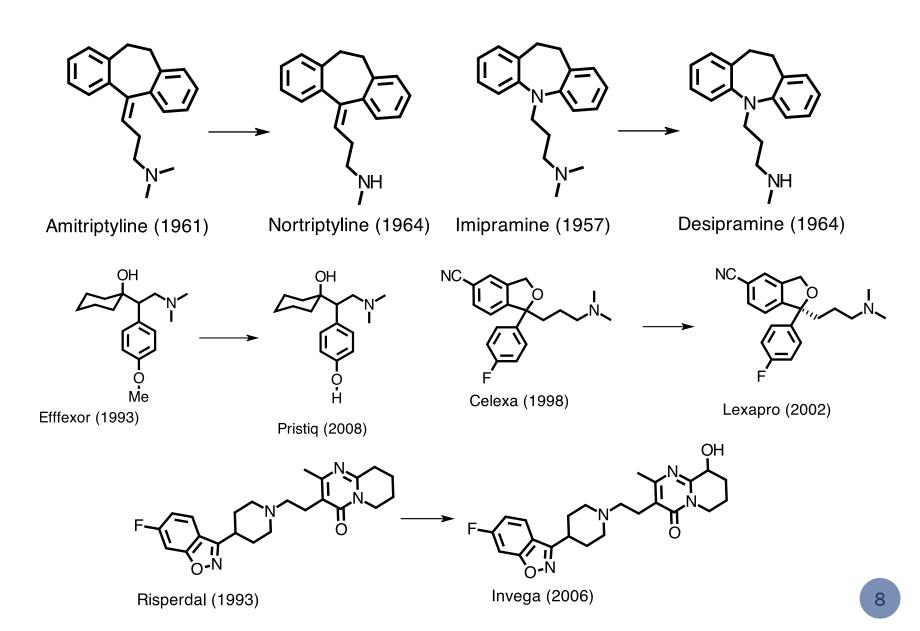
## LB PHARMACEUTICALS COMPANY OVERVIEW

#### Making Smart Chemical Changes to Create Improved Novel Therapeutics

 Lead drug, LB-102, is a methylated version of amisulpride (used in Europe for decades) that treats the multi-billion dollar disease schizophrenia

- Novel chemical structure biological/pharmacological properties which have been shown to be as good as or better than original
- Preliminary in vivo and in vitro data suggest that the effective dose of LB-102 may be lower than that of amisulpride, which could lead to improved safety and tolerability
- Amisulpride and the entire benzamide class of antipsychotics have never been commercially available in the US despite enjoying significant market share throughout Europe
- US composition of matter patent covering LB-102 granted in January 2019 (Patent No: 10,167,256).
   PCT application filed in November 2017 currently being prosecuted
- We have identified and are currently evaluating a number of successful CNS therapies that have never been commercialized in the US and believe this development strategy can yield significant value for shareholders as assets are moved through development

## **EXAMPLES OF METHYLATION**



## **SCHIZOPHRENIA**

- Schizophrenia (SCZ) is a debilitating disease affecting 3 million Americans<sup>1</sup>
  - Characterized by disorganized thought, social withdrawal, and cognitive deficits
- SCZ patients have profoundly diminished qualities of life
  - On average, SCZ patients life expectancy is reduced by 12-15 years<sup>2</sup>
  - SCZ in top 25 causes of disability worldwide<sup>3</sup>
- The economic burden of SCZ in the US has been estimated at \$155 billion per year (\$38 billion in direct costs)<sup>4</sup>
- SCZ thought to be caused by abnormal dopamine  $D_{2/3}$  activity
  - All approved SCZ drugs act at  $D_{2/3}$  receptors
  - First line treatment typically risperidone, quetiapine, or olanzapine
- Up to 60% of SCZ patients do not experience adequate resolution<sup>5</sup>
  - Lack of efficacy and tolerability prime causes of discontinuation
  - If approved, LB-102 could become 2<sup>nd</sup> or 3<sup>rd</sup> line treatment for SCZ

https://www.nimh.nih.gov/health/statistics/prevalence/schizophrenia.shtml

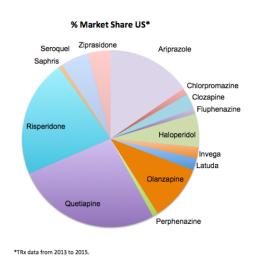
Am. J. Psychiatry, 2013, 170, 324-333

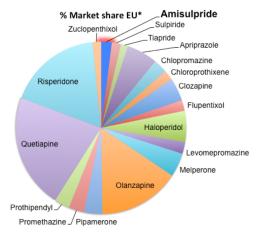
Neuropsychiatr. Dis. Treat., 2016, 12, 357-373

J. Clin. Psychiatry, 2016, 77, 764-771

## SCHIZOPHRENIA LANDSCAPE

US market share<sup>1</sup> by product similar to that of the EU<sup>2</sup>





\*Includes data from: Austria, Estonia, Finland, Germany, Latvia, Lithuania, Netherlands, Norway, Sweden, UK

- Amisulpride maintains an estimated 2% market share of antipsychotics for all indications in the EU (~ 2 million scripts per year<sup>2</sup>; steady usage over past 5 years)
  - Closely related sulpiride (another benzamide not available in the US) also has a 2% market share
- 60 million Rx per year in US for antipsychotics<sup>1</sup>

A 2% market share in the US translates to annual sales in excess of \$1 billion<sup>3</sup>

<sup>1</sup> IMS, US data, 2013 - Q2 2015

<sup>2</sup> IMS, EU data, Q2 2015

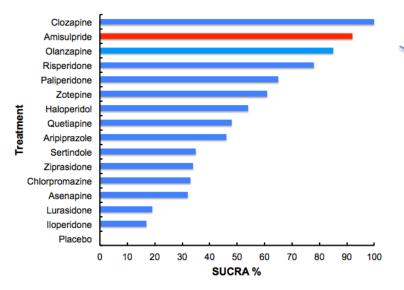
<sup>3</sup> Based on a 2% market share of 60 million antipsychotic Rx per year in US (IMS, US data, 2013 - 02 2015) at an average sales price of \$2,000 per month

## AMISULPRIDE BACKGROUND

- Amisulpride is a schizophrenia drug marketed in Europe since 1986
  - Patented and developed by Synthélabo, a small French company 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 a July 2000 press release, Sanofi stated that it would not pursue development of Solian (amisulpride) in the US
    - FDA informed Sanofi that new US trials with active comparator would be required for marketing approval
    - Based on this FDA feedback and remaining patent life, Sanofi made the business decision not to pursue US approval
- 30 years of clinical use demonstrates an excellent safety/efficacy profile
- European prescriptions steady at 2 million per year\*

## AMISULPRIDE COMPARATIVE EFFICACY

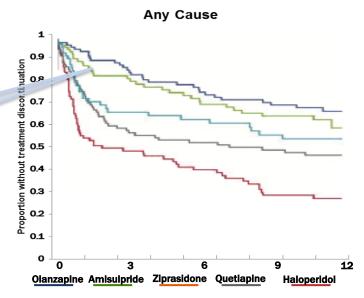
n = 43,000 meta-analysis of 15 SCZ drugs\*



Amisulpride is one of the most effective antipsychotics in the world

EUFEST study, n = 498 clinical trial of 5 SCZ drugs\*\*

Amisulpride has one of the lowest discontinuation rates of any antipsychotic

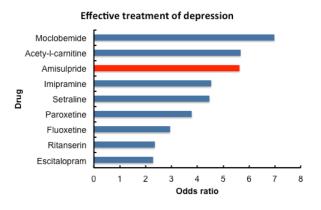


<sup>\*</sup>Leucht et al., Lancet, 2013, 382, 951-962.

<sup>\*\*</sup>Kahn et al., Lancet, 2008, 371, 1085-1097.

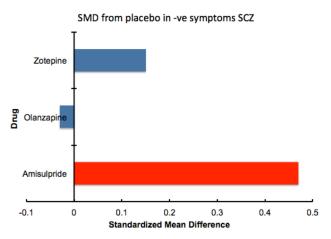
## AMISULPRIDE NEGATIVE SYMPTOMS AND DEPRESSION

Amisulpride's ability to inhibit 5-HT<sub>7</sub> provides anti-depressant properties...



Kriston et al., Depression and Anxiety, 2014, 31, 621-630

#### And renders it effective in treating negative symptoms of SCZ



Krause et al., European Archives of Psychiatry and Clinical Neuroscience, in press

## LB-102: A NOVEL BENZAMIDE

#### Amisulpride

MW = 369.5 cLogP = 3.94

#### LB-102

MW = 383.5 cLogP = 4.41

- LB-102 designed to improve delivery to the brain while minimally affecting receptor binding
- US patent and PCT patent application (filed November 2017) cover composition of matter
- In vitro data suggests that LB-102 has greater membrane permeability than amisulpride
- LB-102 shows equivalent, and in some cases better, efficacy in animal models of schizophrenia compared to amisulpride
- LB-102 shows comparable selectivity profile to amisulpride with no discernible differences at key receptors ( $D_2$ ,  $D_3$ ,  $5HT_2$ ,  $5HT_7$ , etc.)
- LB-102 rat 14-day toxicology profile is consistent with amisulpride. Dog studies in progress

## WHY METHYLATE AMISULPRIDE?

- Comparable efficacy to risperidone and olanzapine (best-in-class antipsychotics) at treating symptoms of SCZ<sup>1</sup>
- Less sedation than nearly all other antipsychotics.<sup>1</sup> In a recent retrospective cohort study, amisulpride was found to have lower risk of self-harm after SCZ diagnosis than olanzapine or risperidone<sup>2</sup>
- In ESCAPE study<sup>3</sup> 78% of SCZ pts switching to amisulpride from risperidone and 56% switching from olanzapine had > 50% improvement in PANSS at 8 weeks
- In recent meta-analysis<sup>4</sup> amisulpride was the only antipsychotic (of 34, including olanzapine and risperidone) that outperformed placebo in treatment of negative symptoms (indicated to treat negative symptoms in the UK)
- In recently published ATLAS study<sup>5</sup> in late onset schizophrenia, amisulpride was found to be well tolerated and highly effective in a population of elderly patients (mean age 80 years)
- Despite a strong record of efficacy and safety and clear differentiation from other anti-psychotics, amisulpride is unavailable to schizophrenia patients in the United States

Based on data generated to date, we believe LB-102 offers all of the advantages of amisulpride with the addition of 20 years of intellectual protection in the US

<sup>1</sup> Leucht et al. Lancet, 2013, 382, 951-962

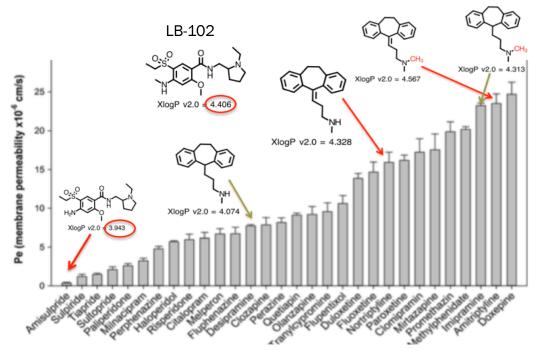
<sup>2</sup> Ma et al. Acta. Psychiatr. Scand., 2018, 1-10

<sup>3</sup> Liang and Yu, Neuropsychiatric Disease and Treatment, 2017, 13, 1163-1173

<sup>4</sup> Krause et al., European Archives of Psychiatry and Clinical Neuroscience, **2018**, https://doi.org/10.1007/s00406-018-0869-3

## LB-102 DESIGNED TO IMPROVE BBB PERMEABILITY

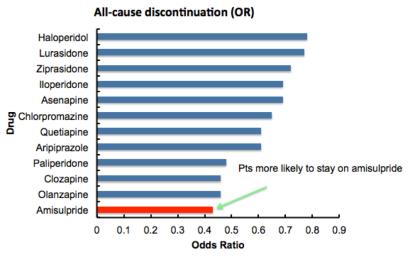
 Of 30 psychiatric medications tested amisulpride was least able to passively diffuse across Blood Brain Barrier (BBB)\*

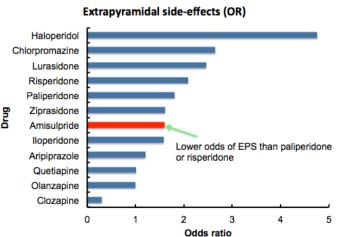


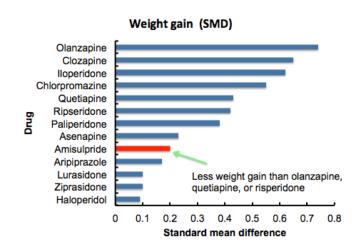
- High doses of amisulpride may be responsible for some of its clinically relevant side effects
- Addition of a single methyl group (e.g. amisulpride to LB-102) to an amine can have a profound impact on BBB permeability
  - Two examples shown above are designamine to imigramine and nortriptyline to amitriptyline

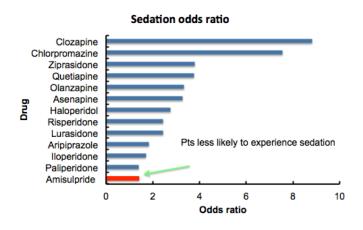
## AMISULPRIDE COMPARATIVE SAFETY

Data from 43,000 patient meta-analysis\*









## AMISULPRIDE SAFETY

#### **QT PROLONGATION**

- All antipsychotics, amisulpride included, have the potential to alter the QT interval
  - Pharmacovigilance data from UK from 2013 to 2017 covering 16,000 patients exposure years showed 18 CV SAEs and 9 examples of QT alteration (also 1 incidence of Parkinsonianism, 1 of EPS, and 1 of galactorrhea)
  - In an in vitro assay LB-102 was found to have no affinity for the hERG receptor, a marker of cardiac depolarization

Preliminary in vivo and in vitro data on LB-102 suggests that the effective dose may be lower than amisulpride

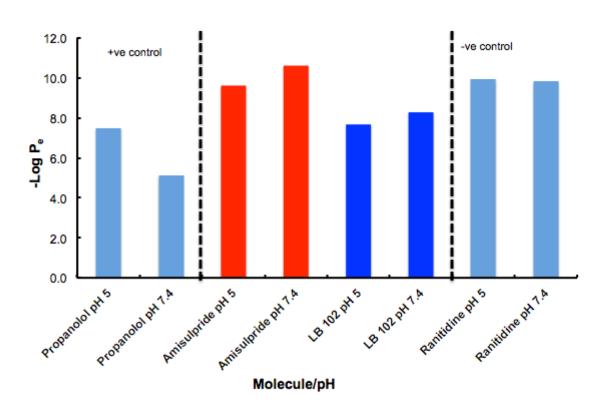
# Examples of QTc prolongation associated with select antipsychotics<sup>a,b</sup>

accordiated with coloct antipoyonetics	
Antipsychotic	Approximate QTc interval prolongation in milliseconds <sup>c</sup>
Aripiprazole	-1 to -4
Clozapine	10
Haloperidol	7 to 15
Mesoridazine	39 to 53
Olanzapine	2 to 6.5
Paliperidone	2 to 4
Quetiapine	6 to 15
Risperidone	3.5 to 10
Sertindole	30
Thioridazine	33 to 41
Ziprasidone	16 to 21
Amisulpride	3.1

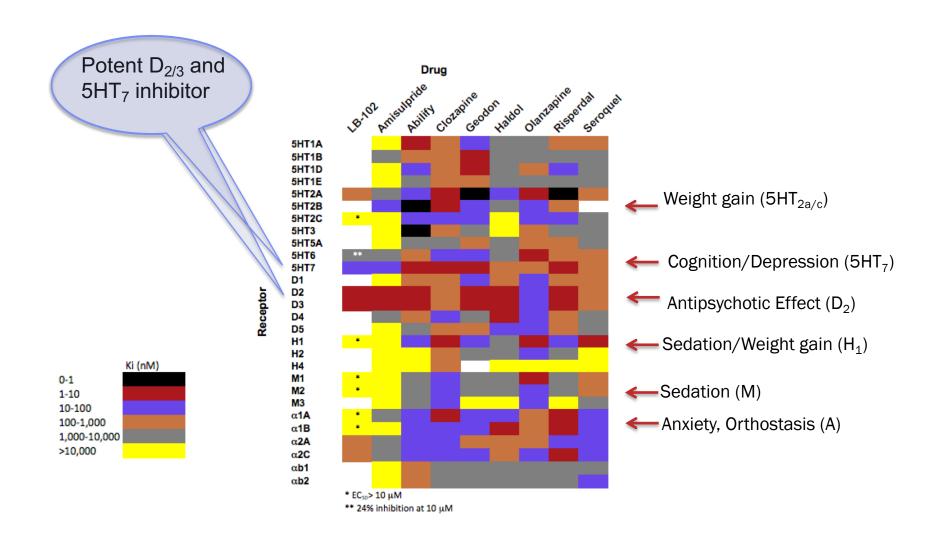
- a. Washington et al, Current Psychiatry, Oct 2012, Vol 11:36-39
- List is not comprehensive. Other antipsychotics may be associated with QTc prolongation
- QTc prolongation interval may depend on the route of administration

## LB-102 IN VITRO MEMBRANE PERMEABILITY DATA

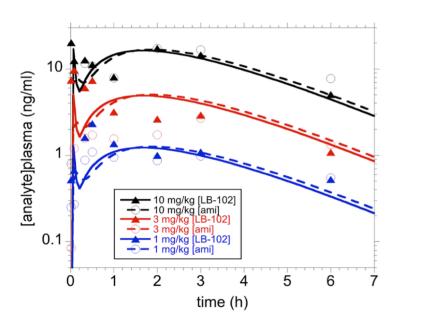
In a PAMPA assay LB-102 was ~200X more permeable than amisulpride

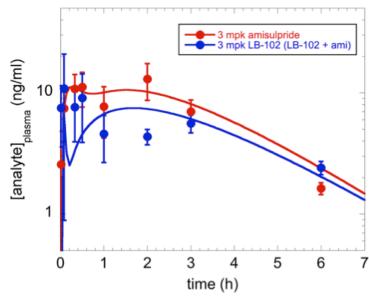


## LB-102 AND AMISULPRIDE RECEPTOR SPECIFICITY



## LB-102 PHARMACOKINETICS EQUIVALENT TO AMISULPRIDE

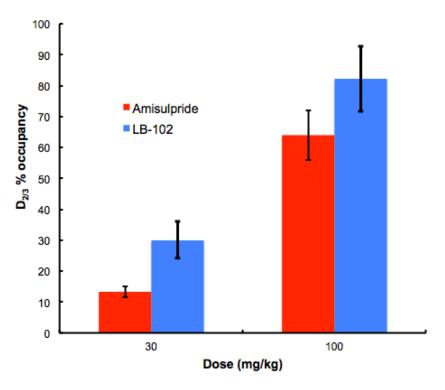




- Total benzamide (LB-102 + amisulpride) plasma exposure of orally dosed LB-102 is similar to amisulpride and is linearly dose dependent in rats and in mice
- Note, LB-102 is ~50% demethylated to amisulpride in rodents
  - Demethylation likely CYP-driven and expected to be lower in humans

# LB-102 RAT BRAIN $D_{2/3}$ RECEPTOR OCCUPANCY (RO)

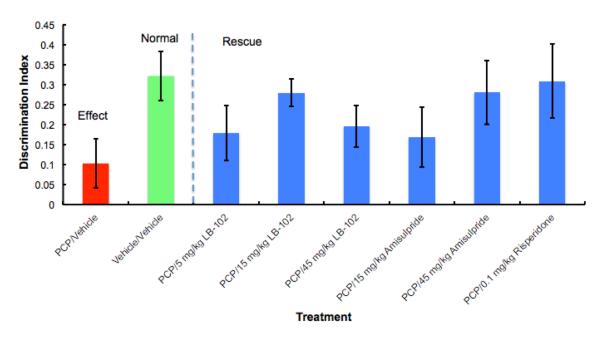
Dopamine % Receptor Occupancy in rat brains (n = 3/group) 12h after PO doses of LB-102 or amisulpride



- Initial in vivo data suggests greater dopamine RO in rat brains for LB-102
- In humans, dopamine RO is highly correlated to improvements in PANSS.

# **NOVEL OBJECT RECOGNITION (NOR) STUDY**

 NOR is a widely published and validated animal model of cognitive impairment in SCZ

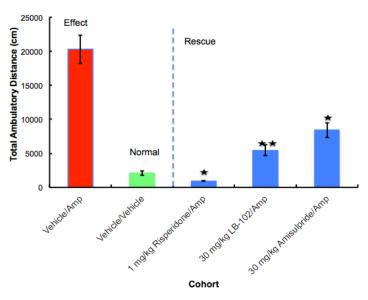


Discrimination index ((time spent exploring novel - time spent exploring familiar)/total exploration time) ± SEM (n = 10/group)

 Study results show LB-102 restored cognitive function to PCP impaired rats in a manner comparable to amisulpride

# **LOCOMOTOR ACTIVITY (LMA) STUDY**

 LMA is a widely published and validated animal model of hyperactivity in SCZ

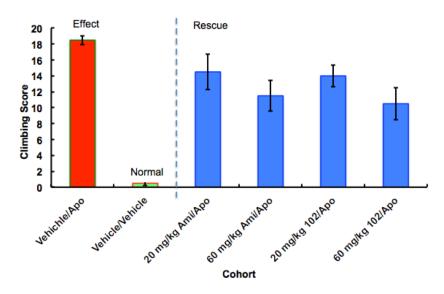


Total ambulatory distance data from an amphetamine induced LMA rat study (n=10/group) measured 6 hours post-dose amphetamine over the course of an hour. \* p < 0.01 v control, \*\* p < 0.05 v amisulpride

 Study results show LB-102 was statistically superior to amisulpride in restoring normal motion to amphetamine impaired rats at 30mg/kg (p < 0.05)

## MOUSE APOMORPHINE INDUCED CLIMBING (AIC) STUDY

 AIC is a widely published and validated animal model of stereotypy in SCZ



Climbing Score + SEM (n = 10/group).

 Study results show LB-102 restored movement to apomorphine impaired rats in a manner comparable to amisulpride

## IN-VIVO TOXICOLOGY CONSISTENT WITH AMISULPRIDE

RESULTS OF LB-102 NON-GLP 4 & 14 DAY TOXICOLOGY STUDIES (MPI RESEARCH)

- Initial 4 day study included groups of 6 rats (3F/3M) treated with 200, 600, 1200, and 2400 mg/kg/d LB-102
  - Rats dosed at 200 and 600 mg/kg/d survived for duration of experiment
- Final results of a 14 day dose range finding study in rats produced a maximum tolerated dose of 200mg/kg/d, consistent with amisulpride
  - In excess of 7x the doses that were effective in LMA and NOR rat models of schizophrenia
- 14 day dose range finding study in dogs in progress, results expected in February 2019
- In a bar balance test, an animal model of EPS, LB-102 was indistinguishable from amisulpride

## LB-102 ANIMAL STUDY CONCLUSIONS

- LB-102 has PK profile indistinguishable from amisulpride
- LB-102 has equivalent/superior dopamine receptor occupancy
- LB-102 displayed efficacy in three rodent models examined (2 in rats, 1 in mice)
  - Cognitive function
  - Hyperactivity
  - Stereotypy
- LB-102 efficacy in animal models comparable/superior to amisulpride, one of the most effective antipsychotics
- MTD in two week rat toxicology study showed LB-102 to be equivalent to amisulpride

# CLINICAL PROOF OF CONCEPT: PHASE 1/2

- Based on FDA guidance at pre-IND meeting, we believe P1 could be conducted with ~ 35 healthy volunteers
  - Single and multiple ascending doses, based on amisulpride's known safety and PK profile
  - PK/PD/Safety endpoint
  - 200 mg/kg/d in rats equivalent to ~3x typical human amisulpride dose (800 mg/d)
- Phase 2 dose-finding study, acute schizophrenia patients
  - PANSS at 4 weeks primary endpoint, and dopamine receptor occupancy secondary endpoints
  - Number of patients to be determined based on resources

## LB-102 SUMMARY

- LB-102 is a novel antipsychotic closely related to amisulpride; US composition of matter patent granted in January 2019; PCT patent application filed in November 2017 currently being prosecuted (affording IP to 2037+)
- In every measure of SCZ to date, LB-102 has been shown to be as good as or better than amisulpride
- With similar TRx to amisulpride in Europe, we believe annual sales could exceed
   \$1 billion
- IND enabling package expected to be complete in Q3 2019 and first in human clinical study expected to start before the end of 2019
- Potential to expand label for use as an augmentation to treat depression-related disorders\*



## THANK YOU