pharmaceuticals

# CORPORATE PRESENTATION

# FEBRUARY 2021

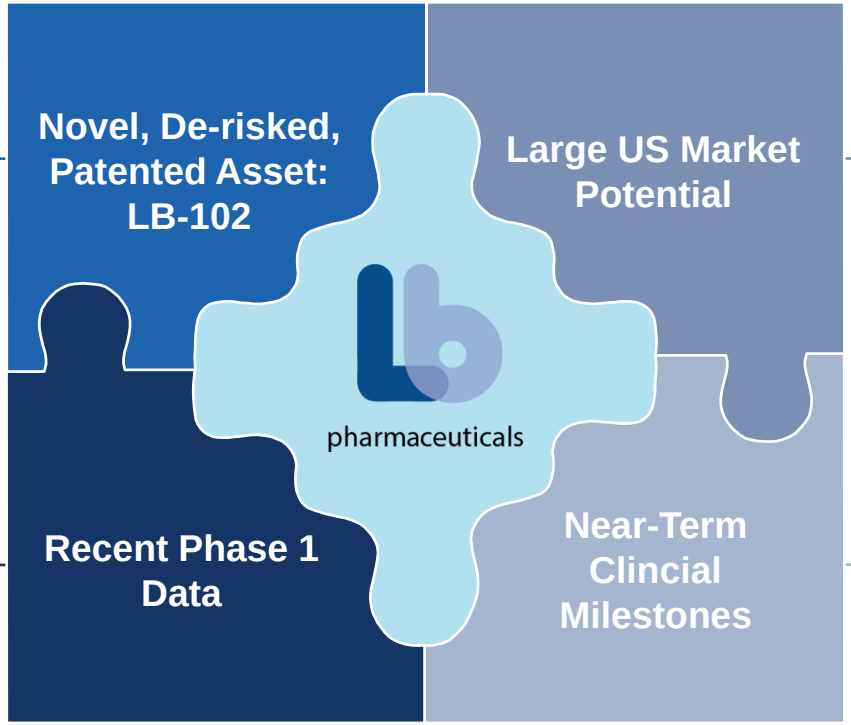
*Making Smart Chemical Changes to Create*
*Improved Novel Therapeutics*

# LB PHARMACEUTICALS INVESTMENT HIGHLIGHTS

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

Lead clinical-stage asset, **LB-102,** is a novel, de-risked, patented benzamide, **leveraging the demonstrated safety and efficacy data** of amisulpride for the treatment of schizophrenia

Phase 1 safety study recently completed in 64 healthy volunteers illustrated that drug is **safe and well-tolerated** and signaled **dopamine target engagement**




LB-102 has **potential to exceed $1 billion in annual US sales**(1)

- Though generic in Europe, amisulpride and closely related benzamides generate ~2 million scripts per year(2)

**Phase 2 study, planned for fall of 2021**, could validate LB-102 as an important therapy for schizophrenia patients

Notes: (1) Based on a 2% market share of ~65 million antipsychotic Rx per year in US (IMS, 2019 data) at an average wholesale price of $1,500 per month; (2) Source: IMS data, trailing four quarters, ending Q2 2016

# MANAGEMENT TEAM

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

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

## 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
- #1 ranked biotech analyst by Wall Street Journal

## 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**

- Managing Partner, Remsen Investors, LP; Angel Investor in LB Pharmaceuticals Inc.
- 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.**

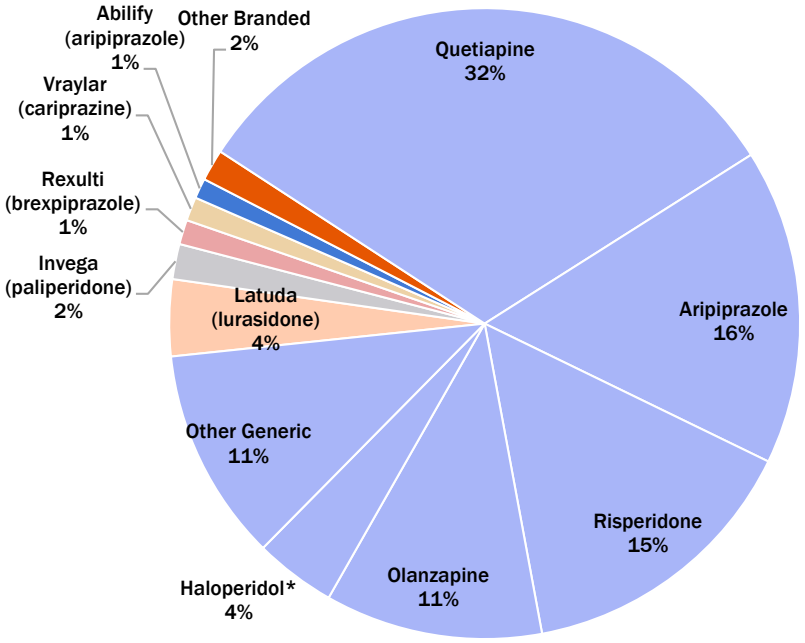
- Professor of Psychiatry and Behavioral Sciences, Stanford University School of Medicine

**Herbert Meltzer, M.D.**

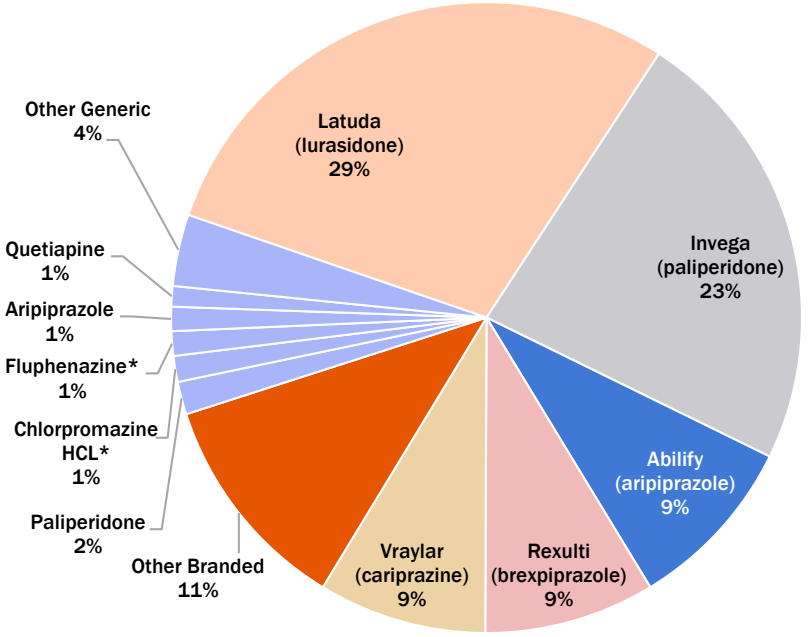
- Professor of Psychiatry & Behavioral Sciences, Pharmacology and Physiology, Northwestern University

# US ANTIPSYCHOTIC MARKET LANDSCAPE

**2019 US Antipsychotic Market[1]: ~67mm Retail TRx**




**2019 US Antipsychotic Market[1]: ~$12bn Sales**




Represents generic TRx / Sales  * Indicates typical (first-generation) product

- While generics are responsible for 89% of prescriptions, branded products still generate ~$11bn in sales annually
- Despite limited efficacy, severe side effects, and a crowded generic market, new branded antipsychotics such as Zyprexa, Seroquel and Abilify each achieved > $5bn in peak sales worldwide
- Economic burden of Schizophrenia in the US estimated ~$150 billion per year[2]

Notes: (1) Source: IMS 2019 data including all dosage forms; (2) Source: *J. Clin. Psychiatry*, *77*, 764-711

# ANTIPSYCHOTIC COMPETITIVE LANDSCAPE

| Product | Europe[1] | | US[2] | |
|---|---|---|---|---|
| | Total TRx (Branded + Generic) *(mm)* | Total TRx (Branded + Generic) Market Share | Total TRx (Branded + Generic) *(mm)* | Total TRx (Branded + Generic) Market Share |
| **Seroquel** *(quetiapine)* | 8.2 | 20.6% | 21.4 | 32.0% |
| **Risperdal** *(risperidone)* | 6.8 | 16.9% | 10.3 | 15.4% |
| **Zyprexa** *(olanzapine)* | 5.9 | 14.7% | 7.5 | 11.2% |
| **Abilify** *(aripiprazole)* | 2.2 | 5.6% | 11.5 | 17.2% |
| **Haldol** *(haloperidol)* | 2.2 | 5.6% | 2.8 | 4.2% |
| **Amisulpride, Sulpiride, and Tiapride** | 1.9 | 4.9% | NA | NA |
| *Clozapine* | 1.6 | 4.1% | 2.0 | 2.9% |

**Given the continued strong market penetration in Europe of amisulpride even after 35 years on the market, we believe that LB-102 will have significant potential in the US market**

Notes: (1) Source: IMS Q3'15 – Q2'16 data from Austria, Estonia, Finland, Germany, Latvia, Lithuania, Netherlands, Norway, Sweden, UK; (2) Source: IMS 2019 data

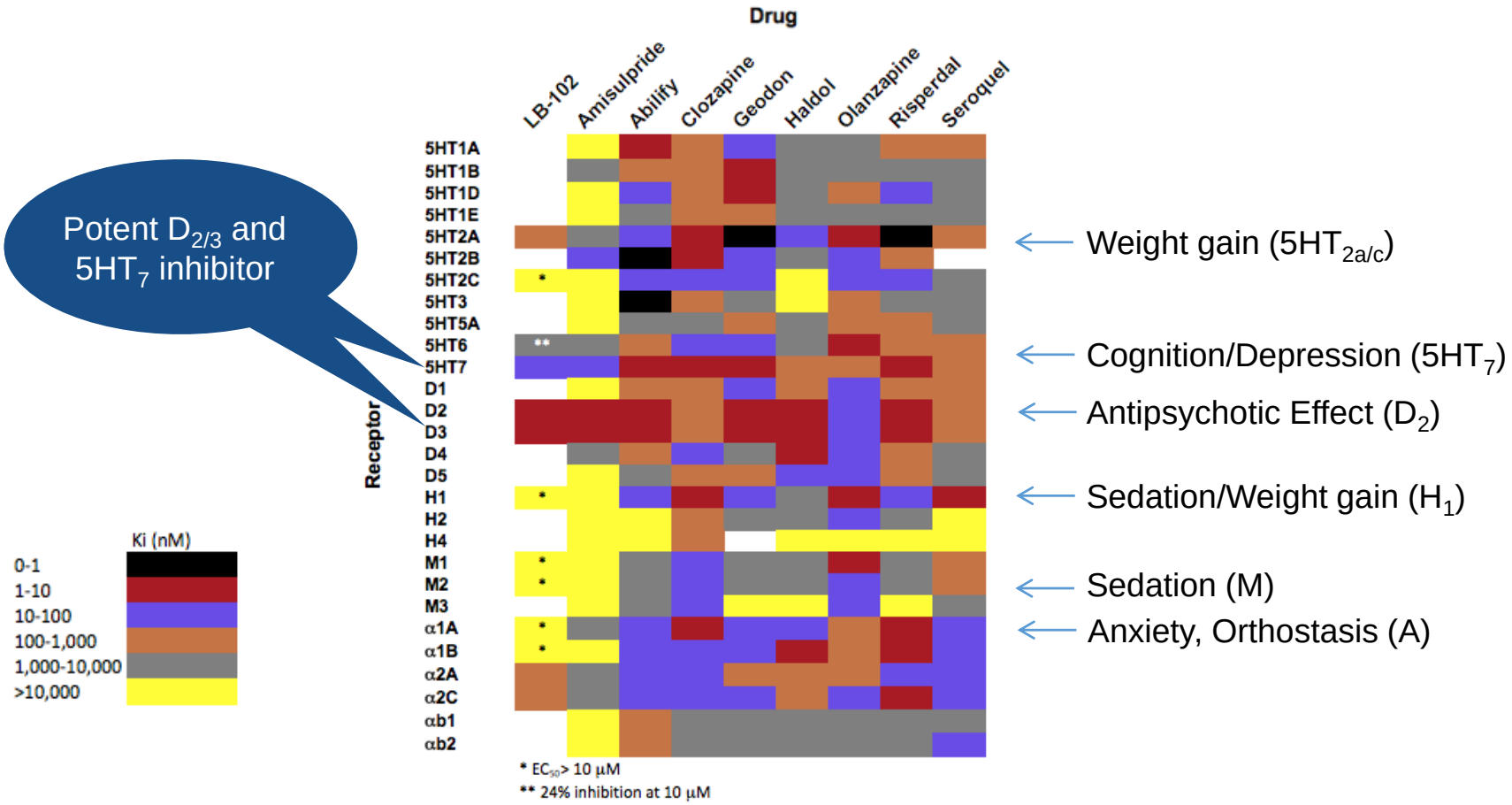
# AMISULPRIDE BACKGROUND

- Amisulpride is a best-in-class benzamide drug marketed for the treatment of schizophrenia in Europe since 1986
  - Patented and developed by Synthélabo (acquired by Sanofi)
  - Selective $D_2$ ($K_i$ = 2.8 nM)/$D_3$ ($K_i$ = 3.2 nM) and $5HT_7$ ($K_i$ = 31 nM) antagonist
  - In a July 2000 press release, Sanofi stated that it would not pursue development of Solian (amisulpride) in the US
    - Based on FDA feedback and remaining patent life, Sanofi made the business decision not to pursue US approval
- European prescriptions of benzamide anti-psychotics steady at 2 million per year(1)
- **35 years of clinical use demonstrates an excellent safety/efficacy profile**

Notes: (1) Source: IMS, Europe data Q2 2016, includes closely related sulpiride and tiapride

# LB-102 AND AMISULPRIDE RECEPTOR SPECIFICITY

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

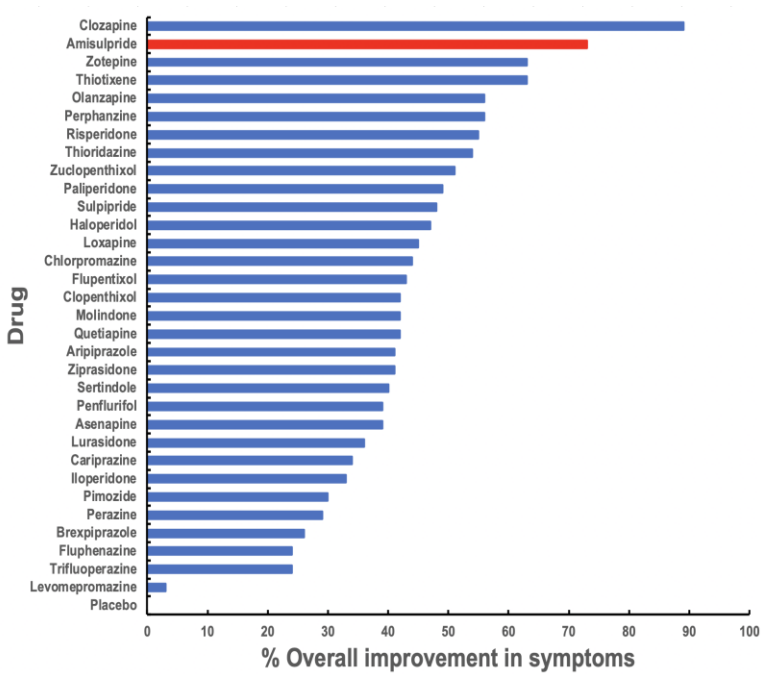



Notes: Ki data from: *The Neuroscientist*, **2000**, *6*, 252-26245rf

# AMISULPRIDE COMPARATIVE EFFICACY

**Meta-Analysis of 32 Schizophrenia (SCZ) Drugs[1]**
**(n = 53,500)**

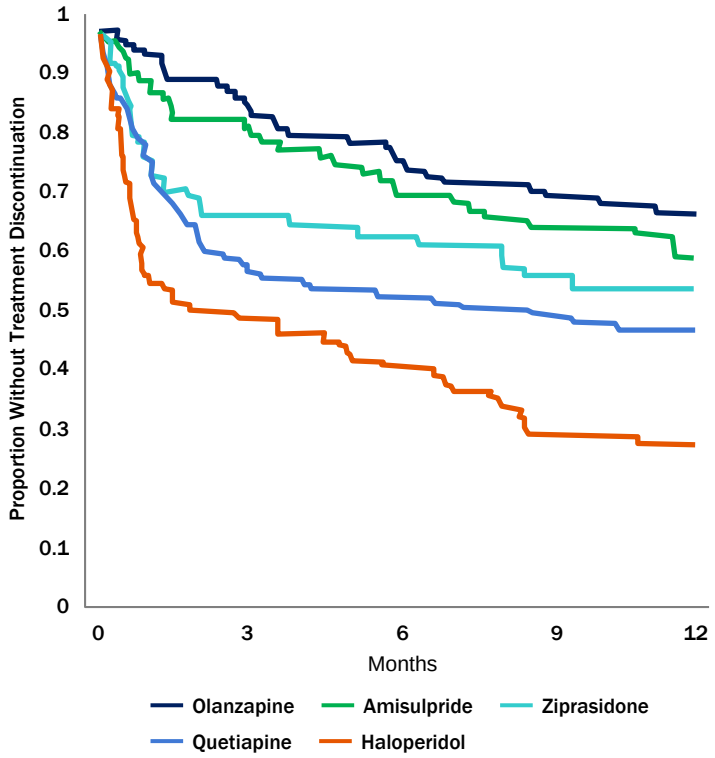
**Antipsychotic Efficacy**




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

**EUFEST Study[2]**
**(Clinical Trial of 5 SCZ Drugs in First Episode)**
**(n = 498)**

**Any Cause Discontinuation**




**Amisulpride has one of the lowest discontinuation rates of any antipsychotic**

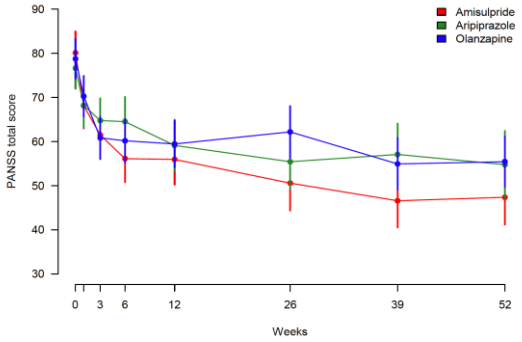
Notes: (1) Source: *Lancet*, **2019**, *394*, 939-951.; (2) Source: *Lancet*, **2008**, *371*, 1085-1097

# AMISULPRIDE CLINICAL STUDIES

Amisulpride has demonstrated efficacy comparable to many of the most well-established schizophrenia products on the market today in numerous clinical studies

**BeSt InTro[1]**
**52 Week Study vs. Aripiprazole and Olanzapine**
**(n = 144)**

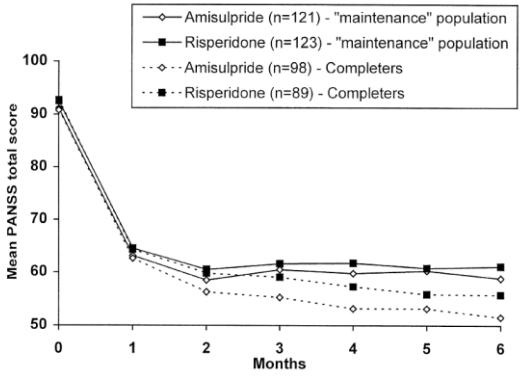
**PANSS Score Over Time**




**Amisulpride is on par / slightly better than two of best selling schizophrenia drugs— aripiprazole and olanzapine**

**Six Month Study vs. Risperidone[2]**
**(n = 309)**

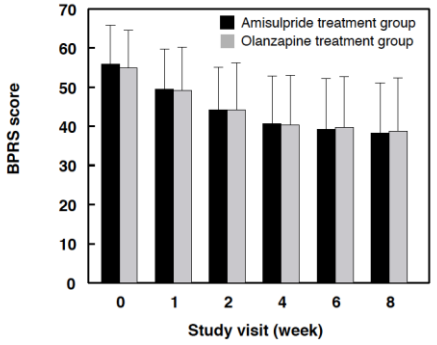
**PANSS Score Over Time**




**Amisulpride is on par with risperidone, one of best selling schizophrenia drugs**

**Two Month Study vs. Olanzapine[3]**
**(n = 377)**

**BPRS Score Over Time**




**Amisulpride is on par with olanzapine, one of best selling schizophrenia drugs**

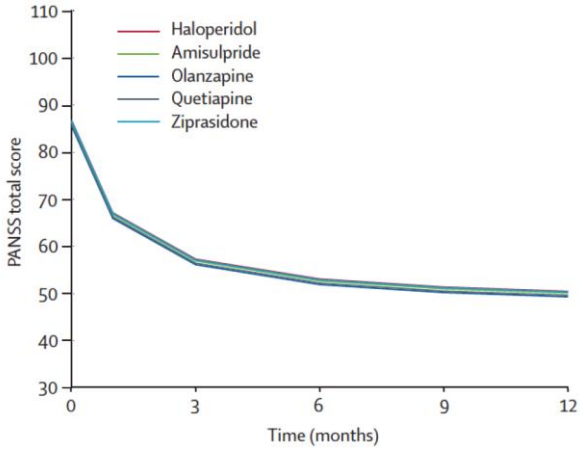
Notes: (1) Source: *Lancet Psychiatry*, **2020**, *7*, 945-954; (2) Source: *Neuropsychopharmacology*, **2002**, *27*, 1071-1081; (3) Source: *Current Medical Res. & Opin.*, **2020**, *18*, 355-362

# AMISULPRIDE CLINICAL STUDIES (CONTINUED)

Amisulpride's MOA ($D_2$ / $D_3$ and $5HT_7$ antagonism with minimal off-target activity) allows for a meaningful reduction in PANSS score, with a more favorable side effect profile

**EUFEST Study[1]**
**(Clinical Trial of 5 SCZ Drugs in First Episode)**
**(n = 498)**

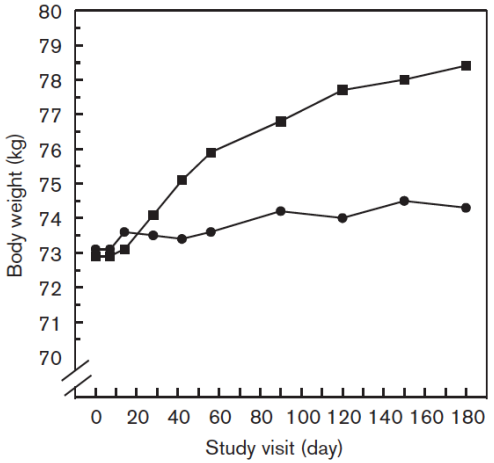
**PANSS Score Over Time**




**Amisulpride is on par with four other best selling schizophrenia drugs**

**Six Month Study vs. Olanzapine[2]**
**(n = 377)**

**Body Weight Over Time**




Evolution of body weight over the study. Data are presented as mean body weight (kg) in patients with acute schizophrenia treated with amisulpride (●) or olanzapine (■).

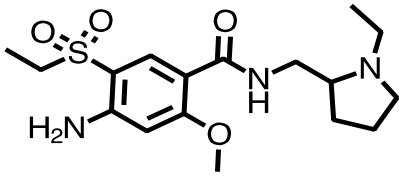
**Both drugs meaningfully improved PANSS, a ~27 point improvement, but amisulpride patients had markedly less weight gain**

Notes: (1) Source: *Lancet*, **2008**, *371*, 1085-1097-954; (2) Source: *Int. Clin, Psychopharmacol.*, **2004**, *19*, 63-69

# LB-102 OVERVIEW

LB-102 is a methylated version of amisulpride

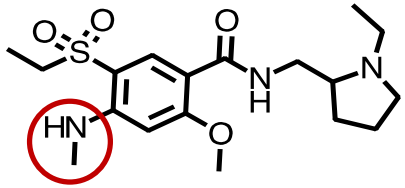
**Amisulpride (1983)**



**Prior to methylation**



**LB-102 (2016)**

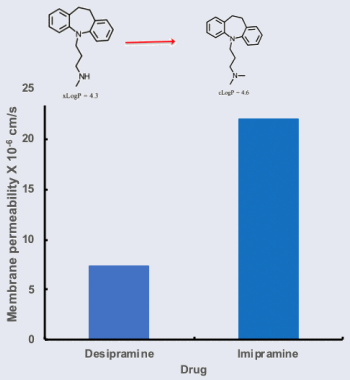
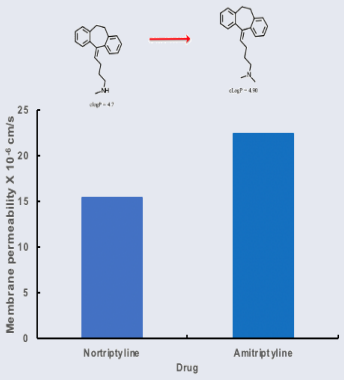


**Amisulpride containing added methyl group**

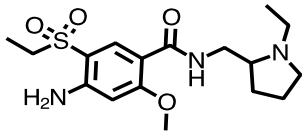
- Novel chemical structure with biological / pharmacological properties designed to improve amisulpride's safety and efficacy
- LB-102 appears to mimic amisulpride's safety profile at lower doses in its Phase 1 clinical trial
- US composition of matter patents covering LB-102 granted in 2019 (Patent Numbers: 10,259,786 and 10,167,256)
  - PCT application and 11 foreign patent applications pending
- We believe LB-102 would be one of the most effective antipsychotics on the US market, if approved, with IP until at least 2037

# LB-102: ENHANCING AMISULPRIDE'S PRODUCT PROFILE

Methylation has been shown to improve membrane permeability without changing receptor binding activity, resulting in some of the most successful psychiatric products

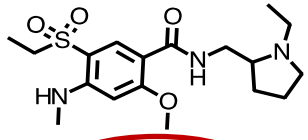
| Membrane Permeability After Methylation | | |
|---|---|---|
| **Demethylated Molecule** | Desipramine | Nortriptyline |
| **Methylated Molecule** | Imipramine (TOFRANIL) | Amitriptyline (ELAVIL) |
| **Membrane Permeability** |  |  |

**Amisulpride**



cLogP = 3.9

**LB-102**



cLogP = 4.4

- Of 30 psychiatric medications tested amisulpride was least able to passively diffuse across model BBB(1)
- Improving BBB permeability could improve efficacy/decrease adverse events

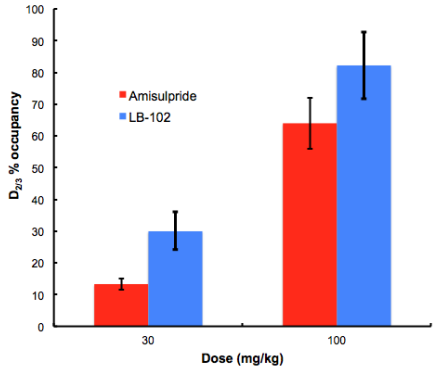
Notes: (1) Source: *The AAPS Journal*, **2014**, *16*, 1247-1258

# LB-102 PRECLINICAL OVERVIEW

In pre-clinical studies, LB-102 has been shown to be comparable or superior to amisulpride

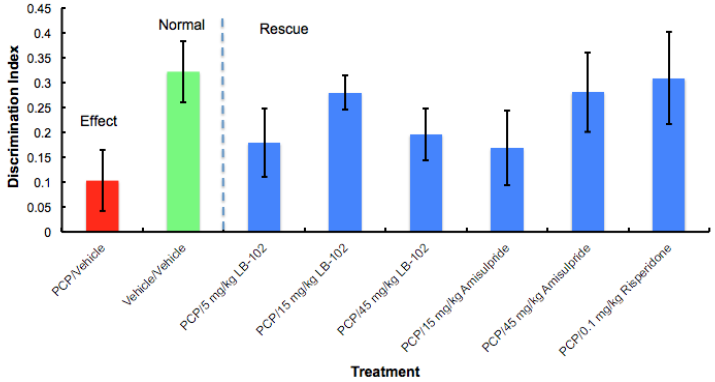
## LB-102 rat brain $D_{2/3}$ Receptor Occupancy (RO)

*Superior(1) dopamine RO relative to amisulpride*




## Novel Object Recognition (NOR) Study

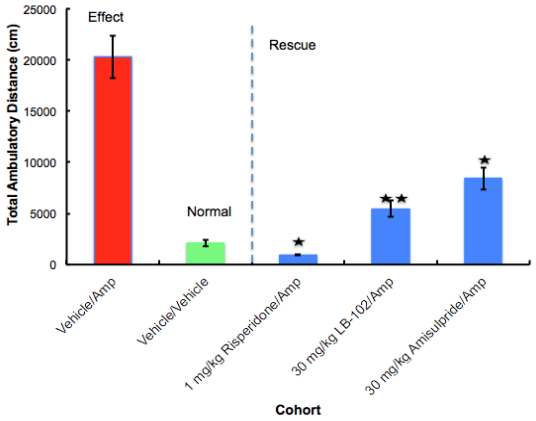
*Improvement in cognitive function relative to baseline*




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

## Locomotor Activity (LMA) Study

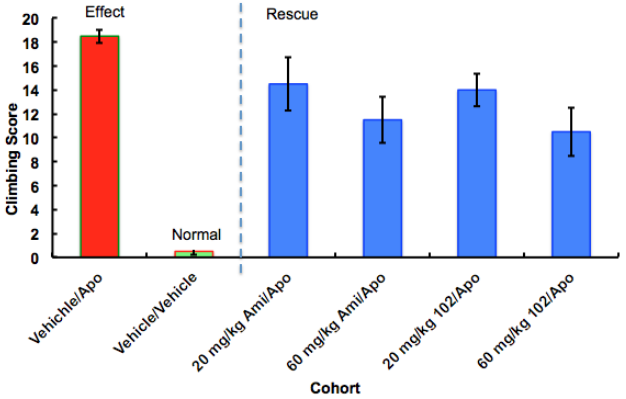
*Statistically significant hyperactivity improvement relative to amisulpride and control*




* p < 0.01 v control, ** p < 0.05 v amisulpride

## Mouse Apomorphine Induced Climbing (AIC) Study

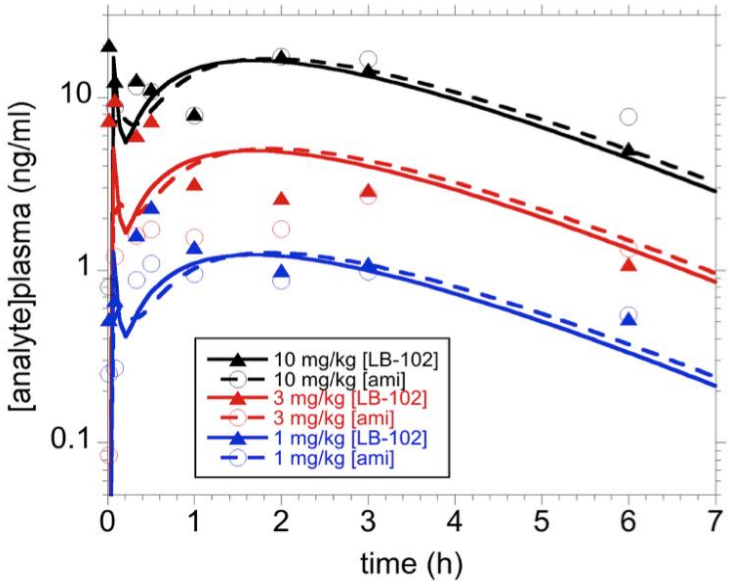
*Comparable improvement in stereotypy relative to amisulpride*

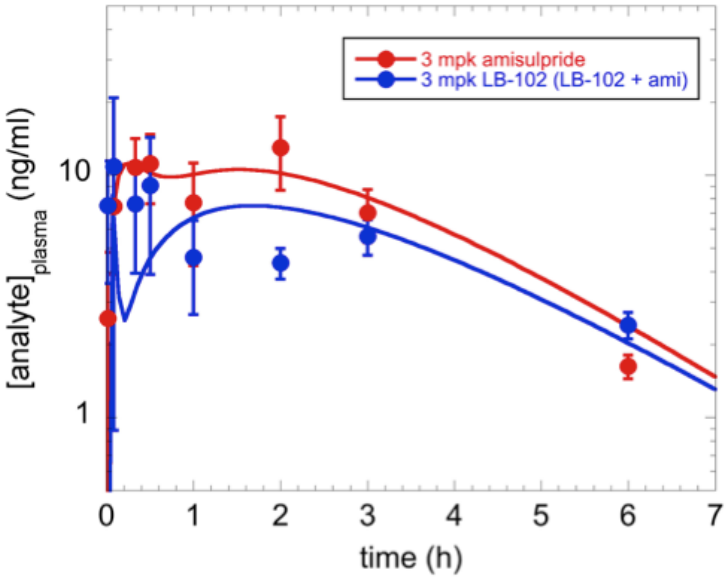



Climbing Score± SEM (n = 10/group).

Notes: Study results presented as part of poster: "Pre-clinical evaluation of two novel benzamides, LB-102 and 103, for the treatment of schizophrenia", ECNP (European Neuropsychopharmacology, 2017, 27 (S4), S922-S923); (1) superiority on a numerical, not statistical basis

# LB-102 PK EQUIVALENT TO AMISULPRIDE



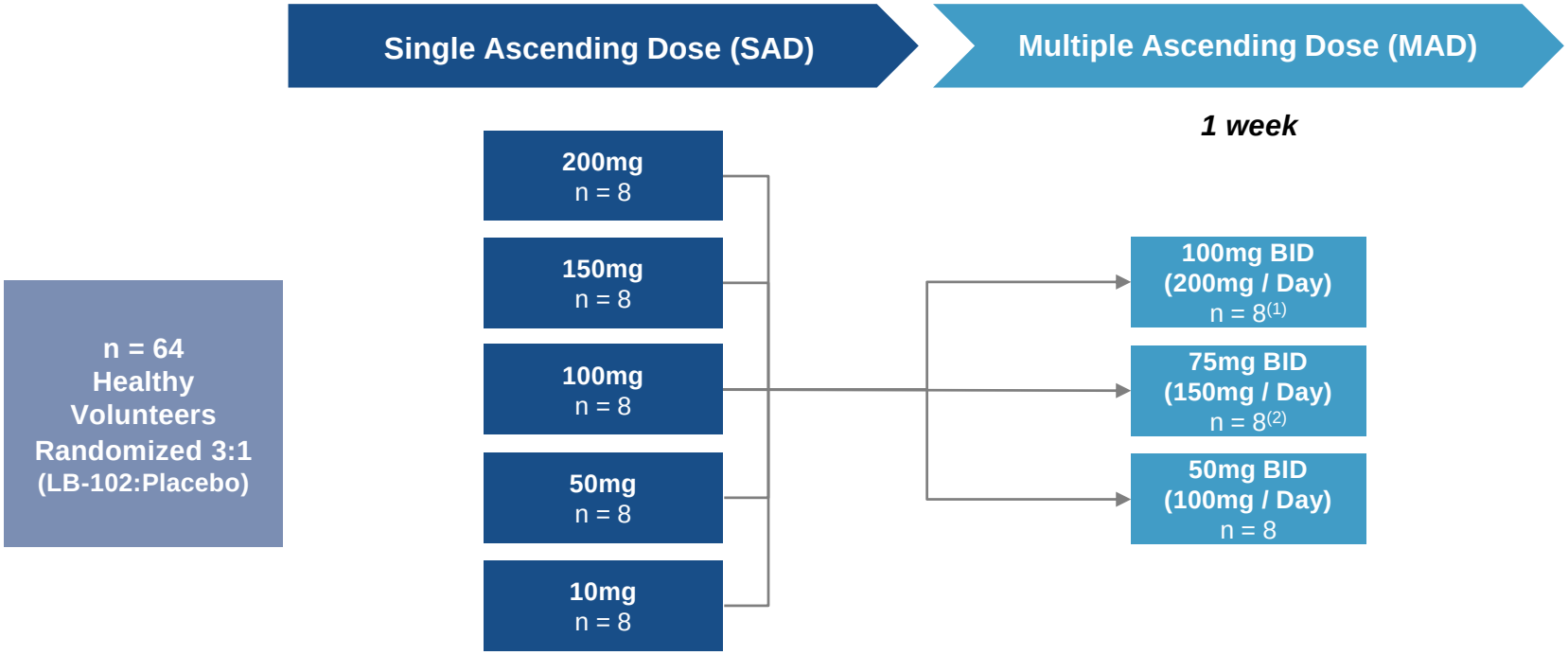




- Total benzamide (LB-102 + amisulpride) plasma exposure of orally dosed LB-102 is similar to amisulpride and is linearly dose dependent in rats and in mice
- Note, LB-102 is ~50% demethylated to amisulpride in rodents
  - Demethylation likely CYP driven and, in LB-102 Phase 1 study, was much lower in humans

# LB-102 PHASE 1 CLINICAL TRIAL OVERVIEW

(All data on following pages are blinded, unaudited, and are subject to change)

- First subject was dosed in January 2020 and the final subject was discharged on July 1, 2020 (NCT04187560)
- **Dosing**: 5 single ascending dose (SAD) cohorts / 3 multiple ascending dose (MAD) (1 week, BID dosing) cohorts
- **Primary Endpoint**: Safety / **Secondary Endpoint**: Pharmacokinetics
- **Single Site**: Medpace in Cincinnati, OH




**Phase 1 results of LB-102 in schizophrenia were announced in September 2020**

Notes: (1) Did not complete as pre-specified number of adverse events was reached; (2) n = 7 completed, one patient dropped out due to adverse events

# LB-102 PHASE 1 ADVERSE EVENTS

## Single Ascending Dose (SAD)

| Dose (mg) | Adverse Event | n | Severity | Related to Drug |
|---|---|---|---|---|
| 10 | Prolactin elevation | 1 | Mild | Definitely |
| | Abdominal cramps | 1 | Mild | Unrelated |
| 50 | Prolactin elevation | 3 | Mild | Definitely |
| | Diarrhea | 1 | Mild | Unlikely |
| | Upper respiratory infection | 1 | Mild | Unrelated |
| 100 | Prolactin elevation | 1 | Mild | Definitely |
| | Urticaria | 1 | Mild | Possibly |
| | Headache | 1 | Mild | Probably |
| | Upper respiratory infection | 1 | Mild | Unrelated |
| | Nausea | 1 | Mild | Probably |
| 150 | Prolactin elevation | 1 | Mild | Definitely |
| | Low back pain | 1 | Mild | Unrelated |
| 200 | QT prolongation | 1 | Mild | Definitely |
| | Acute dystonia | 1 | Moderate | Definitely |
| | Palpitations | 1 | Mild | Unlikely |
| | Nausea | 1 | Mild | Possibly |
| | Gastroesophageal reflux | 1 | Mild | Possibly |
| | Insomnia | 1 | Mild | Probably |
| | Sore throat | 1 | Mild | Unrelated |
| | Headache | 1 | Mild | Unrelated |

## Multiple Ascending Dose (MAD)

| Dose (mg) | Adverse Event | n | Severity | Related to Drug |
|---|---|---|---|---|
| 50 | Dizziness | 1 | Mild | Unrelated |
| | Prolactin elevation | 2 | Mild | Definitely |
| 75 | Prolactin elevation | 2 | Mild | Definitely |
| | Abdominal cramps | 1 | Mild | Unrelated |
| | Migraine headache | 1 | Moderate | Possibly |
| | Acute dystonic reaction | 1 | Moderate | Definitely |
| | Intermittent dizziness | 1 | Mild | Probably |
| | Intermittent nausea | 1 | Mild | Probably |
| | Intermittent drowsiness | 1 | Mild | Probably |
| | Bug bite | 1 | Mild | Unrelated |
| | Insomnia | 1 | Mild | Possibly |
| | Low back pain | 1 | Mild | Unrelated |
| 100 | Acute dystonia | 2 | Moderate | Definitely |
| | Drowsiness | 1 | Mild | Unrelated |
| | Dry mouth | 1 | Mild | Unrelated |
| | Elevated prolactin | 1 | Mild | Definitely |
| | Nausea | 1 | Moderate | Probably |
| | Emesis | 1 | Mild | Possibly |

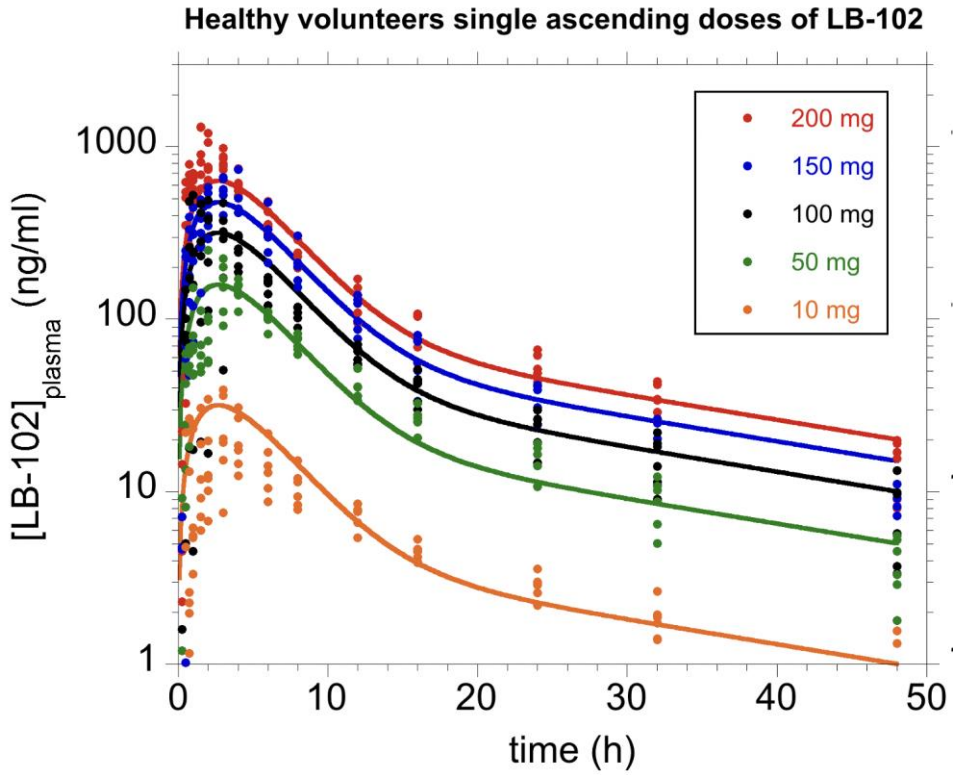
***100 mg BID cohort (200 mg/d) discontinued early due to two moderate AEs (EPS) consistent with excess dopamine engagement***

- Prolactin elevation (PRL), which was reversible and unassociated with clinical consequences, was observed at all doses (consistent with dopamine receptor binding)
- QT prolongation profile consistent with atypical antipsychotics

# 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) | $T_{1/2}$(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 |

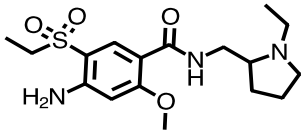


# PLASMA EXPOSURE OF LB-102 > AMISULPRIDE

Rosenzweig[1] reported PK data on 18 healthy volunteers exposed to a single dose 50 mg amisulpride

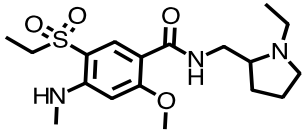
**LB-102 was designed as a more lipophilic version of amisulpride**

**Amisulpride**



**MW = 369.5**
**cLogP = 3.9**

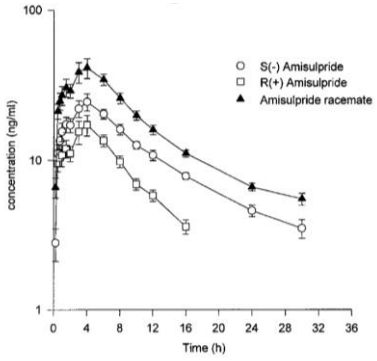
**LB-102**



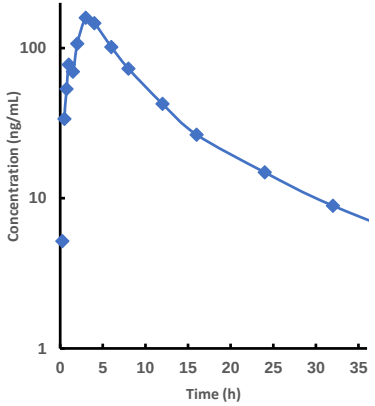
**MW = 383.5**
**cLogP = 4.4**

**Plasma Concentration of 50mg LB-102 vs. 50mg Amisulpride**

**50mg Amisulpride**




**50mg LB-102**

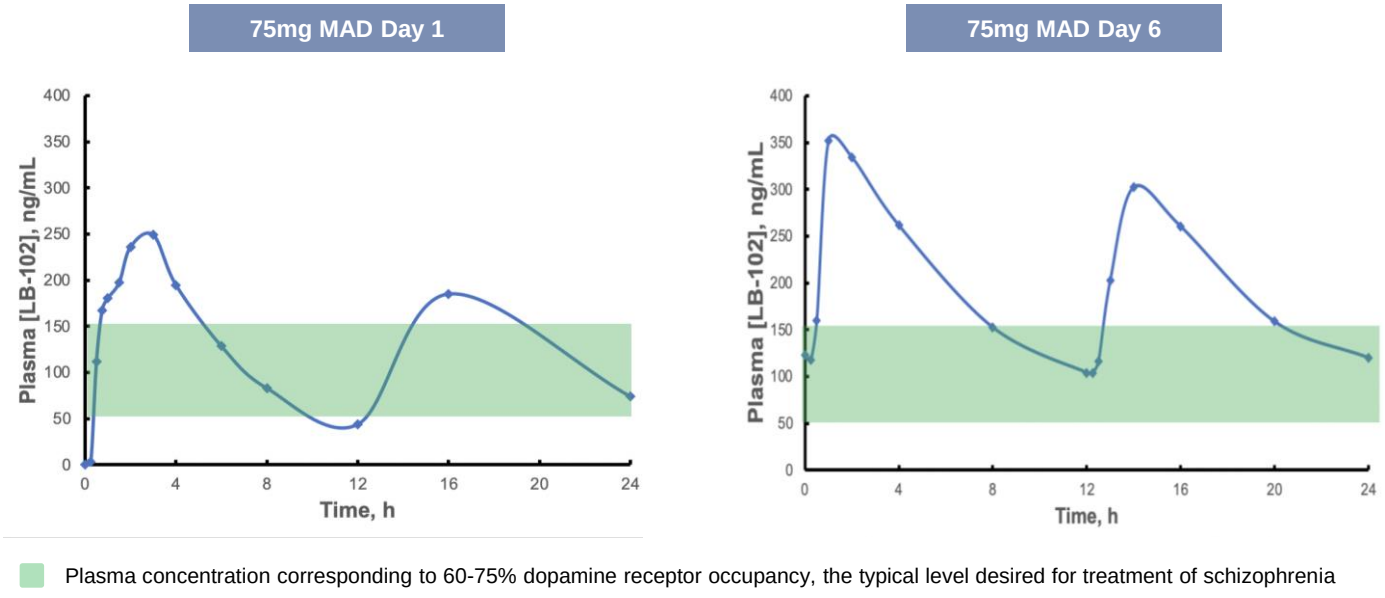



**Observed LB-102 plasma exposure is approximately 2.5x that of amisulpride[2]**

Notes: (1) Source: *Hum. Psychopharmacol. Clin. Exp.*, **2002**, *17*, 1-17; (2) Source: *Drugs*, **2001**, *61*, 2123-2150

# LB-102 PHASE 1 PHARMACOKINETICS (MAD)

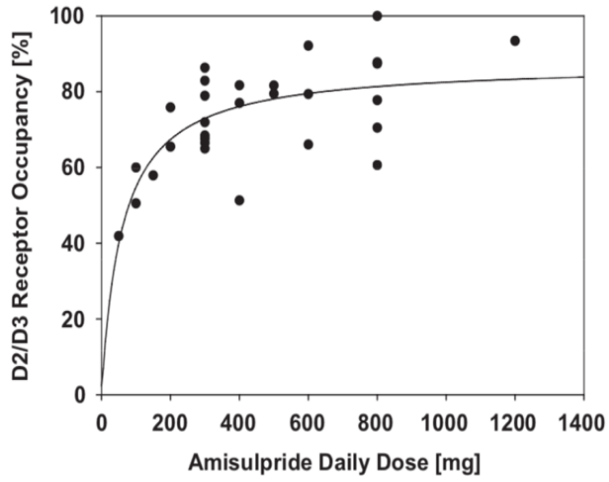
**Blood Plasma Concentrations of LB-102 From MAD Portion of Phase 1 Study**



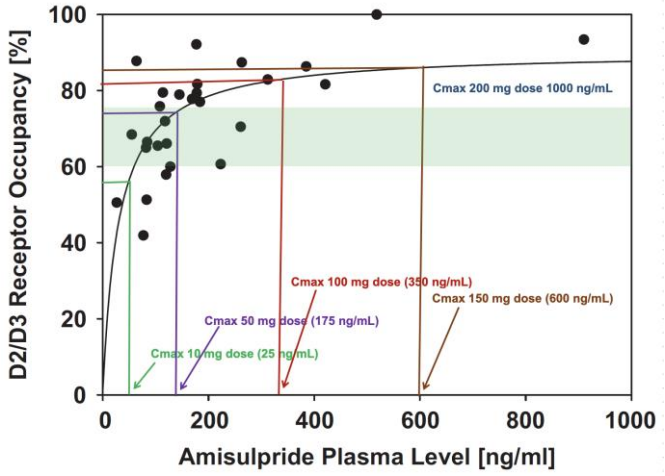

- Higher LB-102 plasma exposure consistent with observed EPS (and greater dopamine binding)
- Steady-state plasma levels observed at Day 3

# LB-102 PHASE 1 EFFICACY SIGNAL

**Amisulpride RO[2]**




**Superimposing Plasma [LB-102]**



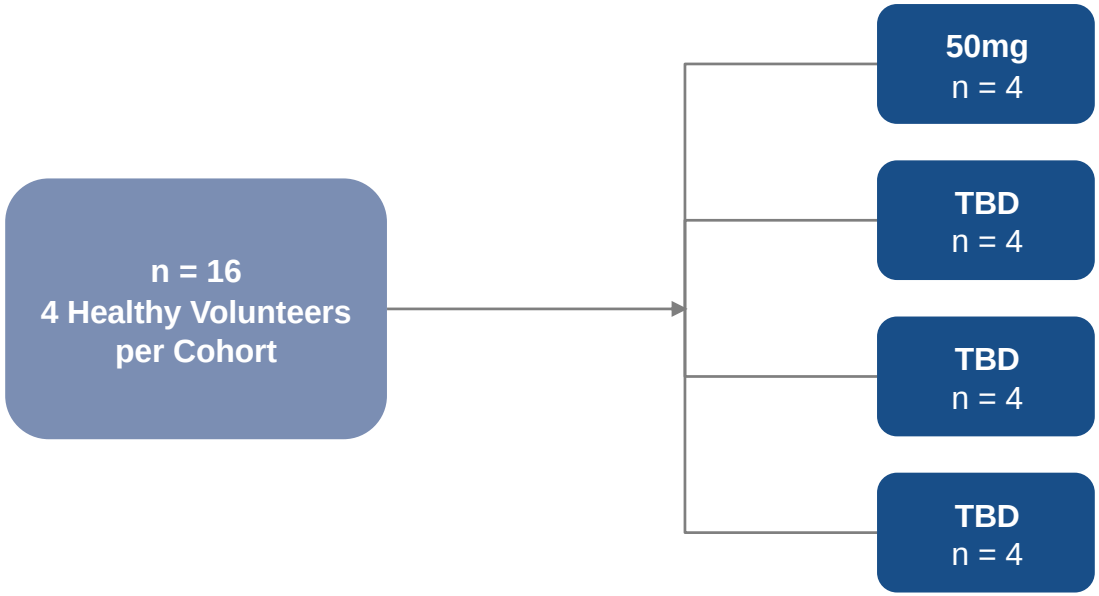

60-75% dopamine receptor occupancy, the typical level desired for treatment of schizophrenia

- Prolactin elevation and EPS are known consequences of dopamine engagement, suggesting that LB-102 is hitting dopamine as planned
- In in vitro studies, LB-102 bound dopamine receptors more strongly than amisulpride[1]
- Data to date (EPS, plasma conc.) suggests that ***50mg to 100mg LB-102 could be effective in treating schizophrenia***

Notes: (1) Source: *ACS Omega*. **2019**, *4*, 14151–14154; (2) Source: *Pharmacopsychiatry*, **2008**, *41*,169–175

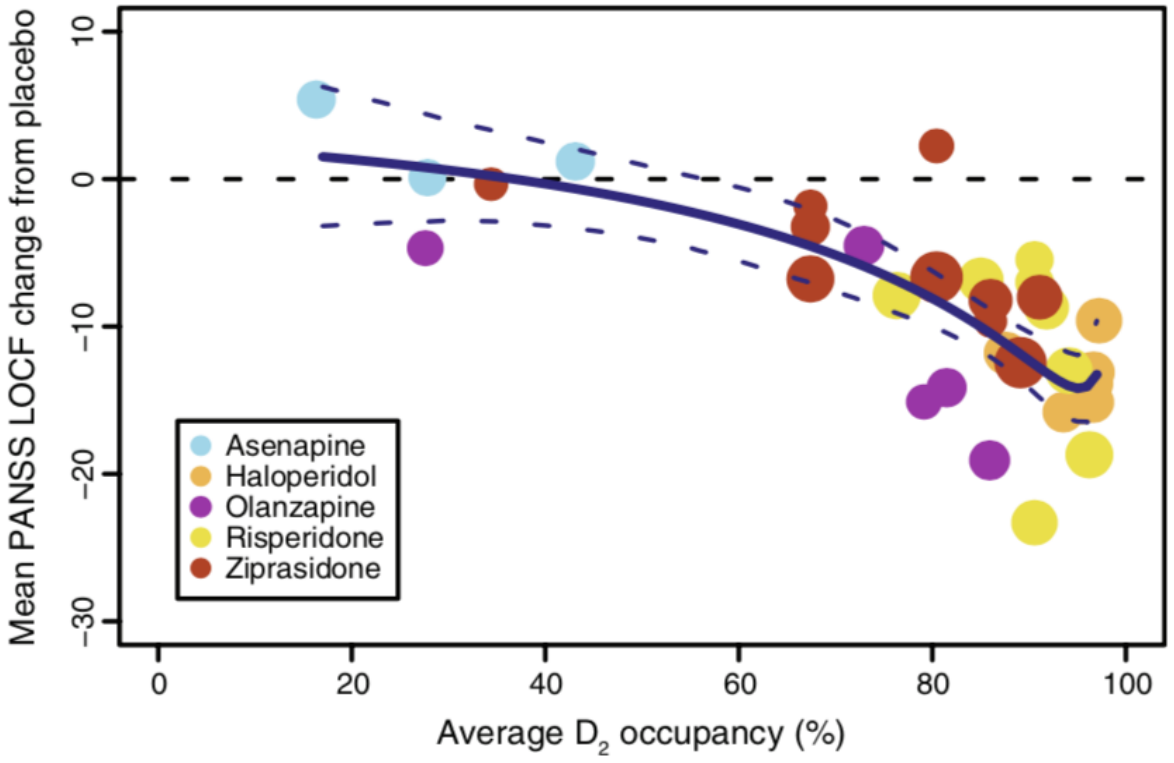
# PET DOPAMINE RECEPTOR OCCUPANCY (RO) STUDY

- PET dopamine receptor occupancy (RO) study initiated in January 2021
  - **Dosing**: Adaptive design with 4 healthy volunteers per cohort; doses dependent on % dopamine RO observed
  - **Study Objectives**: To confirm D2/D3 target engagement and therefore inform Phase 2 dosing



# CORRELATING PANSS WITH DOPAMINE RO

**Dopamine Receptor Occupancy**

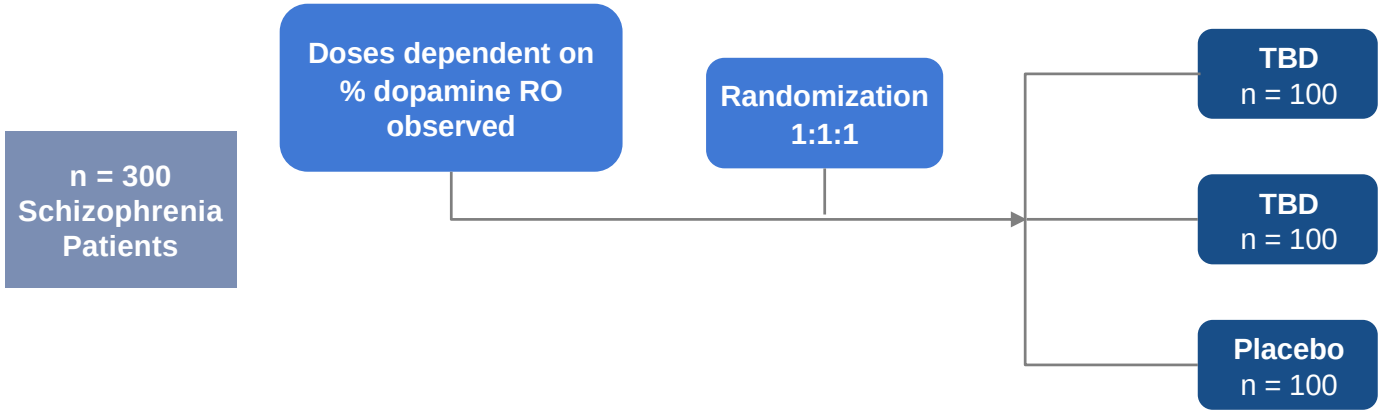



**Dopamine RO a good predictor of PANSS improvement[(1)]**

Notes: (1) Source: *The AAPS Journal*, **2011**, 13, 121-130

# LB-102 PHASE 2 CLINICAL PROGRAM

- **Trial Size:** Expecting to enroll ~300 SCZ patients in ~25 sites
- **Dosing:** Expecting 2 doses LB-102 versus placebo (4 weeks duration, double blind, placebo controlled)
- **Primary Endpoint:** Change in PANSS / **Secondary Endpoint:** CGI-S[(1)]
- Overall development plan will follow well-established criteria for FDA approval of a drug with schizophrenia label (cf. Rexulti, Vraylar, Latuda)
  - FDA regulations specify two well-controlled studies; LB-102 Phase 2 study designed and powered with this in mind
- CMC activities for drug product underway with partner (and LB shareholder) Rivopharm
- Trial initiation planned for fall 2021




**Inclusion Criteria**

- Adults with acute schizophrenia diagnosis
- Adults 18 to 50 years old

**Designed to be powered as one of two registrational studies**

Notes: (1) CGI-S: Clinical Global Impression Scale - Severity

# LB-102 CLINICAL DEVELOPMENT PROJECTED TIMELINE

| Study | Size | Cost | FY 2020 Q2 | FY 2020 Q3 | FY 2020 Q4 | FY 2021 Q1 | FY 2021 Q2 | FY 2021 2H | FY 2022 1H | FY 2022 2H | FY 2023 Q1 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Phase 1 SAD/MAD | N=64 | $1.6 | *Completed* ✓ | | | | | | | | |
| Phase 1B PET | N=16 | $1.0 | | | | | ★ | | | | |
| Phase 2 | N=300 | $33.0 | | | | | | | | | ★ |
| CARC | | $2.5 | | | | | | | | | |
| CMC | | $1.0 | | | | | | | | | |

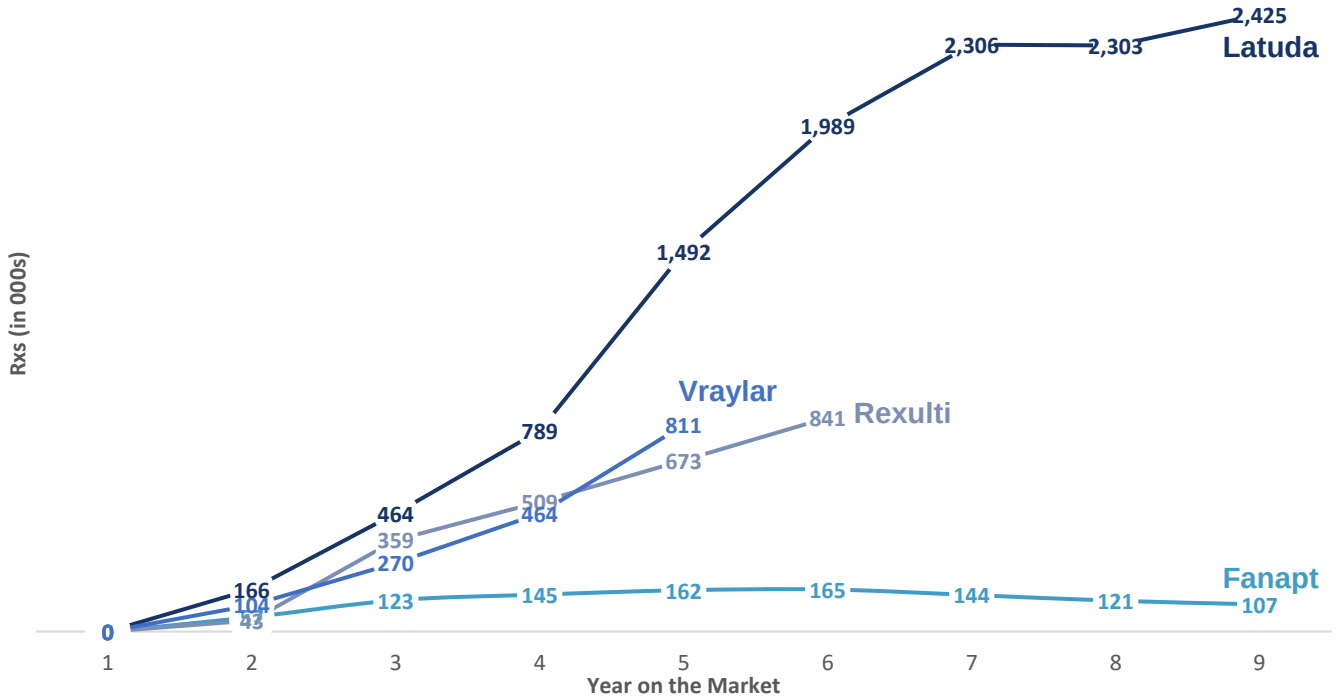
★ - Indicates expected data readout

- Phase 1 study completed; End of Phase 1 meeting with FDA took place in January 2021
- Start of Phase 2 study dependent on close of Series B financing
- CMC activities to support Phase 2 study ongoing (Rivopharm)
- Looking to raise approximately $50mm in a Series B financing to support clinical activity through Phase 2 data readout anticipated in 2023

# LB-102 MARKET POTENTIAL

- Amisulpride and closely related benzamides have ~5% share of the antipsychotics market in the EU[1]
  - Amisulpride alone has ~2% share of the antipsychotics market in the EU[1]
- ~65 million prescriptions per year for antipsychotics in the US
- **Assuming similar penetration to amisulpride in the EU for LB-102 in the US and $1,500/Rx pricing (Average Wholesale Price), LB-102 could generate > $1 billion in peak sales**

## Recent Antipsychotic US Product Launches[2]




Notes: (1) Source: IMS Q3'15 – Q2'16 data from Austria, Estonia, Finland, Germany, Latvia, Lithuania, Netherlands, Norway, Sweden, UK; (2) Source: Equity Research

# PIPELINE EXPANSION POTENTIAL

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

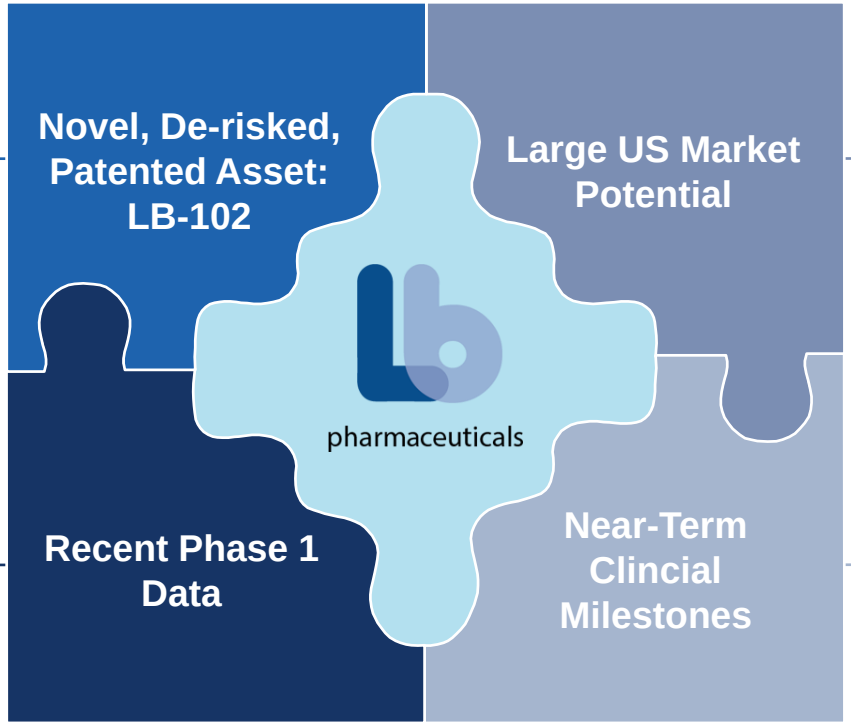
| Product (Indication) | Discovery | Pre-Clinical | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|---|---|
| LB-102 (schizophrenia) | | | | | |
| LB-102 (schizophrenia – negative symptoms) | | | | | |
| LB-102 (schizophrenia - LAI) | | | | | |
| LB-104 (depression) | | | | | |

# LB PHARMACEUTICALS INVESTMENT HIGHLIGHTS

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

Lead clinical-stage asset, **LB-102,** is a novel, de-risked, patented benzamide, **leveraging the demonstrated safety and efficacy data** of amisulpride for the treatment of schizophrenia

Phase 1 safety study recently completed in 64 healthy volunteers illustrated that drug is **safe and well-tolerated** and signaled **dopamine target engagement**




LB-102 has **potential to exceed $1 billion in annual US sales**(1)

- Though generic in Europe, amisulpride and closely related benzamides generate ~2 million scripts per year(2)

**Phase 2 study, planned for fall of 2021**, could validate LB-102 as an important therapy for schizophrenia patients

Notes: (1) Based on a 2% market share of ~65 million antipsychotic Rx per year in US (IMS, 2019 data) at an average wholesale price of $1,500 per month; (2) Source: IMS data, trailing four quarters, ending Q2 2016

pharmaceuticals

# THANK YOU

pharmaceuticals

# APPENDIX

# AMISULPRIDE EFFICACY AND TOLERABILITY

## Reduction in PANSS Negative Subscore

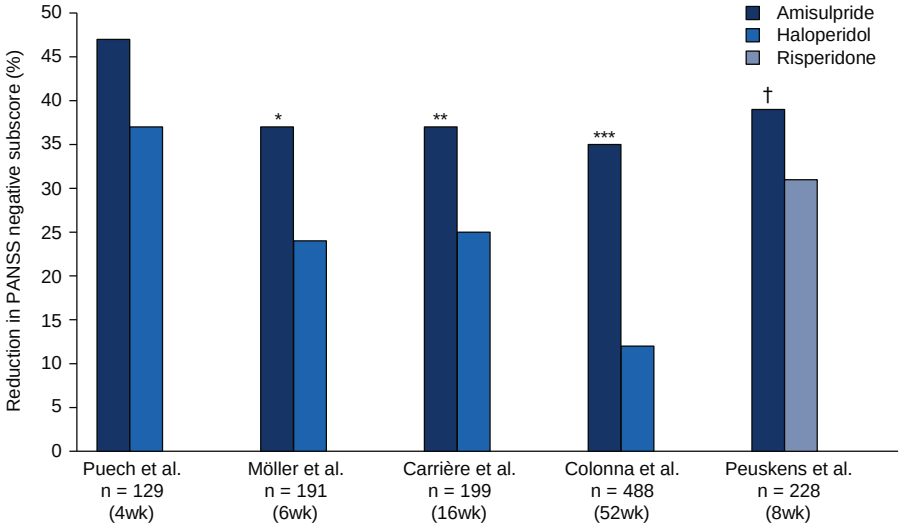



**Fig. 1.** Reduction in the Positive and Negative Syndrome Scale (PANSS) negative subscore in patients with acute exacerbations of schizophrenia treated with amisulpride in randomized, multicenter, double-blind studies. * $p < 0.05$, ** $p = 0.01$, *** $p < 0.001$ *vs* haloperidol; † $p = 0.09$ *vs* risperidone.

## Combined Tolerability

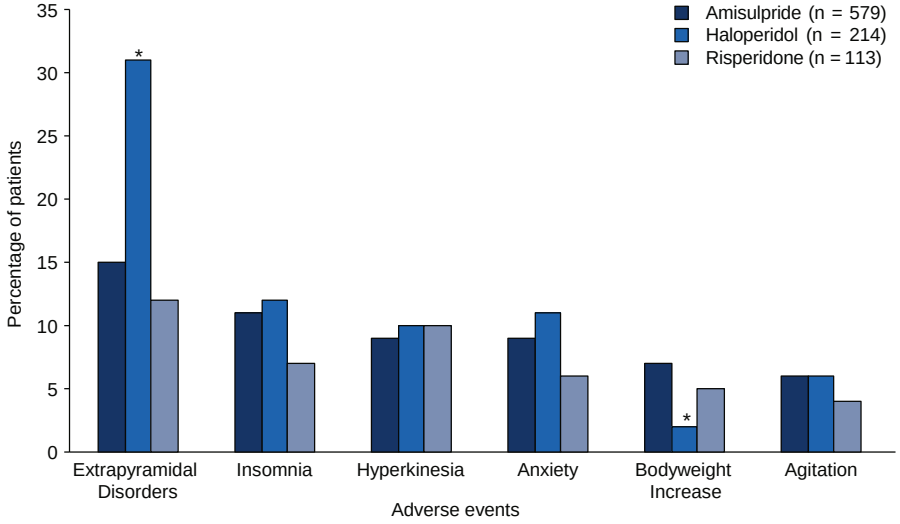



**Fig. 2.** Combined tolerability data in patients with acute exacerbations of schizophrenia treated with amisulpride, haloperidol and risperidone. Amisulpride 100 to 1200 (mean 670) mg/day, haloperidol 5 to 30 (mean 16) mg/day and risperidone 8 mg/day were administered orally. * $p < 0.01$ *vs* amisulpride.

## Combined Tolerability in Patients with Predominantly Negative Symptoms

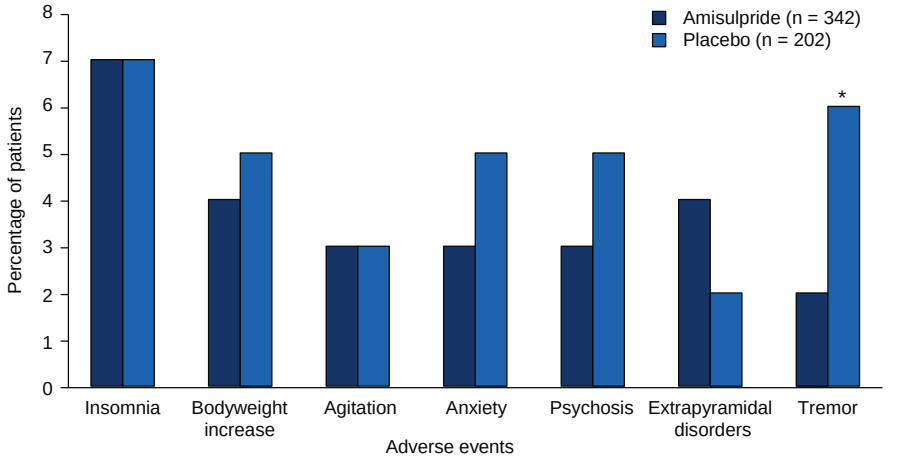



**Fig. 3.** Combined tolerability data in patients with predominantly negative symptoms of schizophrenia treated with amisulpride compared with placebo. Amisulpride was administered orally at a mean dosage of 118 mg/day (<300 mg/day in 87% of patients). * $p < 0.01$ *vs* amisulpride.

Source: *Drugs*, **2001**, *61*, 2123-2150

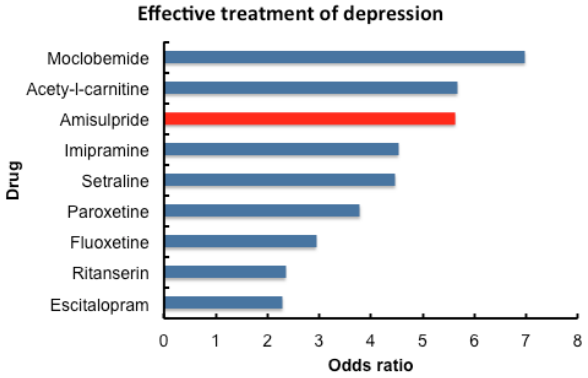
# DEVELOPMENT STAGE SCHIZOPHRENIA LANDSCAPE

| Candidate (Company) | Status | Commentary |
|---|---|---|
| **ALKS 3831**<br>*Olanzapine / samidorphan* (Alkermes) | NDA submitted (Nov 2019) | ▪ PDUFA Date of 11/15/20 for schizophrenia and bipolar I disorder<br>▪ Phase 3 data presented in April 2019 demonstrated statistically significant reduction from baseline in PANSS scores at 4 weeks, compared to placebo<br>▪ Adverse reactions included weight increases (24.8%), somnolence (21.2%), and dry mouth (12.8%) |
| **SEP-36385**<br>(Sunovion) | Phase 3 | ▪ Open label extension study data announced in December 2019 demonstrated clinically meaningful improvements across all efficacy measures, including PANSS total score (-22.6), the CGI-S score (-1.0), and the BNSS total score (-11.3)<br>▪ Pivotal Phase 2 study data announced in December 2018 demonstrated statistically significant and clinically meaningful improvement in the PANSS total score compared to placebo after four weeks of treatment (-17.2 vs. -9.7, respectively; p=0.001; effect size, 0.45)<br>– Adverse reactions included somnolence (6.7% vs 4.8% placebo), agitation (5.0% vs 4.8%) nausea (5% vs 3.2%), diarrhea (2.5% vs 0.8%), and dyspepsia (2.5% vs 0%) |
| **MK-8189**<br>(Merck) | Phase 2 | ▪ Phase 2 data released in December 2018 did not separate from placebo or risperidone, but risperidone separated from placebo on total PANSS(1) |
| **KarXT**<br>(Karuna) | Phase 2 | ▪ Phase 2 data announced in November 2019 demonstrated an 11.6 point improvement over placebo on total PANSS at week five<br>▪ Rates of adverse reactions (somnolence, weight gain, and EPS/akathisia) were similar to placebo |
| **BIIB104**<br>(Biogen) | Phase 2 | ▪ Phase 2b data expected in H2 2021 |
| **LB-102**<br>(LB Pharmaceuticals) | Phase 1 Complete | ▪ Most common adverse reactions were elevated prolactin levels and acute dystonic reactions |

Source: Equity Research, Company Materials; ClinicalTrials.gov
Note: (1) source: *CNS Spectrums*, **2019**, *24*, 41–68
CGI-S: Clinical Global Impression Scale - Severity
BNSS: Brief Negative Symptom Scale

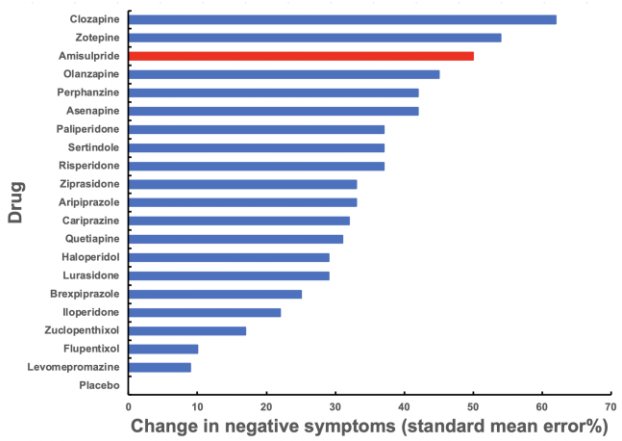
# AMISULPRIDE NEGATIVE SYMPTOMS AND DEPRESSION

Amisulpride's ability to inhibit 5-$HT_7$ provides anti-depressant properties…




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

And may render it effective in treating negative symptoms of SCZ

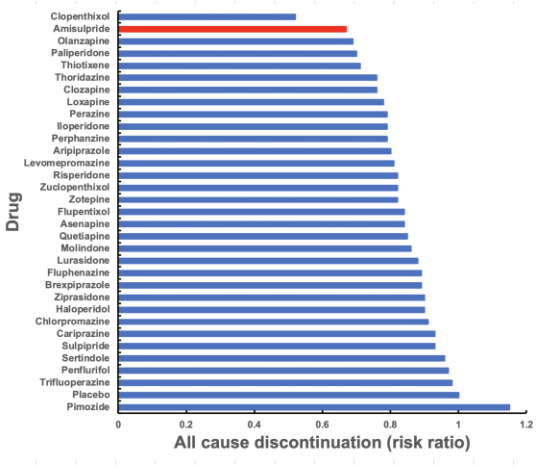



Source: *Lancet*, **2019**, *394*, 393-951

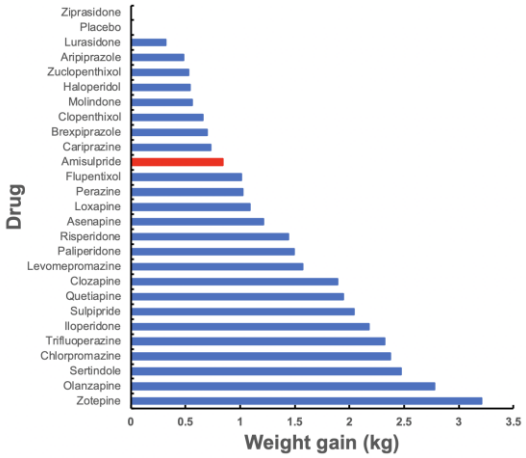
# AMISULPRIDE COMPARATIVE SAFETY

## Data from 53,500 patient meta-analysis[1]

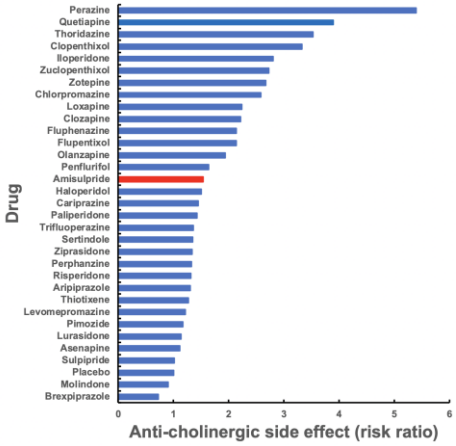
### All Cause Discontinuation by Antipsychotic Agent



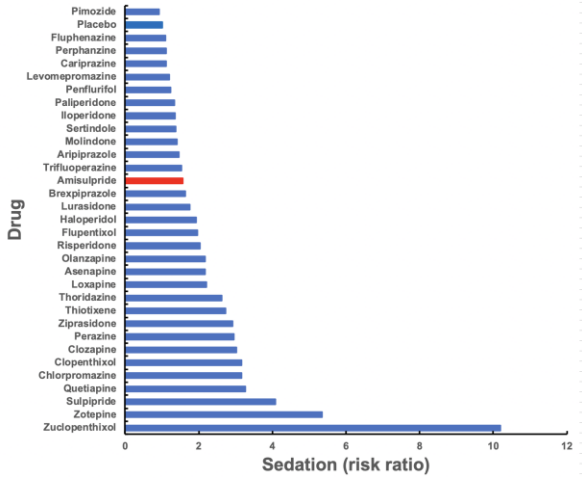

### Weight Gain by Antipsychotic Agent




### Anti-cholinergic Side Effects by Antipsychotic Agent




### Sedation by Antipsychotic Agent




Notes: (1) Source: *Lancet*, **2019**, *394*, 939-951

# SUMMARY OF ANTIPSYCHOTIC QT PROLONGATION

- **All antipsychotics, including amisulpride, have the potential to alter the QT interval**
  - A 16,000 patient amisulpride PV study in the UK from 2013 to 2017 showed 18 CV SAEs and 8 examples of QT alteration, all of which occurred in patients also taking clozapine
  - Data below from *World Journal of Biological Psychiatry* (**2012**, *13*, 318-378) shows QT risk of amisulpride is no different from other commonly used anti-psychotics

| Antipsychotic | Approximate QTc Interval Prolongation(1) *(Milliseconds)* |
|---|---|
| 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 |

Table II. Selected side effects of commonly used antipsychotics. Frequencies and severity of side effects refers to information obtained by drug companies, FDA, additional literature and other guidelines.

| | Antipsychotic medication | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Side effect | Haloperidol | Amisulpride | Aripiprazole | Clozapine | Olanzapine | Paliperidone | Quetiapine | Risperidone | Sertindole | Ziprasidone |
| Akathisia/Parkinsonism | +++ | 0/+ | + | 0 | 0/(+) | 0/++ | 0/(+) | 0/++ | 0/(+) | 0/(+) |
| Tardive dyskinesia | +++ | (+) | (+) | 0 | (+) | (+) | ? | (+) | (+) | ? |
| Seizures | + | 0 | (+) | ++ | 0 | 0 | 0 | 0 | (+) | 0 |
| QT-prolongation | + | (+) | (+) | (+) | (+) | (+) | (+) | (+) | +++ | ++ |
| Glucose abnormalities | (+) | (+) | 0 | +++ | +++ | ++ | ++ | ++ | + | 0 |
| Lipid abnormalities | (+) | (+) | 0 | +++ | +++ | ++ | ++ | ++ | + | 0 |
| Constipation | + | ++ | 0 | +++ | ++ | ++ | + | ++ | + | 0 |
| Hypotension | ++ | 0 | + | (+) | (+) | ++ | ++ | ++ | (+) | 0 |
| Agranulocytosis | 0/(+) | 0/(+) | 0/(+) | + | 0/(+) | 0/(+) | 0/(+) | 0/(+) | 0/(+) | 0/(+) |
| Weight Gain | + | + | (+) | +++ | +++ | ++ | ++ | ++ | ++ | (+) |
| Prolactin elevation | +++ | +++ | 0 | 0 | (+) | ++ | (+) | ++ | (+) | 0 |
| Galaktorrhoea | ++ | ++ | 0 | 0 | + | ++ | 0 | ++ | (+) | 0 |
| Dysmenorrhoea | ++ | ++ | 0 | 0 | + | ++ | (+) | ++ | (+) | (+) |
| Sedation | + | 0/(+) | 0 | +++ | +/++ | + | ++ | + | (+) | 0/(+) |
| MNS | + | ? | (+) | (+) | (+) | (+) | (+) | (+) | (+) | ? |

0 = no risk; (+) = occasionally, may be no difference to placebo; + = mild (less 1%); ++ = sometimes (less 10%), +++ frequently (> 10%); ? = no statement possible due to lacking data. Weight gain during 6 – 10 weeks: + = low (0–1.5 kg); ++ = medium (1.5 – 3 kg); +++ = high (> 3 kg).

Notes: (1) Washington et al, *Current Psychiatry*, **Oct 2012**, Vol 11:36-39; list is not comprehensive, other antipsychotics may be associated with QTc prolongation

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