pharmaceuticals

CORPORATE PRESENTATION

SEPTEMBER 2021

Making Smart Chemical Changes to Create Improved Novel Therapeutics

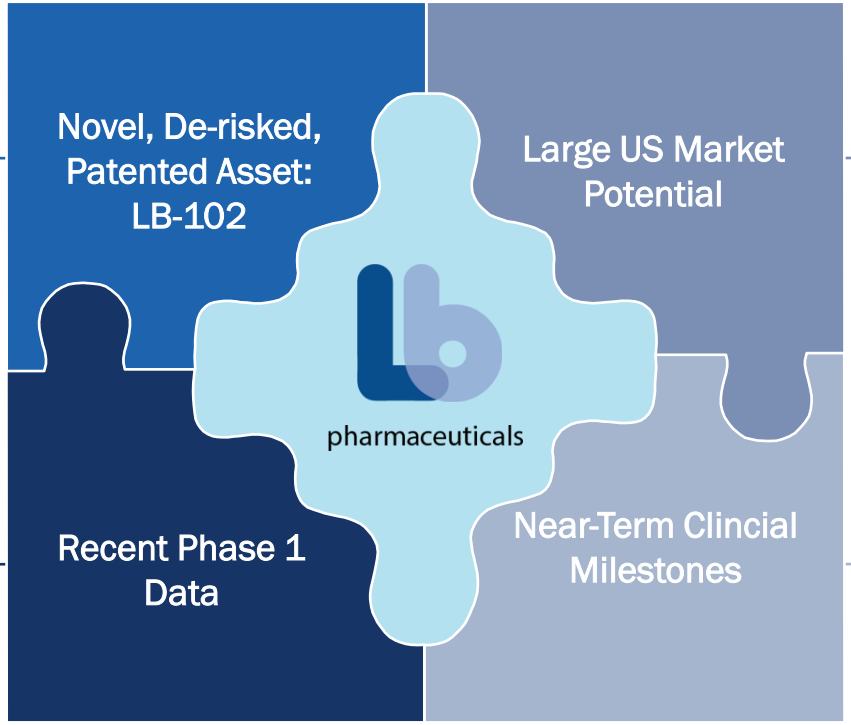
LB PHARMACEUTICALS INVESTMENT HIGHLIGHTS

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 completed in 64 healthy volunteers illustrated that drug is **safe and well-tolerated** and signaled **dopamine target engagement**

Phase 1b dopamine receptor occupancy study completed in September 2021 confirming proof of concept



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 Q1 of 2022, 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

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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

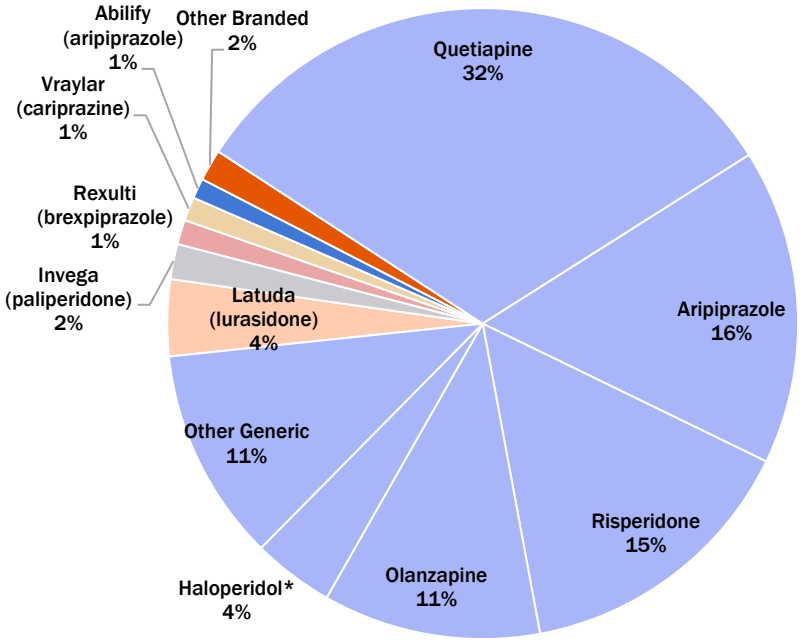
SCHIZOPHRENIA

- Schizophrenia (SCZ) is a chronic and debilitating disease affecting approximately 1% of the US population[1]
- SCZ patients have profoundly diminished quality of life
- Despite over 20 FDA approved drugs, there is a great need for additional treatments
  - 10% - 30% of patients with schizophrenia show little symptomatic improvement after multiple trials of first-generation antipsychotics[2]
  - An additional 30% - 60% experience partial or inadequate improvement or unacceptable side effects during antipsychotic therapy[2]
  - Up to 75% of patients cycle through multiple antipsychotics within 18 months[3]
- Typical antipsychotic side effects are associated with significantly reduced likelihood of compliance[4]

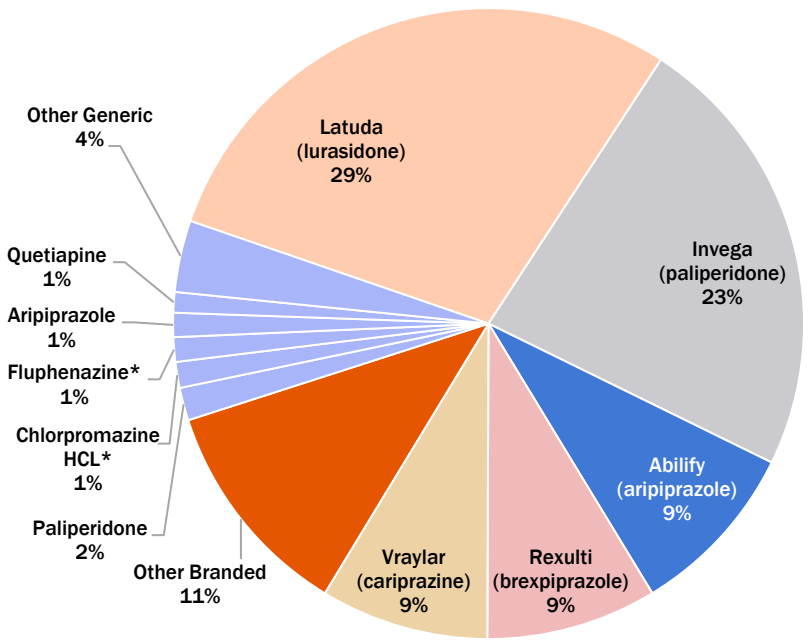
1 https://sardaa.org/resources/about-schizophrenia/
2 Patel et al. P&T 2014 Sep; 39(9): 638–645.
3 Lieberman JA, Stroup TS, et al. N Engl J Med. 2005;353(12):1209-1223.
4 Dibonaventura M et al. BMC Psychiatry. 2012;12:20.

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

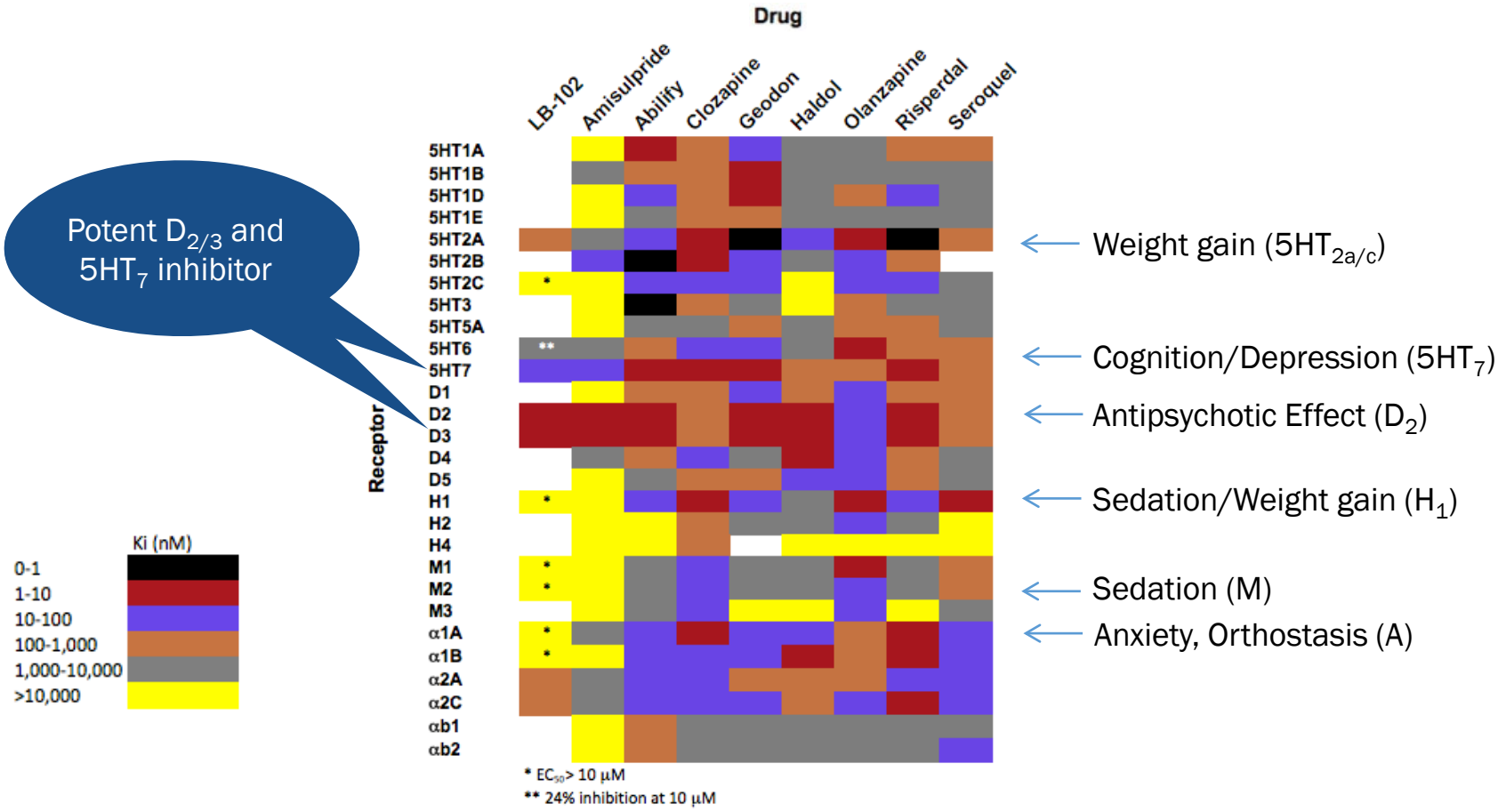
AMISULPRIDE BACKGROUND

- Amisulpride is a best-in-class benzamide 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

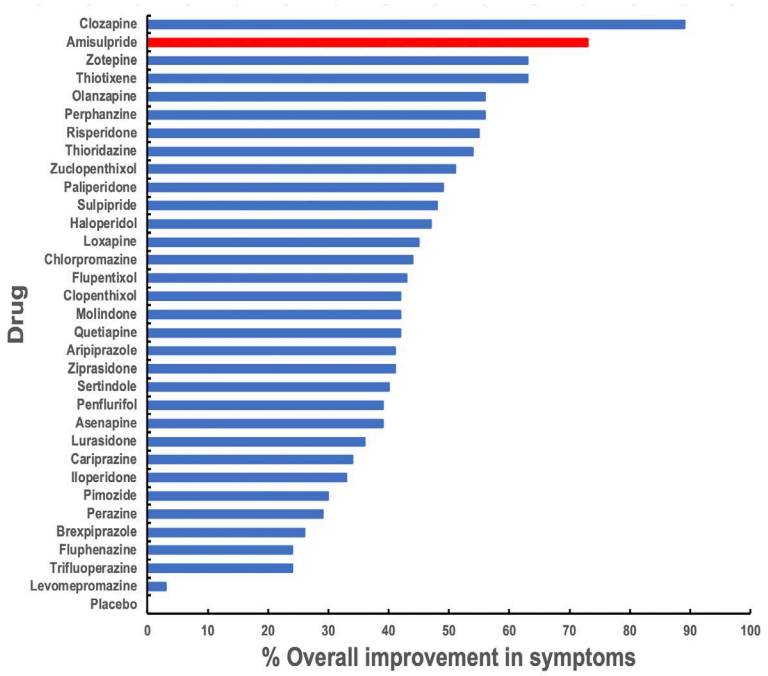


Notes: Ki data from: *The Neuroscientist*, **2000**, 6, 252-26245rf

AMISULPRIDE COMPARATIVE EFFICACY

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

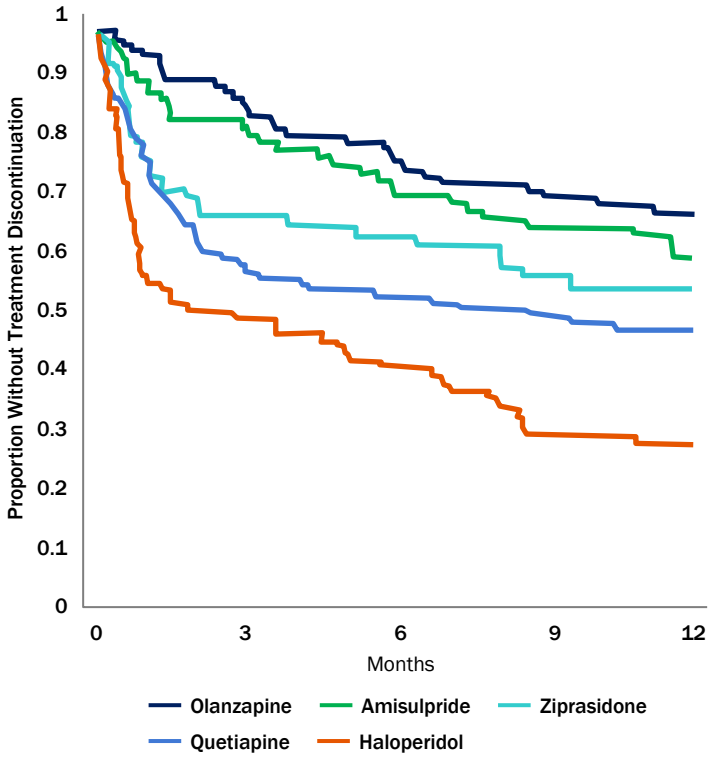
Antipsychotic Efficacy



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

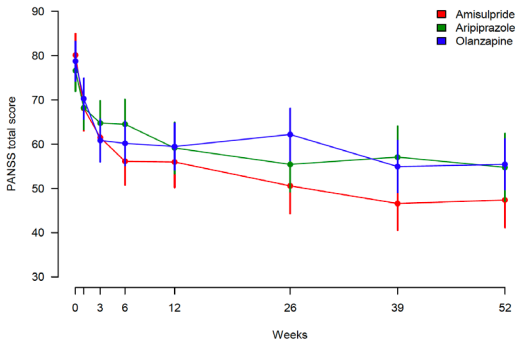
Notes: (1) Source: *Lancet*, **2019**, *394*, 939-951.; (2) Source: *Lancet*, **2008**, *371*, 1085-1097

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)

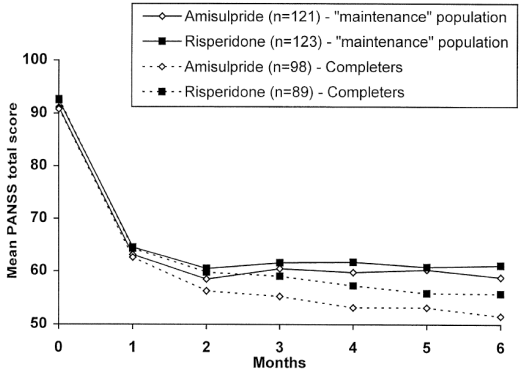
PANSS Score Over Time



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

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

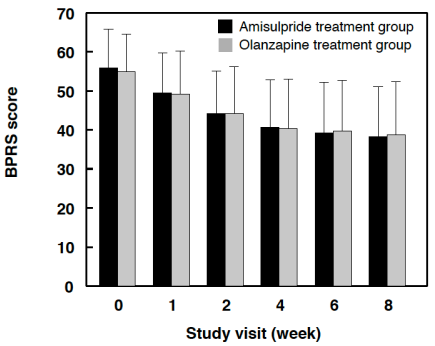
PANSS Score Over Time



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

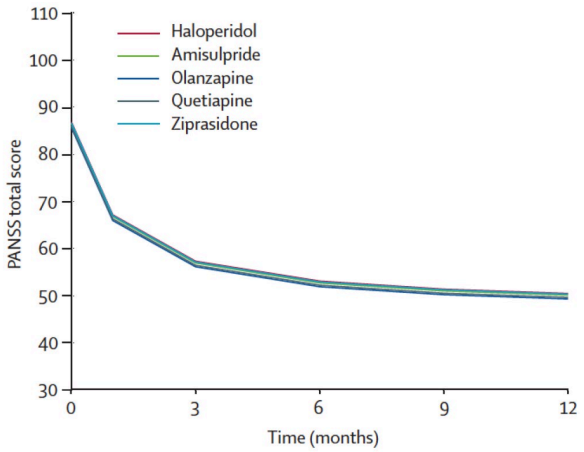
Notes: (1) Source: *Lancet Psychiatry*, **2020**, *7*, 945-954; (2) Source: *Neuropsychopharmacology*, **2002**, *27*, 1071-1081; (3) Source: *Current Medical Res. & Opin.*, **2020**, *18*, 355-362

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 favorable side effect profile

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

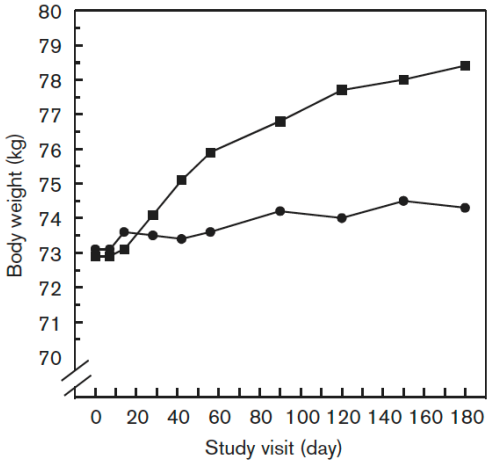
PANSS Score Over Time



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

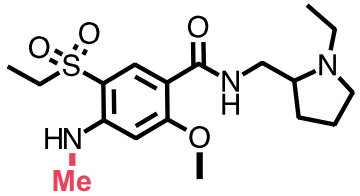
LB-102 OVERVIEW

LB-102 is a methylated version of amisulpride

Amisulpride (1983)

Prior to methylation

LB-102 (2016)

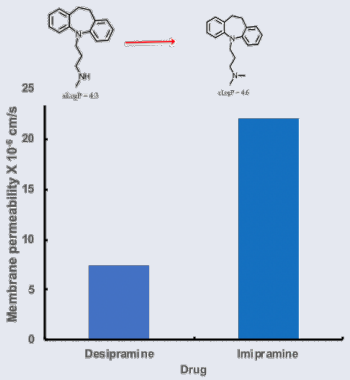
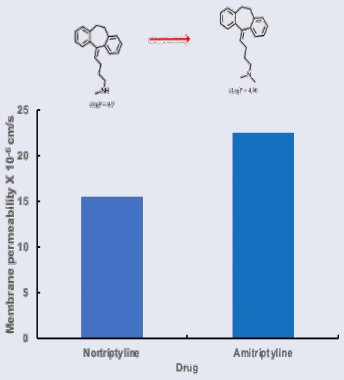


Amisulpride containing added methyl group

- Novel chemical structure with biological / pharmacological properties designed to improve amisulpride's safety and efficacy
- LB-102 mimicked amisulpride's safety profile at lower doses in its Phase 1 clinical trial
- 3 US composition of matter patents covering LB-102 issued (Patent Numbers: 10,167,256, 10,259,786, and 10,689,338)
  - PCT application and 19 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	**LB-102**
	cLogP = 3.9	**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

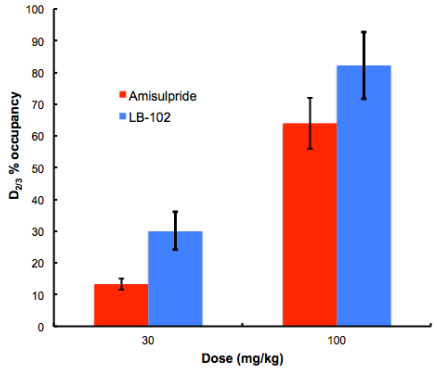
Notes: (1) Source: *The AAPS Journal*, **2014**, *16*, 1247-1258

LB-102 PRECLINICAL OVERVIEW

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

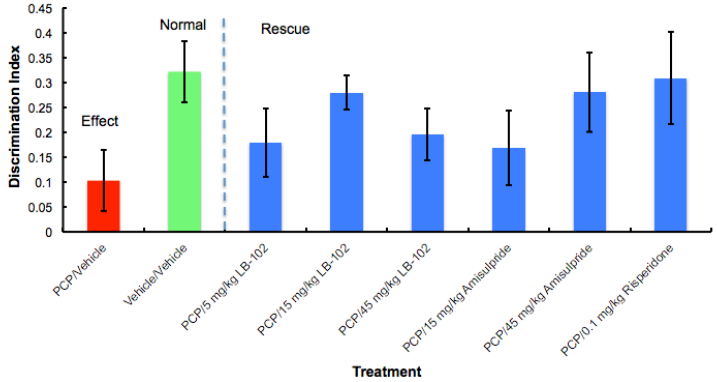
LB-102 rat brain $D_{2/3}$ Receptor Occupancy (RO)

Superior(1) dopamine RO relative to amisulpride



Novel Object Recognition (NOR) Study

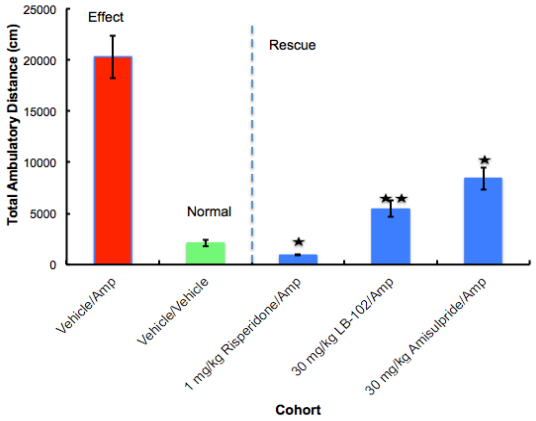
Improvement in cognitive function relative to baseline



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

Locomotor Activity (LMA) Study

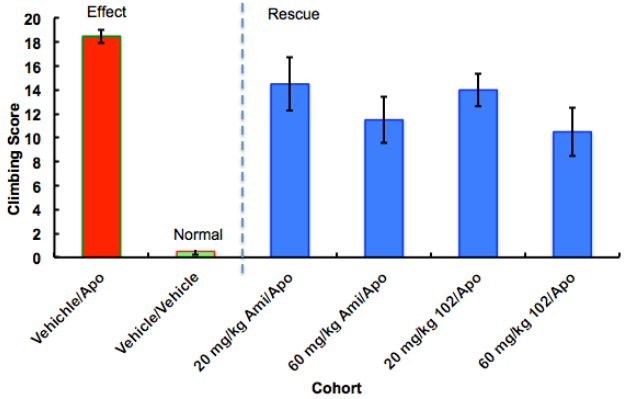
Statistically significant hyperactivity improvement relative to amisulpride and control



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

Mouse Apomorphine Induced Climbing (AIC) Study

Comparable improvement in stereotypy relative to amisulpride

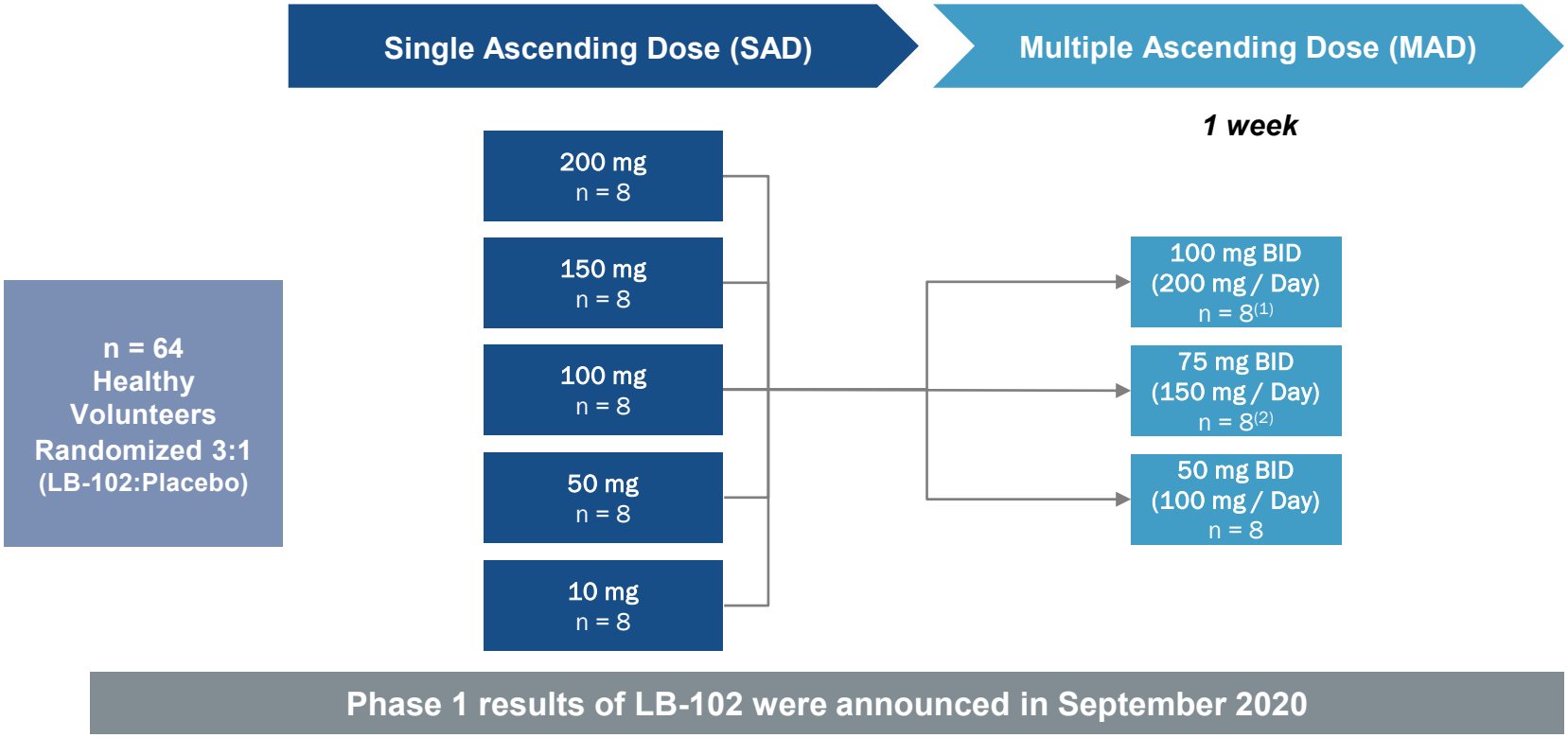


Climbing Score± SEM (n = 10/group).

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 PHASE 1 CLINICAL TRIAL OVERVIEW

- **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 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

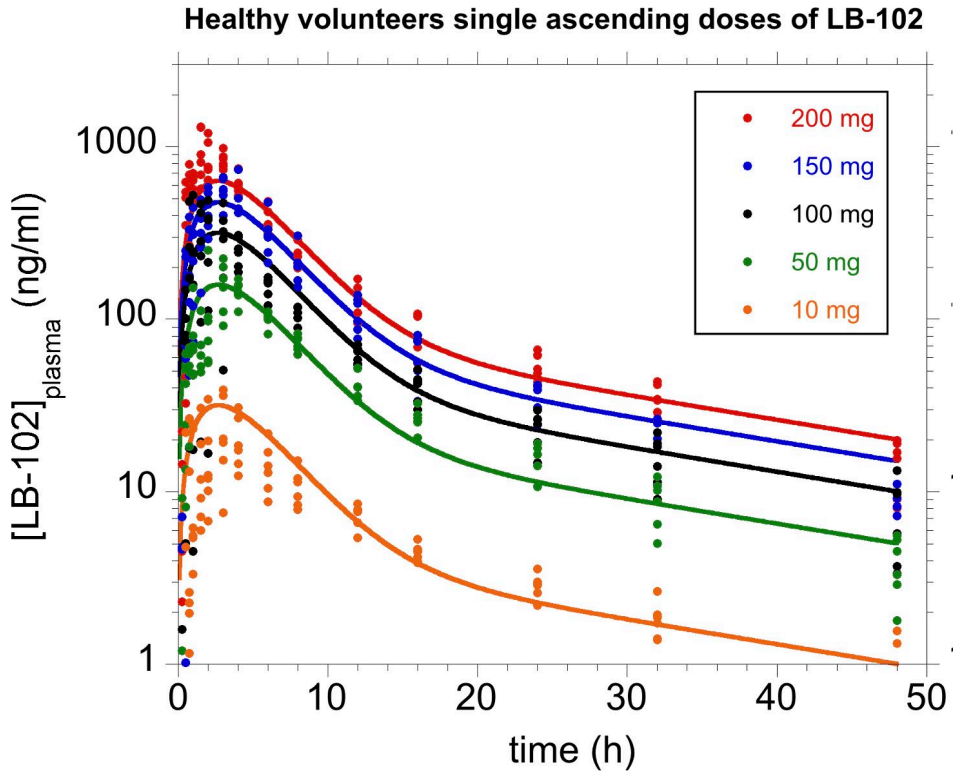
		Single ascending dose					Multiple ascending dose		
Adverse event	**Placebo**	**10 mg**	**50 mg**	**100 mg**	**150 mg**	**200 mg**	**50 mg BID**	**75 mg BID**	**100 mg BID**
n	**16**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
Elevated prolactin		2	3	1	1	1	2	2	1
Diarrhea			1						
Upper respiratory 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								

- Dosing in 200 mg/d MAD cohort was stopped after 3 days due to two occurrences of EPS (acute dystonia)
  - ≥ 2 grade 2 AEs in same organ class was a stopping rule
- Prolactin elevation (PRL), which was reversible and unassociated with clinical consequences, was observed at all doses (consistent with D_2 receptor binding)
  - Uncorrelated with dose, consistent with Glatard *et al.*, *Clin. Pharmacokinet.*, **2020**, *59*, 371-382
- QT prolongation profile consistent with atypical antipsychotics and did not meet stopping criteria outlined in study

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

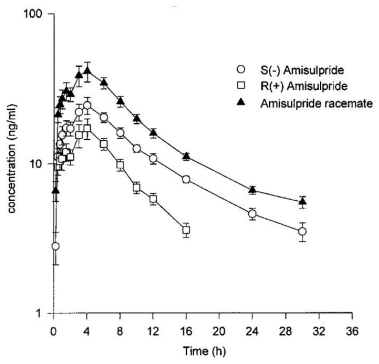
MW = 369.5
cLogP = 3.9

LB-102

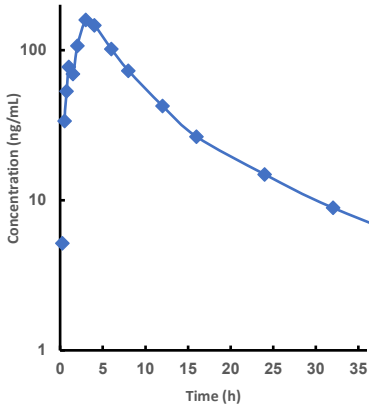
MW = 383.5
cLogP = 4.4

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

50 mg Amisulpride



50 mg LB-102

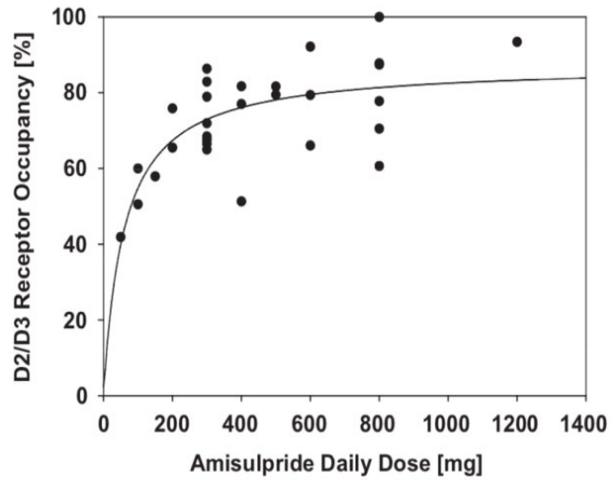


Observed LB-102 plasma exposure is approximately 2.5x that of amisulpride[2]

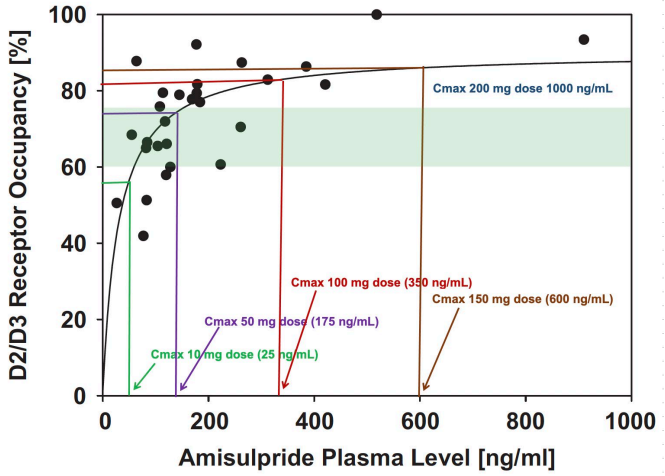
Notes: (1) Source: *Hum. Psychopharmacol. Clin. Exp.*, **2002**, *17*, 1-17; (2) Source: *Drugs*, **2001**, *61*, 2123-2150

LB-102 PHASE 1 EFFICACY SIGNAL

Amisulpride RO[1]



Superimposing Plasma [LB-102]



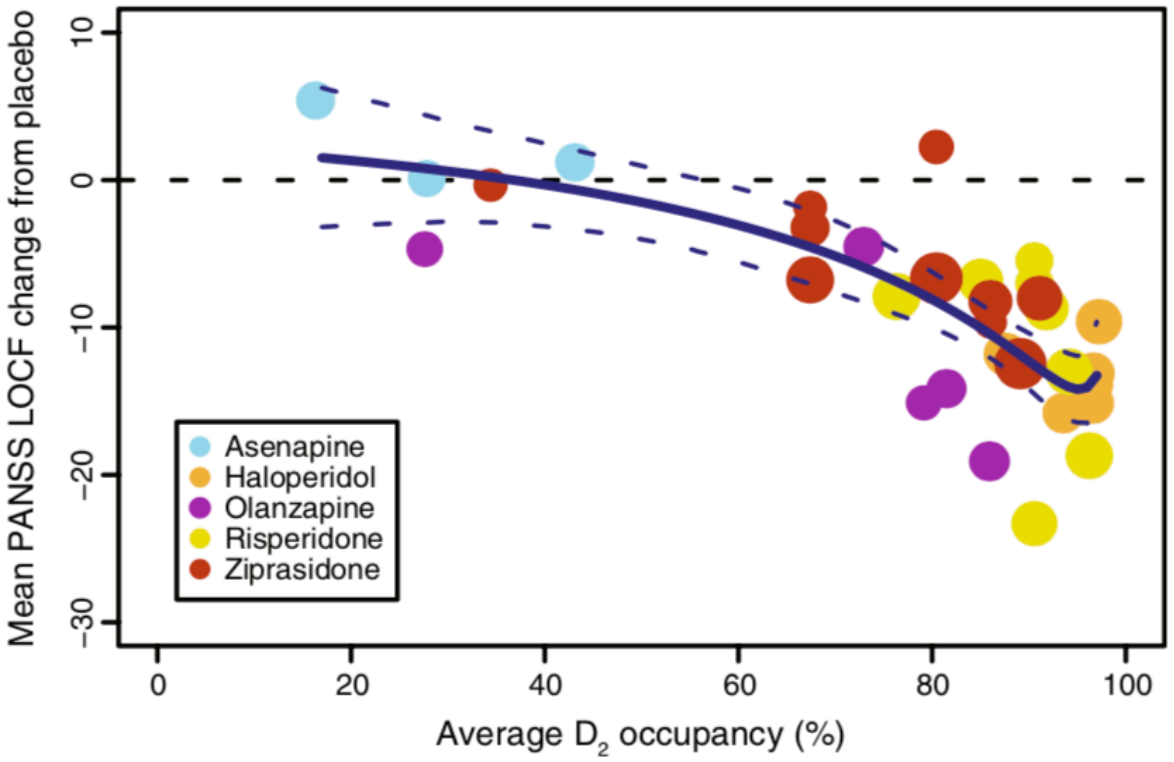
60-75% dopamine receptor occupancy, the typical level desired for treatment of schizophrenia

- Prolactin elevation and EPS are known consequences of dopamine engagement, suggesting that LB-102 is hitting dopamine as expected
- Circumstantial evidence (EPS, plasma conc., PRL) suggests that a daily dose of 50 mg to 100 mg LB-102 could be effective in treating schizophrenia
  - Amisulpride is typically dosed at 400 mg to 800 mg per day
- Our expectation was that 100 mg LB-102 would produce just over 80% dopamine RO
  - Lower bound associated with increased risk of EPS
- Phase 1b PET study was designed to test this hypothesis

Notes: (1) Source: *Pharmacopsychiatry*, **2008**, *41*,169–175

CORRELATING PANSS WITH DOPAMINE RO

Dopamine Receptor Occupancy

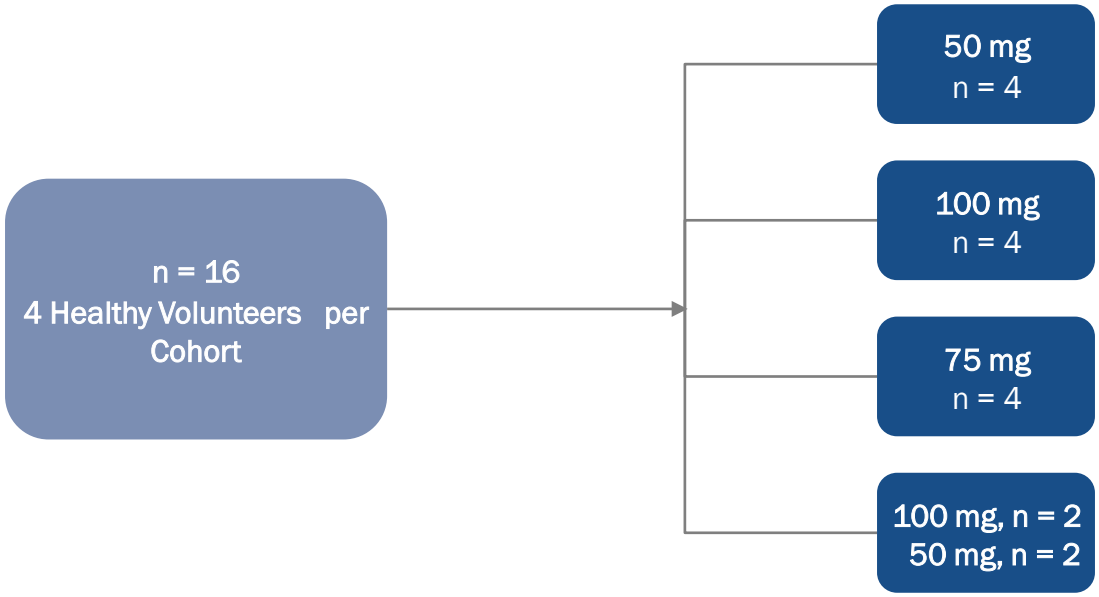


Dopamine RO a good predictor of PANSS improvement[1]

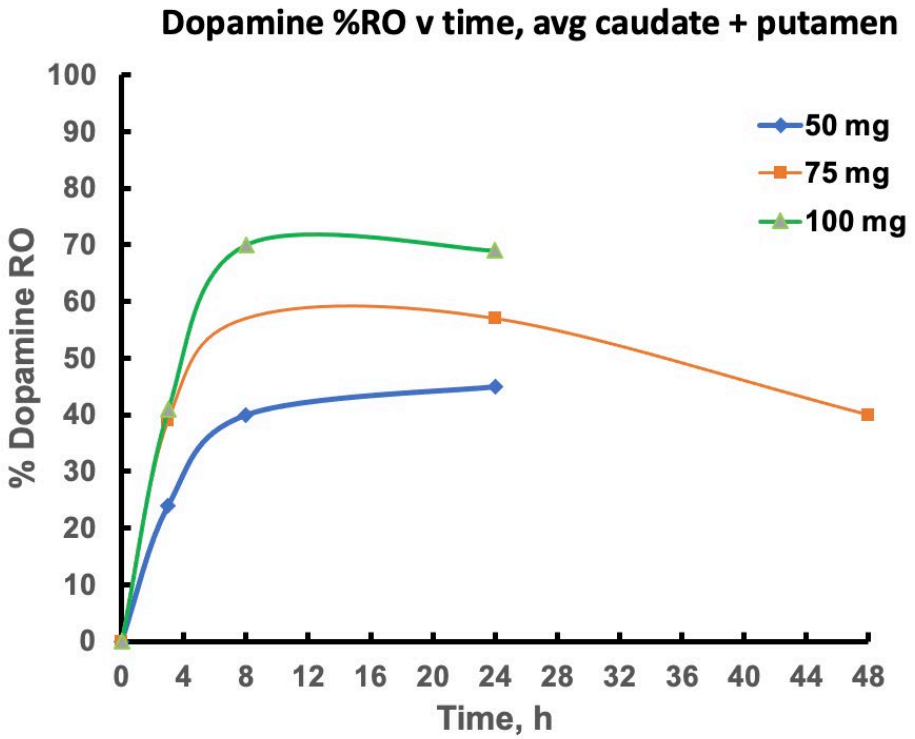
Notes: (1) Source: *The AAPS Journal*, **2011**, 13, 121-130

LB-102 PHASE 1b PET IMAGING STUDY

- PET dopamine receptor occupancy (RO) study initiated earlier this year (NCT04588129)
  - **Dosing**: Adaptive design with 4 cohorts of 4 healthy volunteers per cohort receiving LB-102; doses dependent on % dopamine RO observed
    - Multiple PET scans per subject using ^{11}C raclopride as tracer
  - **Study Objectives**: To confirm D_2/D_3 target engagement and inform Phase 2 dosing

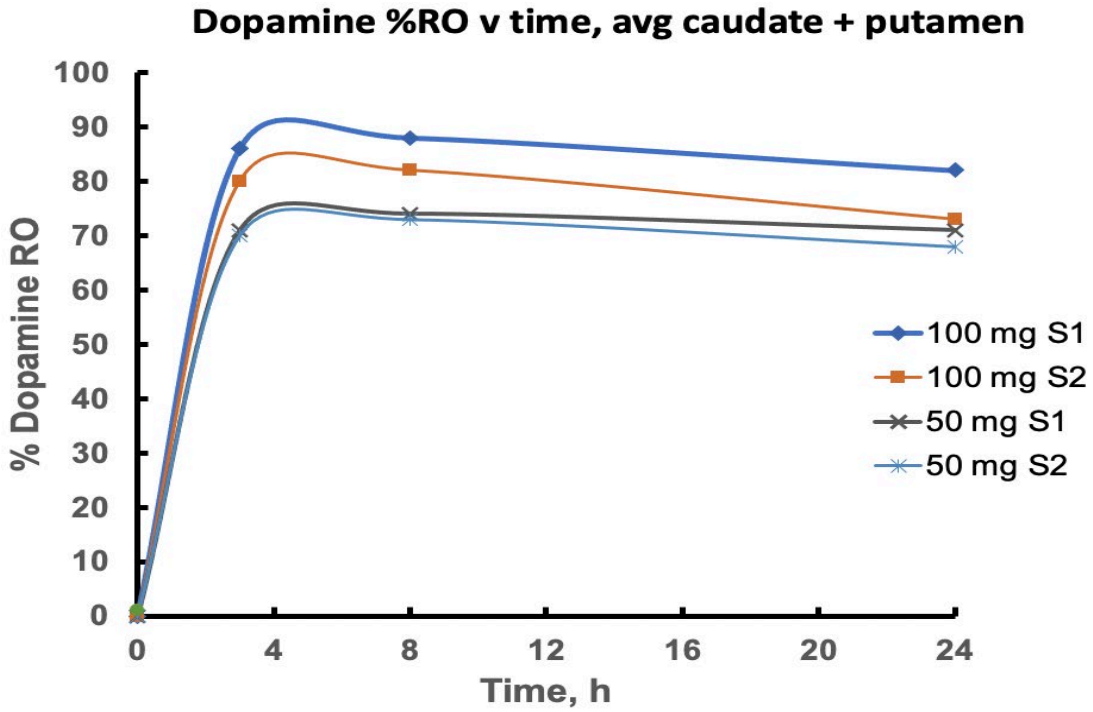


PHASE 1b - COHORTS 1 - 3, SINGLE DOSE



- Cohorts 1 (100 mg) and 2 (50 mg) subjects scanned at 2.5, 7.5, and 23.5 hrs post-dosing
- Cohort 3 (75 mg) subjects scanned at 2.5, 23.5, and 47.5 hrs post-dosing
- Goal was to have dopamine RO between 60% and 75%

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



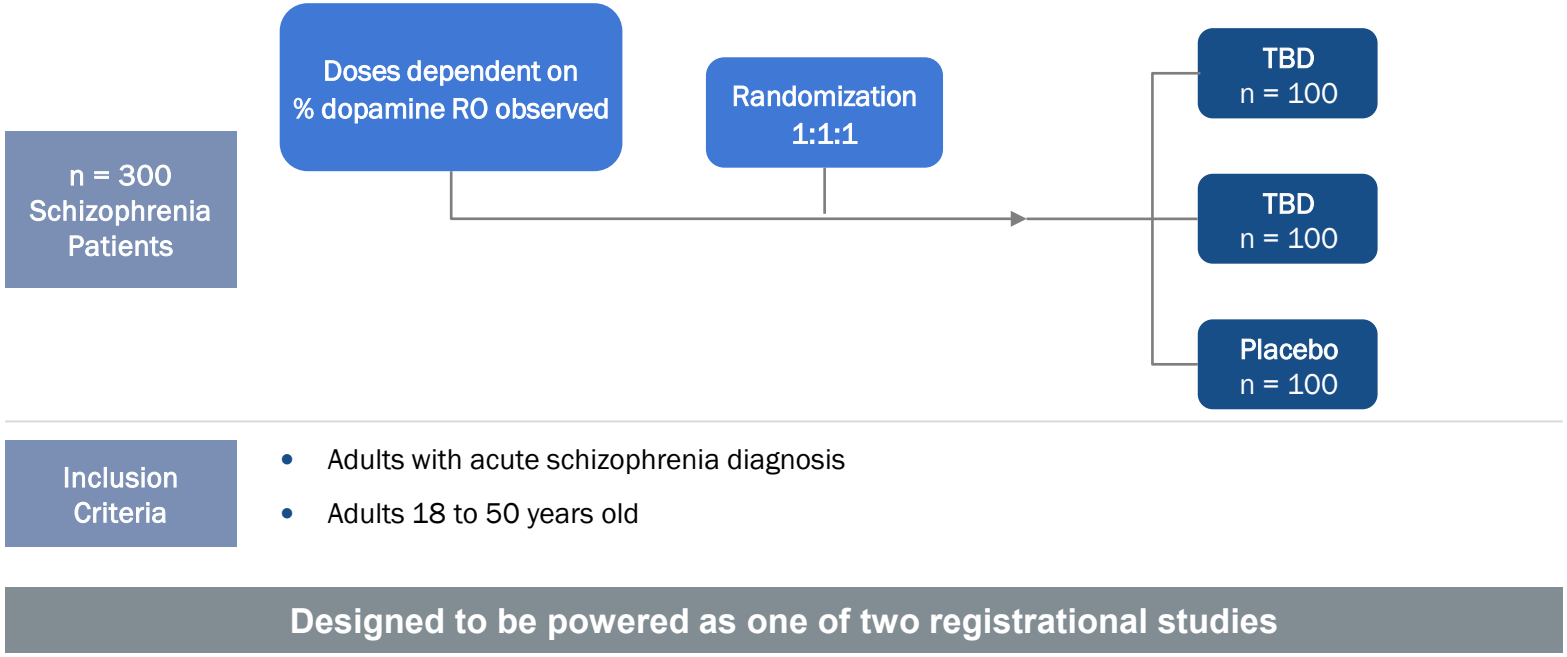
- Subjects scanned 2.5, 7.5, and 23.5 hrs post-fourth day dosing
  - Dopamine RO observed at 50 mg was in the range of the desired RO for an effective schizophrenia drug
  - There were no observations of EPS

PHASE 1b - KEY TAKEAWAYS

- Total of eight AEs, all minor, in 16 subjects dosed
  - Importantly no observations of EPS
- Unambiguously seeing dopamine receptor occupancy in desired range at 50 mg to 100 mg dose
- Confirms hypothesis from Phase 1 study
- Expected range of dosing in upcoming Phase 2 study to be less than 100 mg per day
  - Phase 1a established an MTD of 200 mg per day
  - 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
- **Dosing:** Expecting 2 doses LB-102 versus placebo (4 weeks duration in-patient, double blind, placebo controlled)
- **Primary Endpoint:** Change in PANSS
- Overall development plan will follow well-established criteria for FDA approval of a schizophrenia drug (cf. Rexulti, Vraylar, Latuda)
  - FDA requires two well-controlled studies for approval; LB-102 Phase 2 study designed and powered with this in mind
- CMC activities for drug product ongoing with partner (and LB shareholder) Rivopharm
- Trial initiation planned for Q1 2022



LB-102 CLINICAL DEVELOPMENT PROJECTED TIMELINE

Study	Size	Cost	FY 2020	FY 2021 Q1	FY 2021 Q2	FY 2021 Q3	FY 2021 Q4	FY 2022 1H	FY 2022 2H	FY 2023 1H	FY 2023 2H
Phase 1a SAD/MAD	n = 64	$1.6	*Completed*								
Phase 1b PET	n = 16	$1.5					★				
Phase 2	n = 300	$33.0									★
CARC		$2.5									
CMC		$1.0									

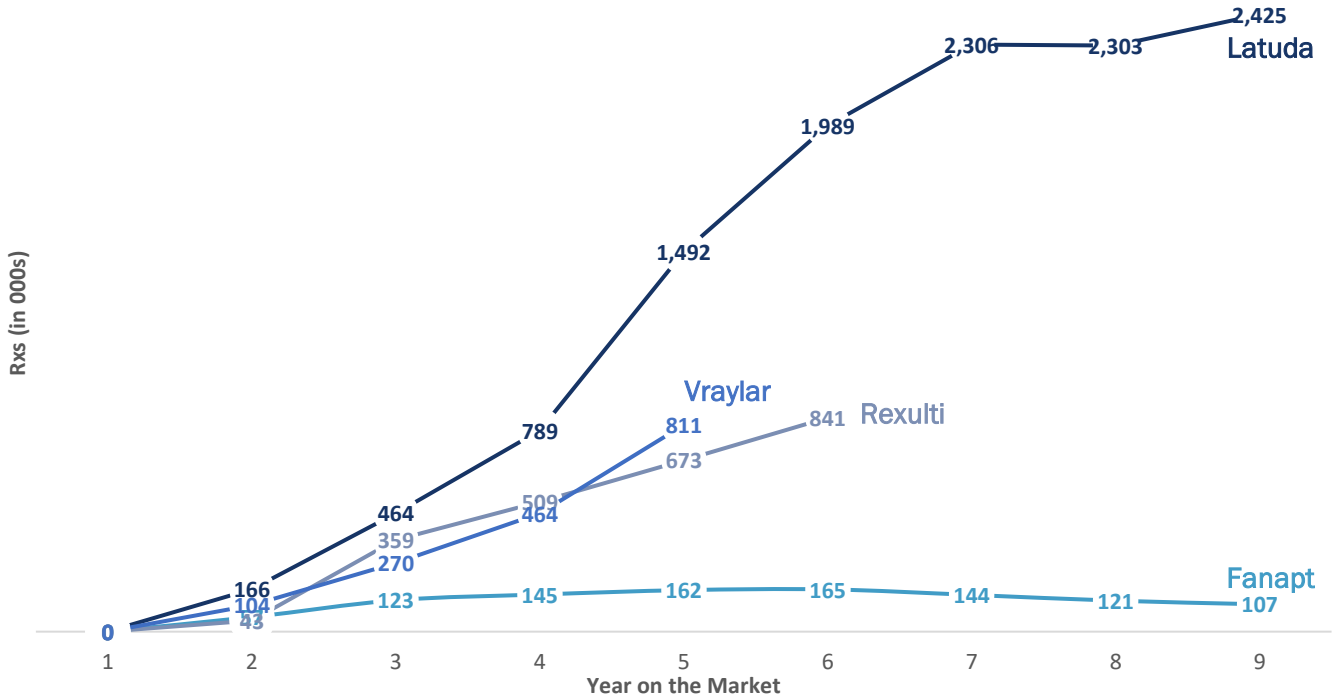
★ - Indicates expected data readout

- 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
- Looking to raise $60mm + in a Series B financing to support clinical activity through Phase 2 data readout anticipated by end of 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)					

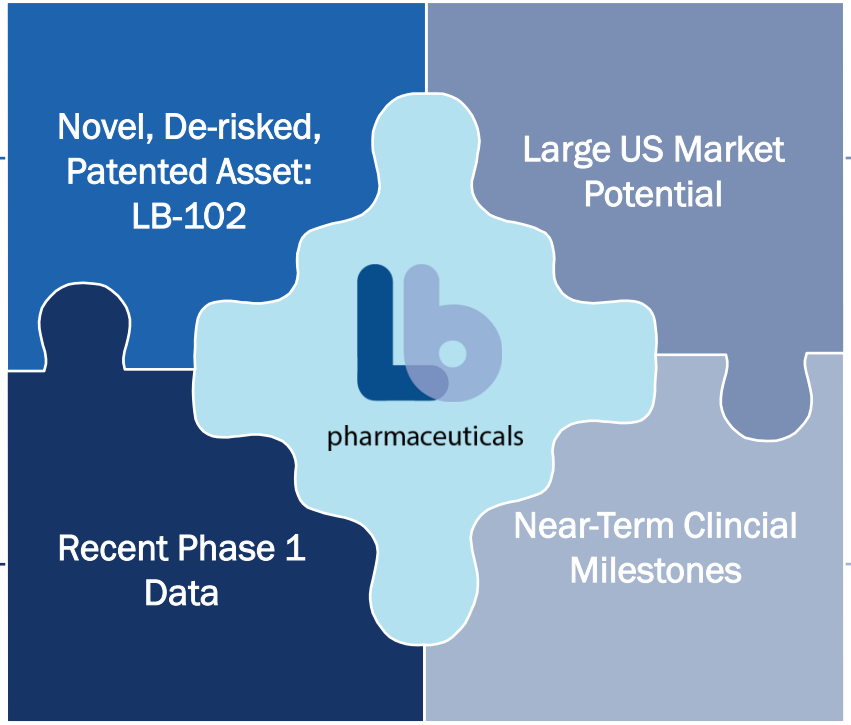
LB PHARMACEUTICALS INVESTMENT HIGHLIGHTS

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 completed in 64 healthy volunteers illustrated that drug is **safe and well-tolerated** and signaled **dopamine target engagement**

Phase 1b dopamine receptor occupancy study completed in September 2021 confirming proof of concept



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 Q1 of 2022, 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

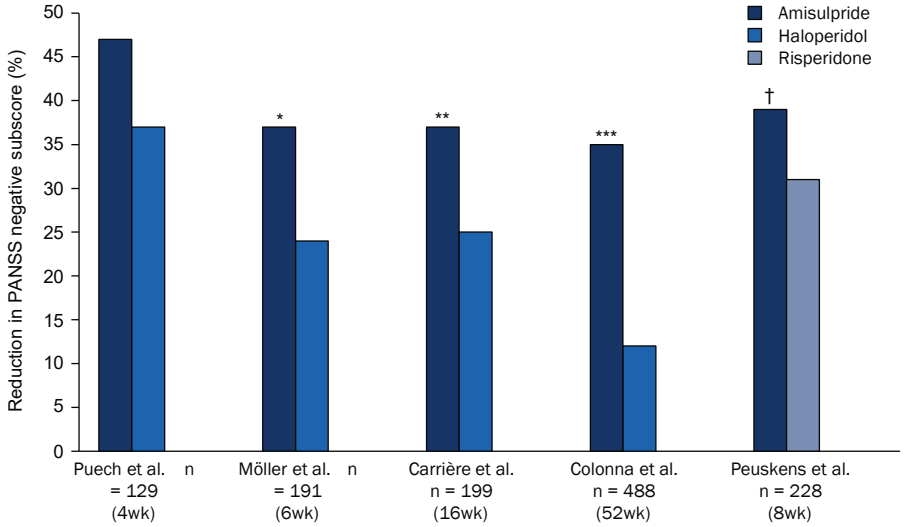


Fig. 1. Reduction in the Positive and Negative Syndrome Scale (PANSS) negative subscore in patients with acute exacerbations of schizophrenia treated with amisulpride in randomized, multicenter, double-blind studies. * $p < 0.05$, ** $p = 0.01$, *** $p < 0.001$ *vs* haloperidol; † $p = 0.09$ *vs* risperidone.

Combined Tolerability

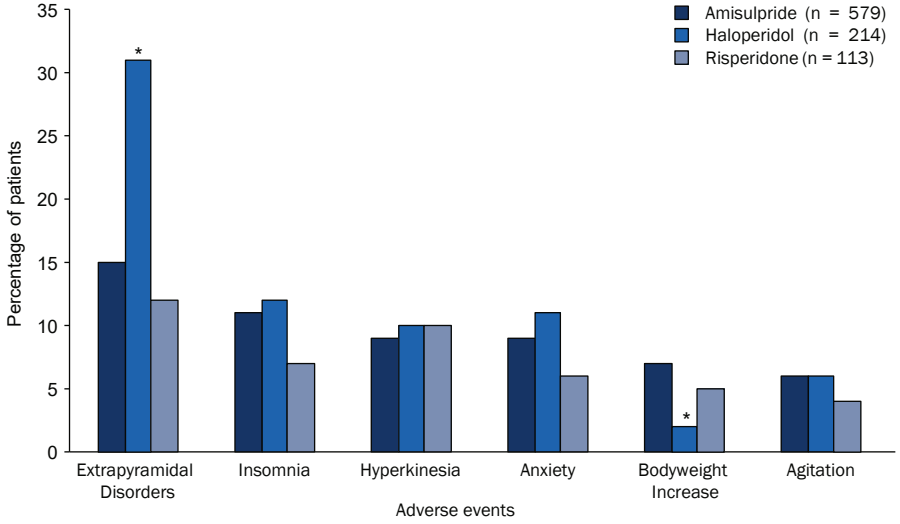


Fig. 2. Combined tolerability data in patients with acute exacerbations of schizophrenia treated with amisulpride, haloperidol and risperidone. Amisulpride 100 to 1200 (mean 670) mg/day, haloperidol 5 to 30 (mean 16) mg/day and risperidone 8 mg/day were administered orally. * $p < 0.01$ *vs* amisulpride.

Combined Tolerability in Patients with Predominantly Negative Symptoms

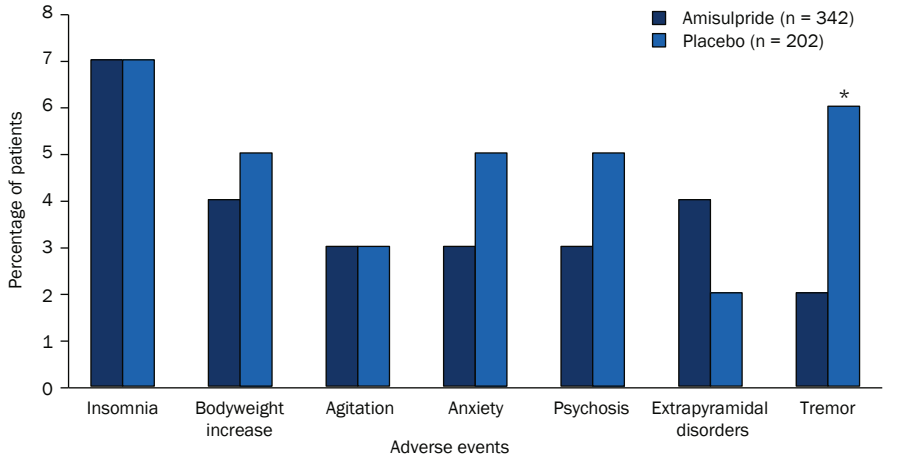


Fig. 3. Combined tolerability data in patients with predominantly negative symptoms of schizophrenia treated with amisulpride compared with placebo. Amisulpride was administered orally at a mean dosage of 118 mg/day (<300 mg/day in 87% of patients). * $p < 0.01$ *vs* amisulpride.

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

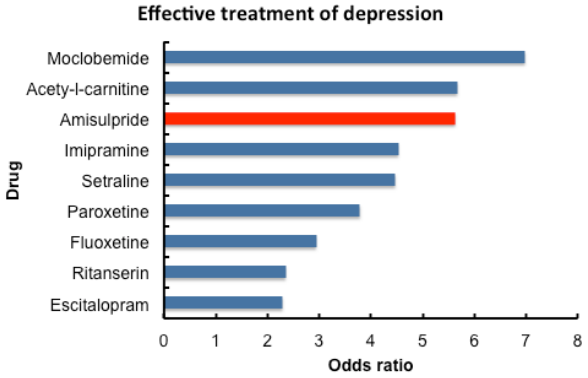
DEVELOPMENT STAGE SCHIZOPHRENIA LANDSCAPE

Candidate (Company)	Status	Commentary
ALKS 3831 *Olanzapine / samidorphan* (Alkermes)	NDA submitted (Nov 2019)	▪ PDUFA Date of 11/15/20 for schizophrenia and bipolar I disorder ▪ Phase 3 data presented in April 2019 demonstrated statistically significant reduction from baseline in PANSS scores at 4 weeks, compared to placebo ▪ Adverse reactions included weight increases (24.8%), somnolence (21.2%), and dry mouth (12.8%)
SEP-36385 (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) ▪ 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) – 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 (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 (Karuna)	Phase 2	▪ Phase 2 data announced in November 2019 demonstrated an 11.6 point improvement over placebo on total PANSS at week five ▪ Rates of adverse reactions (somnolence, weight gain, and EPS/akathisia) were similar to placebo
BIIB104 (Biogen)	Phase 2	▪ Phase 2b data expected in H2 2021
LB-102 (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

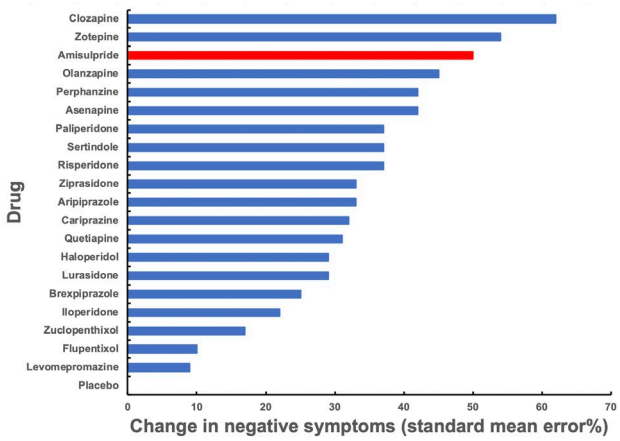
AMISULPRIDE NEGATIVE SYMPTOMS AND DEPRESSION

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

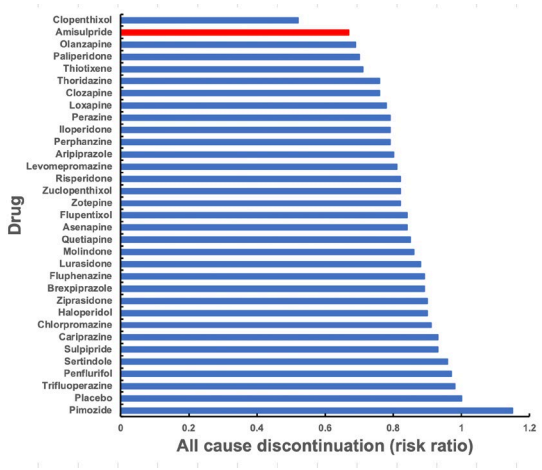


Source: *Lancet*, **2019**, *394*, 393-951

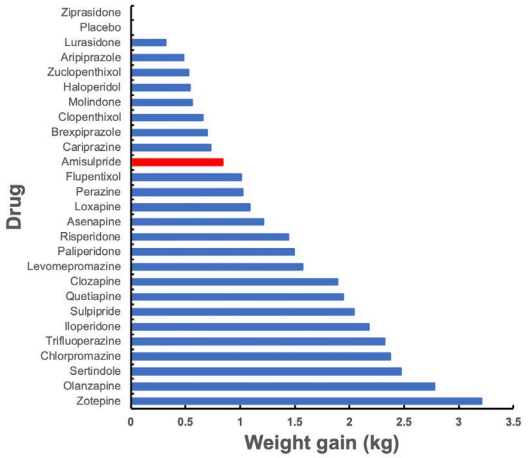
AMISULPRIDE COMPARATIVE SAFETY

Data from 53,500 patient meta-analysis(1)

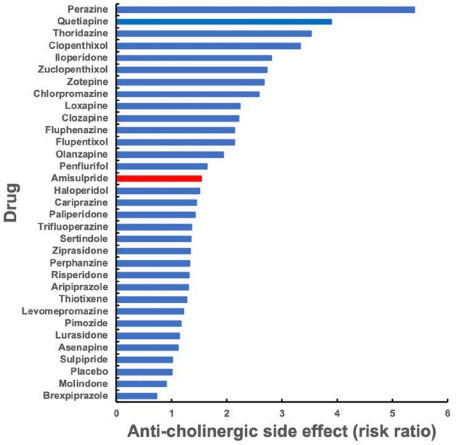
All Cause Discontinuation by Antipsychotic Agent



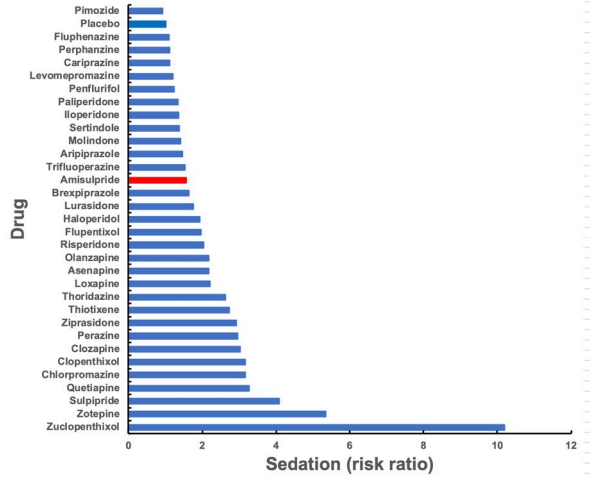
Weight Gain by Antipsychotic Agent



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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