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2.6.1 INTRODUCTION

LB Pharmaceuticals, Inc. is developing LB-102, a benzamide-derived antipsychotic for the treatment of schizophrenia. LB-102 is a new chemical entity. The initial clinical study is a Phase 1 single ascending dose (once daily treatment) and multiple ascending dose (MAD) study assessing safety, tolerability and pharmacokinetics. The MAD phase will involve twice daily oral dosing for 6.5 days (total of 13 doses). The chemical structure of LB-102 is shown below.

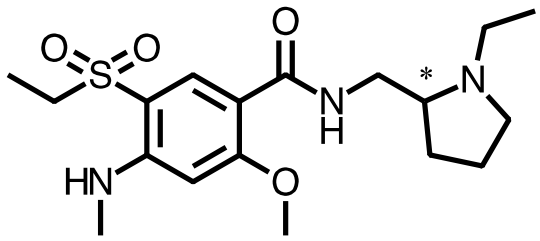

Figure 1: Chemical Structure of LB-102

LB-102 is a novel benzamide; it is a racemic mixture with one asymmetric center, as indicated by an asterisk in Figure 1. The *S*-enantiomer is referred to as LB-103 and the *R*-enantiomer is referred to as LB-104. LB-102 is synthesized by the addition of a methyl group to the aniline nitrogen of amisulpride (LB-101) (Figure 2).

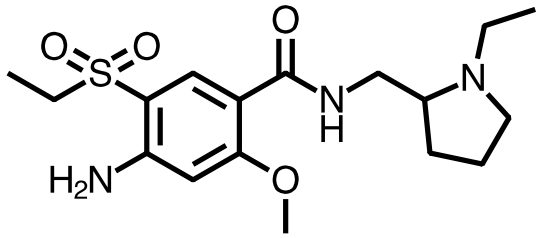

Figure 2: Chemical Structure of Amisulpride

LB-102 was designed to be an improved version of the benzamide antipsychotic, amisulpride, with increased permeability across the blood-brain-barrier. It is anticipated that with the increased penetration the plasma concentrations needed for efficacy will be lower thereby decreasing the magnitude and frequency of adverse events typically observed in patients treated with amisulpride.

Amisulpride was originally developed in France in the 1980s and is currently approved for use in more than 50 non-US countries worldwide for the treatment of schizophrenia and in certain countries for the treatment of dysthymia (IMS, 2015; Mann et al., 1984; Thominet et al., 1983). Amisulpride elicits its activity in part by selectively blocking the human dopaminergic D_2 (K_i = 2.8 nM) and D_3 (K_i = 3.2 nM) receptors with negligible affinity for the D_1, D_4, and D_5 receptor subtypes (K_i > 1,000 nM) and in part by its activity against the 5-HT_7 receptor (15 nM K_i). Because LB-102 is metabolized to amisulpride, clinical information on this drug is relevant to this submission (additional details are discussed in Section 2.6.1.1).

Schizophrenia is a chronic and severe mental disorder that has significant adverse social, cognitive/mental, physical and, quality of life consequences. Core symptoms include hallucinations, delusions, and thought disorders (Lin and Lane, 2019; Pietrini et al., 2019). Schizophrenia is reported to be a high morbidity and high mortality disease affecting 1% of the world's population (Lin and Lane, 2019); Nuno et al., (2019) report a global lifetime prevalence of 0.3 to 0.7%.

The specific etiology of schizophrenia remains unknown even after decades of research (Patel et al., 2014), though obstetric complications (Canon et al., 2002) (including low birth weight, complications in pregnancy and/or delivery), environmental factors (March et al., 2008), genetic factors (Moskvina et al., 2009), motivational salience (Schultz, 2007), and protein insolubility (Nucifora et al., 2019) have all been postulated as potential causes. Overall, genetics offers little insight into the cause of schizophrenia, with at least 108 genetic loci associated with the disorder (Schizophrenia Working Group, 2014). None of these putative causes of schizophrenia adequately explains the occurrence of the disorder.

Hafner (2019) noted a gender difference in age of first sign through age of first hospital admission, with males being affected earlier than females. For males, peak age of onset occurs between approximately 15 and 24 years and declines thereafter whereas for females the peak occurs between approximately 20 and 30 years followed by a decline and a second peak at 45 to 49 years.

The standard pharmacologic mechanism of action for antipsychotic drugs is antagonism of dopamine (D_2) receptors in the limbic system of the brain (Joyce and Meader-Woodruff, 1997; Meltzer and Stahl, 1976; Wulff et al., 2015). These treatment modalities have remained largely unchanged since antipsychotics began use clinically in the 1950s. In addition to the predominance of dopamine antagonists in treating schizophrenia, there are published reports that the 5-HT_7 and other serotonin receptors may also play a role (Galici et al., 2008; Hedlund 2009; Pouzet et al., 2002). Second generation antispychotics (SGAs), also known as atypical antipsychotics, produce efficacy via this dual inhibition of both dopamine D_2 receptors and serotonin receptors (Racz et al., 2018). These SGAs are preferred by patients and clinicians and are used by the majority of individuals.

As noted above, current treatment options for schizophrenia continue to involve antipsychotic medications, such as first generation dopamine D_2 receptor antagonists, but clinical symptoms still occur with these drugs, and are typically reported in up to 60% of patients (Obi-Nagata et al., 2019). These drugs are also associated with significant adverse effects including parkinsonism, akasthisia, dystonia, and prolactinemia. Newer, atypical antipsychotics have a dual mode of action targeting both dopamine D_2 and serotonin $5HT_2$ receptors. However, even these pharmaceuticals have adverse effects that often make them intolerable. In fact, many patients refuse to take the available medications due to the side effects and/or the limited treatment response (Lin and Lane, 2019).

LB-102 represents a potential improved alternative to the current antipsychotic medications, both first and second generation drugs (such as amisulpride), based on its improved lipophilicity which is anticipated to allow easier and increased penetration into the brain, which could require lower doses for effective treatment.

The remaining modules present the nonclinical pharmacology, pharmacokinetics, and toxicology data on LB-102.

2.6.1.1 Amisulpride Clinical Summary

Amisulpride is a racemic benzamide (Figure 3) originally developed in France in the 1980s (Thominet et al., 1983) and is now approved in more than 50 countries worldwide (IMS, 2015). Because amisulpride is a metabolite of LB-102, information on its safety and effectiveness can provide an understanding of potential effects with LB-102.

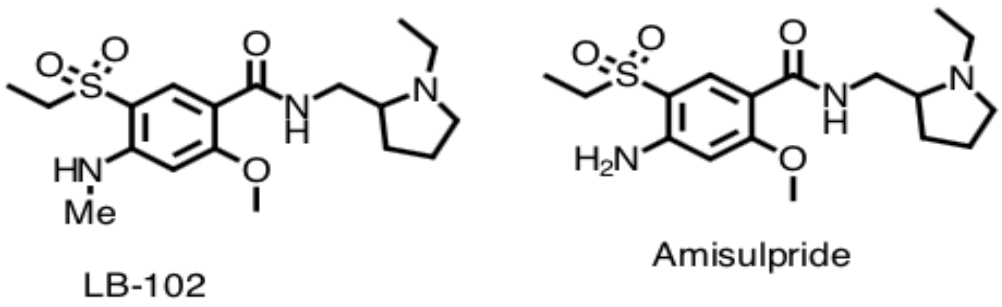

Figure 3: Chemical Structure of LB-102 Compared to Amisulpride

Amisulpride is approved primarily to treat schizophrenia but is also approved for the treatment of dysthymia in Brazil, Italy, Latvia, and Slovakia (IMS, 2015). Trade names include Solian, Amazeo, Amipride, Amival, Soltus, Sultipac, and Sulprix.

This document provides a brief summary of the pharmacology and pharmacokinetics of amisulpride. In addition, a discussion of safety and efficacy data on this drug for the treatment of schizophrenia is presented focusing on the key clinical trials as well as a comparison to other antipsychotics currently in use.

2.6.1.1.1 Pharmacology and Pharmacokinetics

Dopamine antagonists are the clinical standard of care for improving symptoms of schizophrenia (Meltzer and Stahl, 1976; Joyce and Meador-Woodruff, 1997; Wulff et al., 2015). Amisulpride binds selectively to the human dopaminergic D_2 (K_i 2.8 nM) and D_3 (K_i 3.2 nM) receptor subtypes while lacking affinity for D_1, D_4, and D_5 receptor subtypes. Unlike classical and atypical neuroleptics, amisulpride displays low affinity for alpha-adrenergic, histamine receptor subtypes, muscarinic receptors, and sigma sites (Shoemaker et al., 1997). Amisulpride also binds 5-HT_{2B} and HT_7 receptors with low double digit nM K_i (Abbas et al., 2009). This binding to serotonin receptors is thought to result in amisulpride's ability to treat depressive disorders, though it is only approved for such in a few countries, and to account for its cognitive effects in schizophrenia.

In rodents, amisulpride preferentially blocks post-synaptic D_2 receptors in the limbic structures (responsible for affective and cognitive processes) preferentially over those in the striatum (responsible for extrapyramidal effects). In addition, amisulpride does not induce catalepsy and it does not produce D_2 hypersensitivity after repeated treatment. Amisulpride preferentially blocks

pre-synaptic D_2/D_3 dopamine receptors, producing the dopamine release that is responsible for its disinhibitory effects. In animal preclinical models of schizophrenia amisulpride has been demonstrated to mimic current antipsychotics in the amphetamine induced hyperactivity (Perrault et al., 1997) and conditioned avoidance response (Natesan et al., 2008) models.

Amisulpride is minimally metabolized: it has two inactive metabolites, accounting for approximately 4% of the dose. The elimination half-life of amisulpride is ~12 hours after an oral dose, with steady state concentrations being reached between 48 and 72 hours. Amisulpride is frequently dosed once daily but doses above 400 mg/day may be given in divided doses. Plasma protein binding of amisulpride is low (17%), reducing the likelihood of drug interactions due to displacement. Amisulpride has not been shown to have any effect on the major cytochrome P-450 enzymes (Rosenzweig et al., 2002).

2.6.1.1.2 Clinical Studies

The following section describes key published clinical data on amisulpride.

In 2013, Leucht and coworkers published a meta-analysis (Leucht et al., 2013). of 212 clinical studies, including 43,000 subjects, that compared the efficacy and adverse event profiles of 15 widely used antipsychotics. Drugs were rated using a SUCRA ranking (Surface Under the Cumulative Ranking), a measure that compares efficacy of drug to an intervention that is always the best (i.e., amisulpride is 92% as effective as Clozapine and 20% more effective than risperidone). Each of the top 15 drugs (and a placebo), are presented in Figure 4. It is notable that amisulpride scores second highest to clozapine in this measure.

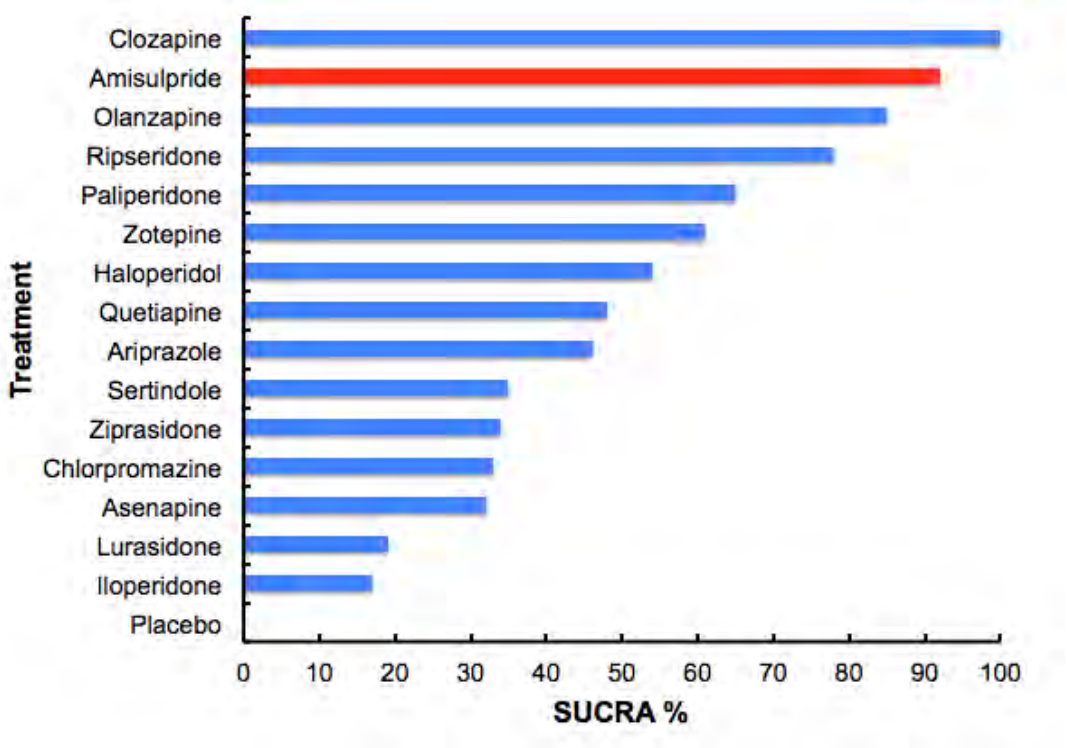

Figure 4: SUCRA Scores Comparing Efficacy of 15 Antipsychotic Drugs and Placebo (Leucht et al., 2013)

Of the 15 drugs evaluated, amisulpride had the lowest rate of discontinuation, compared to placebo, for any reason (Figure 5).

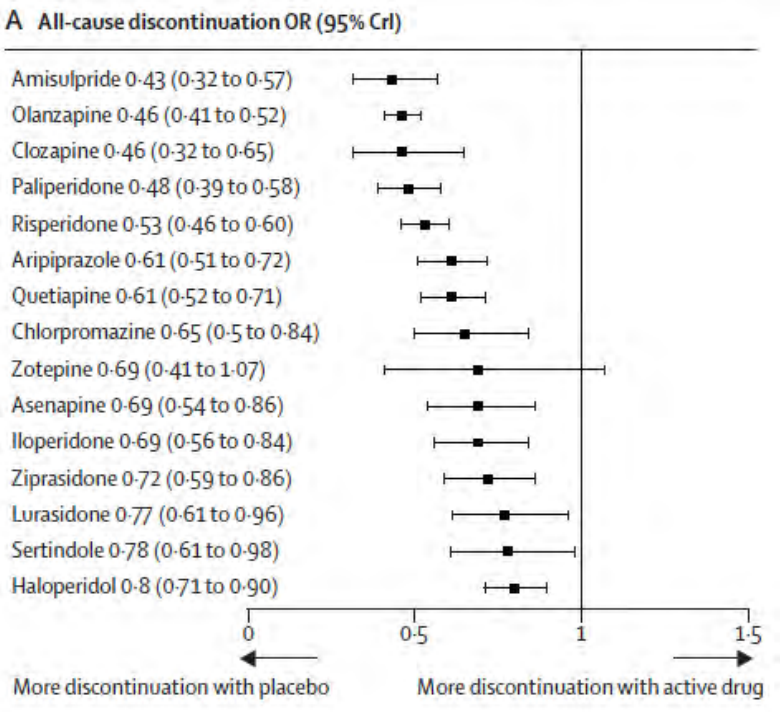

Figure 5: Forest Plot Showing Odds Ratio (OR) of Discontinuation for Any Reason, Compared to Placebo, for 15 Antipsychotics Evaluated (Leucht et al., 2013)

The EUFEST (Kahn et al., 2008) clinical study enrolled 498 first episode schizophrenia patients randomized to receive haloperidol (mean dose 3 mg/d), amisulpride (mean dose 451 mg/d), olanzapine (mean dose 13 mg/d), quetiapine (mean dose 499 mg/d), or ziprasidone (mean dose 107 mg/d) for one year. One year discontinuation rates, the primary endpoint for this study and an important measure of efficacy, are presented in Figure 6. Overall, amisulpride compared favorably to all drugs and only Olanzapine had a numerically lower discontinuation rate.

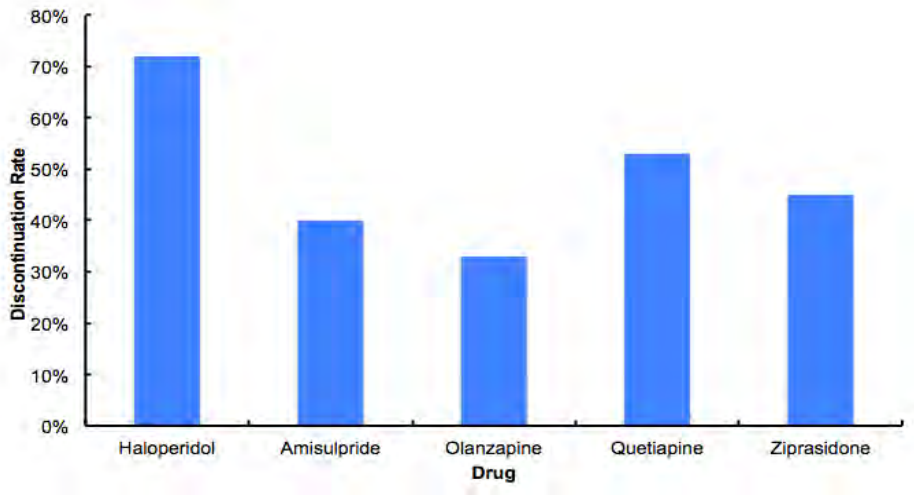

Figure 6: Discontinuation Rates at One Year for Antipsychotics in EUFEST Study (Kahn et al., 2008)

Importantly, as depicted in Figure 7, amisulpride and olanzapine had the lowest rates of discontinuation for lack of efficacy.

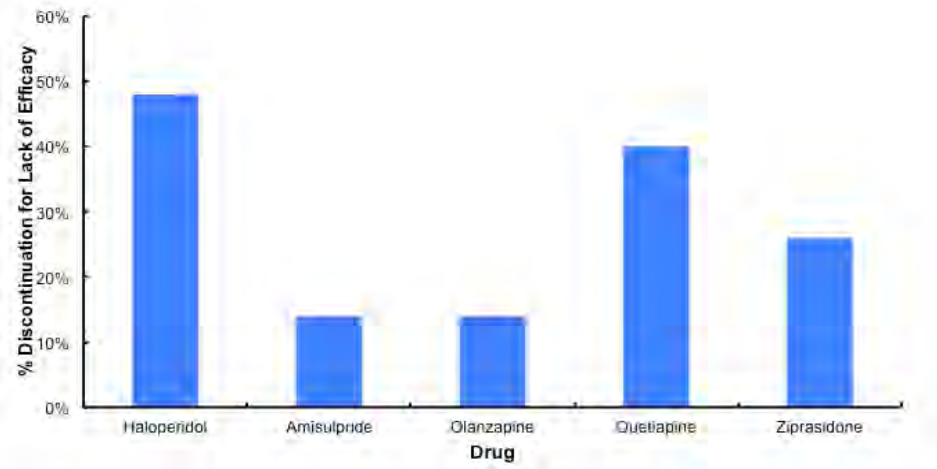

Figure 7: Discontinuation Rates at One Year Due to Lack of Efficacy for Antipsychotics in EUFEST Study (Kahn et al., 2008)

Collectively the data from the EUFEST study show that amisulpride is an effective and safe schizophrenia treatment as measured by discontinuation rates. Table 1 summarizes adverse events noted in the EUFEST study.

Table 1: Summary of Safety Data from EUFEST Study (Kahn et al., 2008)

	Haloperidol	Amisulpride	Olanzapine	Quetiapine	Ziprasidone	p value
Admission to psychiatric hospital						
Admitted to hospital after randomisation/at risk for admission	14/64 (22%)	14/88 (16%)	18/89 (20%)	14/60 (23%)	4/60 (7%)	0·094
Admissions to hospital after randomisation/total patient-years at risk for admission (rate)	16/31·5 (0·51)	18/52·4 (0·34)	29/60·0 (0·48)	18/36·0 (0·50)	6/34·0 (0·18)	0·055
Adverse events						
Any serious adverse event	5/103 (5%)	3/104 (3%)	5/105 (5%)	3/104 (3%)	0/82 (0%)	*
Extrapyramidal symptoms (SHRS)†						
Akathisia	19/73 (26%)	15/94 (16%)	10/97 (10%)	11/85 (13%)	19/68 (28%)	0·007
Dystonia	1/73 (1%)	3/94 (3%)	0/97 (0%)	1/85 (1%)	2/68 (3%)	*
Parkinsonism	25/73 (34%)	16/94 (17%)	6/97 (6%)	9/85 (11%)	11/68 (16%)	<0·0001
Dyskinesia	2/73 (3%)	1/94 (1%)	0/97 (0%)	0/85 (0%)	0/68 (0%)	*
Sexual dysfunction (UKU)†						
Men	15/48 (31%)	14/48 (29%)	15/60 (25%)	16/57 (28%)	19/35 (54%)	0·101
Women	11/24 (46%)	21/45 (47%)	18/38 (47%)	10/28 (36%)	11/33 (33%)	0·774
Weight‡						
Overweight (BMI ≥25 kg/m²)	16/43 (37%)	31/72 (43%)	45/83 (54%)	25/55 (45%)	14/43 (33%)	0·585
Weight gain >7% from baseline	23/43 (53%)	45/72 (63%)	71/83 (86%)	36/55 (65%)	16/43 (37%)	0·053
Weight change from baseline (kg)	7·3 (1·8)	9·7 (1·7)	13·9 (1·7)	10·5 (1·8)	4·8 (1·9)	<0·0001
Prolactin (U/L)§						
Hyperprolactinaemia¶	12/27 (44%)	42/47 (89%)	29/58 (50%)	15/37 (41%)	12/24 (46%)	0·017
Change from baseline						
Mean (SE)	−0·4 (0·3)	0·5 (0·2)	−0·2 (0·1)	−0·2 (0·1)	−1·2 (0·4)	
Median (IQR)	0·0 (−0·3 to 0·1)	0·5 (0·1 to 1·4)	−0·2 (−0·6 to 0·1)	−0·1 (−0·4 to 0·1)	−0·4 (−2·7 to 0·1)	
Per month in study	−0·04 (0·03)	0·12 (0·04)	−0·03 (0·02)	−0·04 (0·02)	−0·16 (0·05)	<0·0001
Fasting glucose (mmol/L)§						
Hyperglycaemia‖	6/33 (18%)	11/53 (21%)	19/63 (30%)	9/41 (22%)	7/32 (22%)	0·794
Change from baseline						
Mean (SE)	0·4 (0·2)	0·5 (0·1)	0·5 (0·1)	0·5 (0·1)	0·2 (0·2)	
Median (IQR)	0·3 (0·0 to 0·9)	0·5 (0·0 to 1·0)	0·5 (0·1 to 1·0)	0·4 (0·0 to 0·9)	0·3 (−0·2 to 0·9)	
Per month in study	0·04 (0·03)	0·07 (0·02)	0·07 (0·02)	0·06 (0·02)	0·04 (0·02)	0·699
Cholesterol (mmol/L)§						
Hypercholesterolemia**	15/33 (45%)	24/53 (45%)	37/66 (56%)	12/43 (28%)	17/32 (53%)	0·276
Change from baseline						
Mean (SE)	0·5 (0·3)	0·7 (0·2)	0·8 (0·1)	0·6 (0·1)	0·4 (0·2)	
Median (IQR)	0·7 (−0·2 to 1·3)	0·5 (0·1 to 1·4)	0·7 (0·2 to 1·3)	0·6 (0·1 to 1·1)	0·3 (−0·2 to 1·0)	
Per month in study	0·04 (0·05)	0·11 (0·02)	0·11 (0·02)	0·07 (0·02)	0·04 (0·02)	0·144
HDL (mmol/L)§						
Low concentration of HDL††	6/32 (19%)	15/53 (28%)	16/65 (25%)	8/43 (19%)	5/32 (16%)	0·894
Change from baseline						
Mean (SE)	−0·1 (0·1)	−0·2 (0·0)	−0·1 (0·0)	−0·1 (0·1)	−0·1 (0·0)	
Median (IQR)	−0·1 (−0·2 to 0·1)	−0·1 (−0·3 to 0·1)	−0·1 (−0·4 to 0·0)	0·0 (−0·2 to 0·1)	−0·1 (−0·2 to 0·1)	
Per month in study	−0·02 (0·01)	−0·02 (0·01)	−0·02 (0·01)	−0·01 (0·01)	−0·01 (0·01)	0·894
LDL (mmol/L)§						
High concentration of LDL‡‡	16/31 (52%)	23/52 (44%)	35/66 (53%)	13/42 (31%)	13/32 (41%)	0·602
Change from baseline						
Mean (SE)	0·5 (0·2)	0·7 (0·2)	0·7 (0·1)	0·7 (0·1)	0·3 (0·1)	
Median (IQR)	0·4 (0·0 to 1·5)	0·5 (−0·1 to 1·2)	0·6 (0·3 to 1·3)	0·7 (0·1 to 1·0)	0·1 (−0·2 to 0·9)	
Per month in study	0·05 (0·04)	0·11 (0·03)	0·09 (0·02)	0·09 (0·02)	0·03 (0·02)	0·303
Fasting insulin (mU/L)§						
Change from baseline						
Mean (SE)	2·0 (1·4)	8·6 (3·1)	2·5 (3·9)	2·1 (1·2)	0·1 (2·0)	
Median (IQR)	3·0 (−2·3 to 6·0)	2·5 (−0·3 to 11·5)	4·0 (0·3 to 11·0)	1·0 (−1·0 to 3·5)	0·0 (−3·0 to 4·0)	
Per month in study	0·31 (0·24)	1·04 (0·36)	0·58 (0·35)	0·11 (0·14)	−0·13 (0·25)	0·080
Triglycerides (mmol/L)§						
Hypertriglyceridaemia§§	13/33 (39%)	19/53 (36%)	26/66 (39%)	11/42 (26%)	10/32 (31%)	0·908
Change from baseline						
Mean (SE)	0·2 (0·1)	0·5 (0·1)	0·3 (0·1)	0·3 (0·1)	0·1 (0·2)	
Median (IQR)	0·1 (−0·2 to 0·8)	0·4 (0·1 to 0·9)	0·3 (−0·1 to 0·7)	0·2 (−0·2 to 0·7)	0·1 (−0·3 to 0·4)	
Per month in study	0·02 (0·02)	0·07 (0·02)	0·04 (0·02)	0·04 (0·02)	0·02 (0·02)	0·439
Electrocardiographical findings						
Prolonged QTc interval¶¶	1/19 (5%)	1/42 (2%)	3/43 (7%)	2/22 (9%)	0/21 (0%)	0·459
Concomitant drug						
Lithium	0/103 (0%)	0/104 (0%)	3/105 (3%)	3/104 (3%)	0/82 (0%)	*
Mood stabilisers/anticonvulsants	26/103 (25%)	19/104 (18%)	25/105 (24%)	26/104 (25%)	17/82 (21%)	0·096
Antidepressants	19/103 (18%)	13/104 (13%)	30/105 (29%)	6/104 (6%)	8/82 (10%)	<0·0001
Hypnotics or sedatives	17/103 (17%)	17/104 (16%)	24/105 (23%)	24/104 (23%)	15/82 (18%)	0·366
Anxiolytic drugs	53/103 (51%)	56/104 (54%)	58/105 (55%)	50/104 (48%)	36/82 (44%)	0·170
Anticholinergic drugs	46/103 (45%)	35/104 (34%)	23/105 (22%)	20/104 (19%)	18/82 (22%)	<0·0001

Data are n/N (%) or mean (SE), unless otherwise indicated. SHRS=St Hans rating scale. UKU=udvalg for kliniske undersøgelser. Denominators fluctuate because of incomplete data. p values are based on tests that compare all treatment groups (four degrees of freedom), accounting for time at risk and adjusting for country. *p values could not be estimated because of low numbers of events. †Percentages are based on the number of patients with at least one follow-up assessment (SHRS and UKU: 1, 3, 6, 9, 12 months)—patients scored positive on at least one evaluation. The analyses on extrapyramidal symptoms were also adjusted for the use of anticholinergic drugs before extrapyramidal symptoms. UKU: cases scored moderate/severe on severity of sexual dysfunction. ‡Percentages and change scores are based on the patients with at least one follow-up assessment (3, 6, 9, 12 months). The maximum weight measured during follow-up was analysed for overweight and weight gain; mean weight change scores were estimated at 12 months. §Percentages are based on the number of patients with at least one assessment after baseline (6 and 12 months). The highest lab value measured during follow-up and the corresponding blood collection date were selected for the analyses. For HDL we selected the lowest lab value. ¶Hyperprolactinaemia: men >0·38 U/L; women >0·53 U/L (men >18 ng/mL; women >25 ng/mL; to convert values in ng/mL to U/L we arbitrarily used a conversion factor of 0·0212). ‖Hyperglycaemia: fasting glucose concentration ≥5·55 mmol/L. **Hypercholesterolaemia: cholesterol concentration ≥5·17 mmol/L. ††Low concentration of HDL <1·03 mmol/L. ‡‡High concentration of LDL ≥3·36 mmol/L. §§Hypertriglyceridaemia: triglyceride concentration ≥1·69 mmol/L. ¶¶QTc prolongation at 12 months: men >450 mseconds, women >470 mseconds.

The Schizophrenia Outpatients Health Outcomes (SOHO) (Novick et al., 2009) study was an open label trial that included recovery and remission data on 6,642 patients with a maximum follow up period of 36 months. Patients entered the study if they had been recently switched to Olanzapine or another antipsychotic. The primary aim of this study was to compare the efficacy of Olanzapine to other available antipsychotics and, accordingly, the Olanzapine arm was intentionally larger than the other treatment arms. The primary medications used by clinicians other than Olanzapine (n=2,501) included Risperidone (n=966), amisulpride (n=208, mean dose at 12 months = 388 mg/d), Quetiapine (n=292), and Clozapine (n=272). Amisulpride was numerically better on a number of efficacy measures compared to the other antipsychotics as depicted in Figure 8.

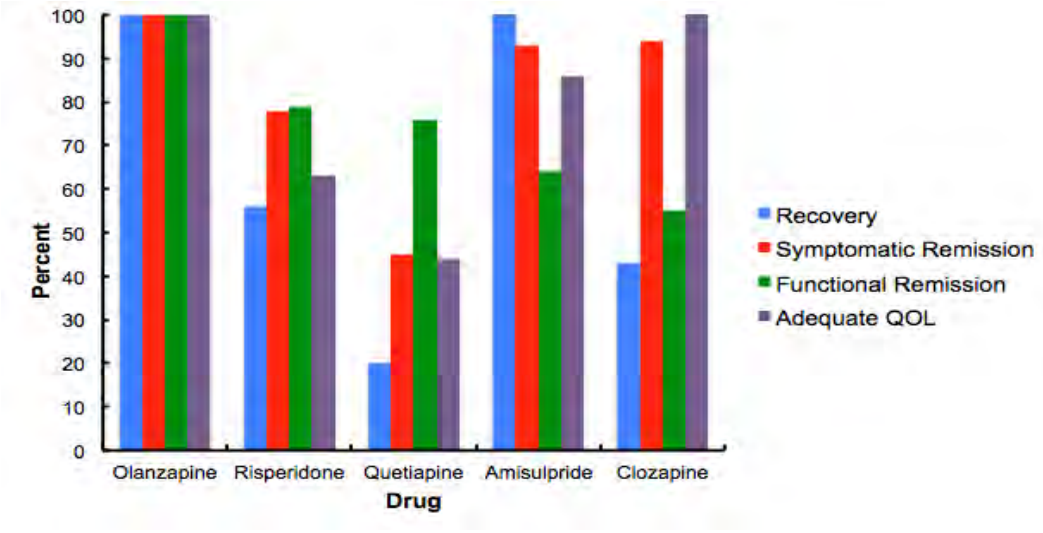

Figure 8: Percent of Patients in SOHO Study Achieving Various Endpoints in SOHO Study (Novick et al., 2009)

Other more traditional drug trials have compared amisulpride head to head against atypical antipsychotics such as Risperidone or Olanzapine. Sechter and coworkers (Sechter et al., 2002) conducted a 6 month, randomized, double blind trial comparing 4 to 10 mg/d Risperidone (n=158) to 400 to 1000 mg/d amisulpride (n=152) on measures of efficacy and safety. Amisulpride was shown to be non-inferior to Risperidone on the change in Positive and Negative Syndrome Scale (PANSS) as shown in Figure 9. Both treatments were well tolerated and had low incidences of extrapyramidal symptoms. Amisulpride was associated with less weight gain and endocrine/sexual symptoms.

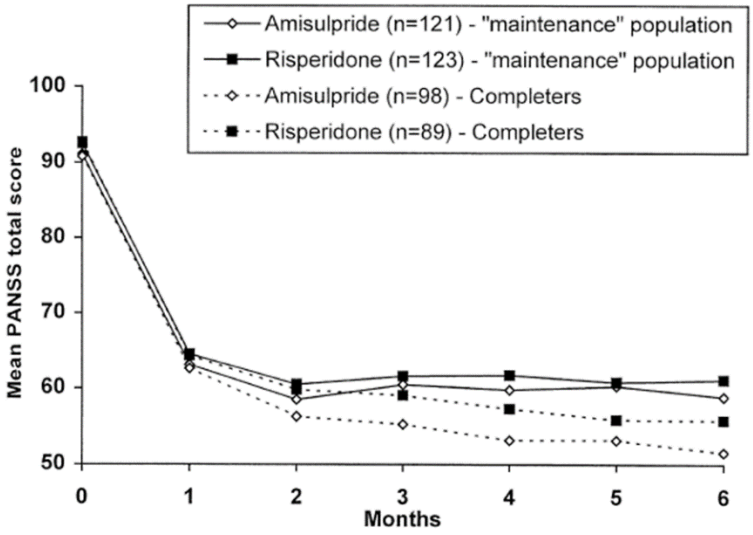

Figure 9: PANSS as a function of Time (Sechter et al., 2002)

There were no significant differences between amisulpride and Risperidone on safety measures in this study.

In 2002 Martin and coworkers (Martin et al., 2002) published results of a randomized, double blind, head to head study comparing 200 to 800 mg/d amisulpride (n=189) to 5 to 20 mg/d olanzapine (n=188) over 8 months. The primary outcome of this study was change in Brief Psychiatric Rating Scale (BPRS) with other outcomes reported including change in PANSS, body weight, and adverse events. There were no differences between amisulpride and olanzapine in the change in BPRS score at any time point (Figure 10).

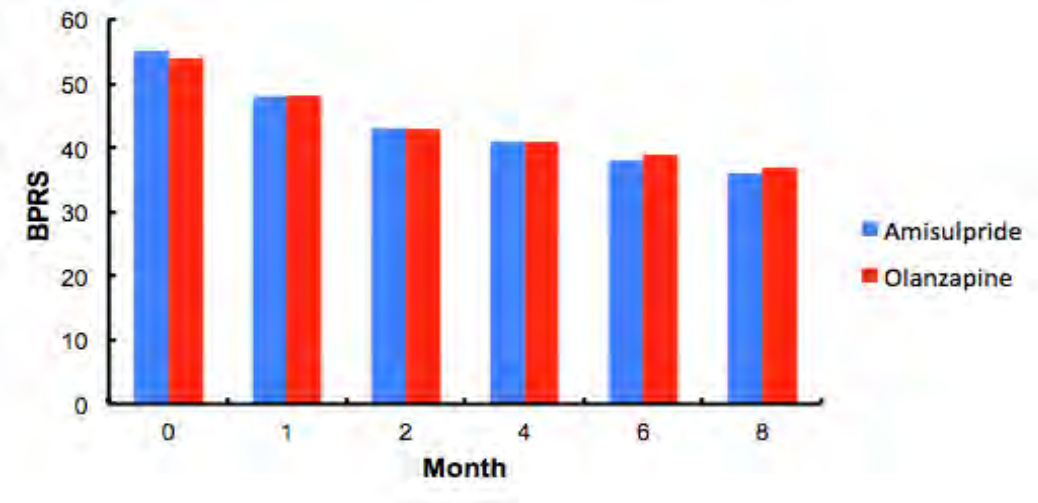

Figure 10: Comparison of BPRS After Treatment with Amisulpride or Olanzapine (Martin et al., 2002)

PANSS scores decreased by a mean of 39% in the amisulpride arm and 38% in the Olanzapine arm. There were 8 withdrawals due to AEs in amisulpride treated patients compared to 7 in Olanzapine treated patients. There was no significant difference in extrapyramidal symptoms in this study. Olanzapine produced significantly greater weight gain than was observed in the amisulpride arm (Figure 11).

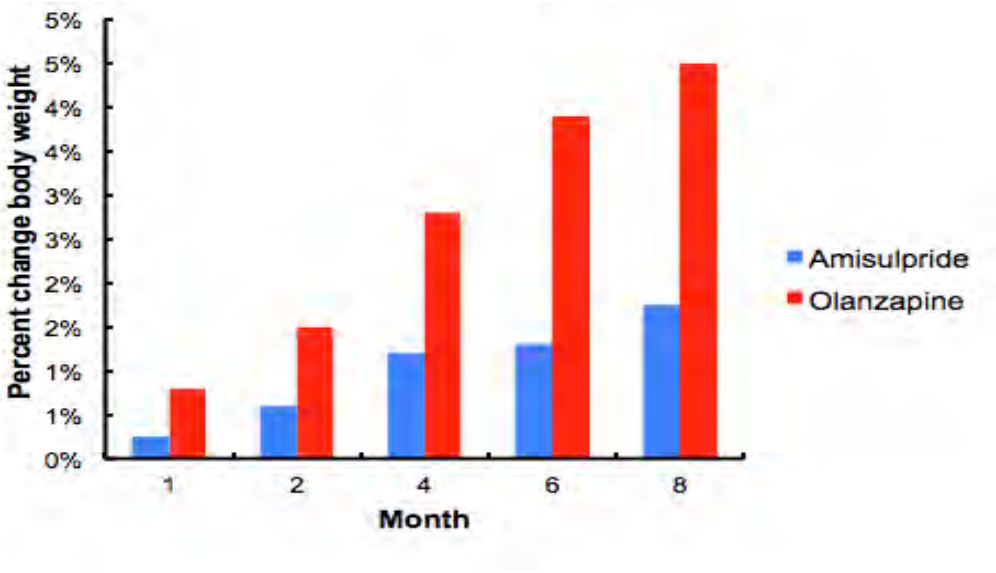

Figure 11: Percent Weight Gain by Month for Amisulpride and Olanzapine (Martin et al., 2002).

Amisulpride has been demonstrated to have a significant impact on the negative symptoms of schizophrenia which include impaired social functioning, lack of spontaneous speech, loss of interest in pleasurable activities, and cognitive deficits.

Danion and coworkers, (Danion et al., 1999), conducted a 12 week study of low doses of amisulpride 50 mg/day (n = 84), 100 mg/day (n = 75) vs. placebo (n = 83) following a 4 week washout period in patients who were diagnosed with a schizophrenia subtype that presents primarily with negative symptoms. The Scale for the Assessment of Negative Symptoms (SANS) was used as the primary rating instrument in this study. As shown, patients treated with either dose showed substantial improvements in negative symptoms compared to placebo. In addition, amisulpride was statistically superior to placebo in all secondary measures, including: SAPS total score, BPRS, and Montgomery-Asperg Depression Rating Scale (MADRS) total score.

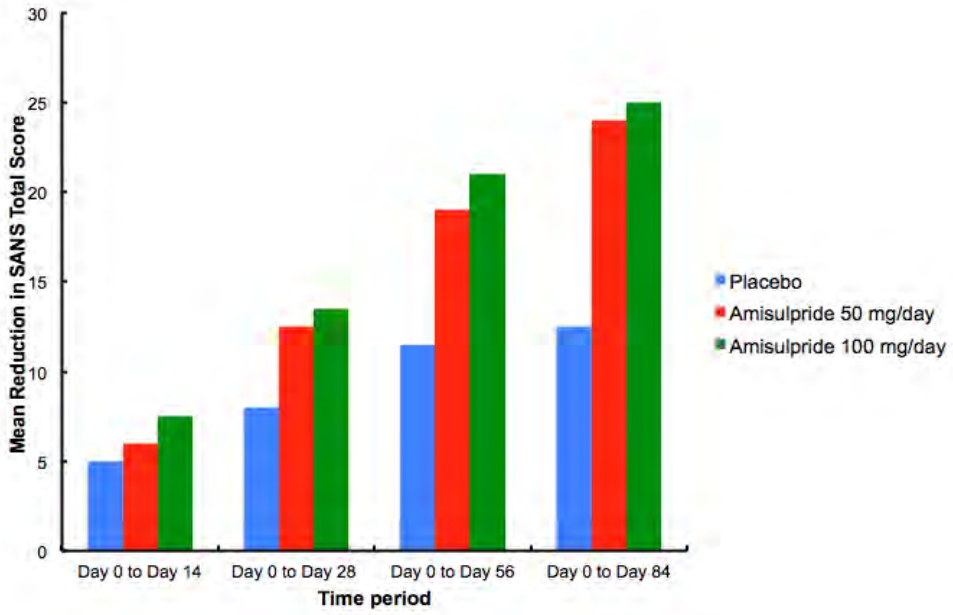

Figure 12: Changes in SANS Scores from Baseline after Treatment with Amisulpride Compared to Placebo (Danion et al., 1999)

In a study published in 1999 (Peuskens et al., 1999), 228 patients with acute exacerbated schizophrenia were randomized to receive either 800 mg/d amisulpride or 8 mg/d risperidone. After 2 months patients in the amisulpride group had their BPRS scores improve by 38 points, on par with the 40 point improvement in the Risperidone group. Both amisulpride demonstrated good safety profiles in this study.

2.6.1.1.3 Conclusion

In summary, amisulpride has been demonstrated to be a safe, effective (on par with Olanzapine and Risperidone as well as other schizophrenia drugs that have been used by millions of patients over decades) treatment for schizophrenia. In all assays, in vitro and in vivo, carried out to date indistinguishable to superior to amisulpride suggesting that it has less clinical risk than an entirely novel new chemical entity.

2.6.1.2 References

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