Target Health LLC

261 Madison Avenue, 24th Floor, New York, NY 10016

Ekta Sheth, MS, BPharm
Sr. Manager, Regulatory Affairs

February 1, 2021

Tiffany Farchione, M.D., Director (Acting)
U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Office of Neuroscience
Division of Psychiatry
5901-B Ammendale Road
Beltsville, MD 20705-12666

RE: IND 137581, LB-102, For the Treatment of Schizophrenia
Serial 0017
IND Annual Report - Reporting Period: December 5, 2019 – December 4, 2020

Dear Dr. Farchione:

Reference is made to IND 137581, LB-102, for the treatment of Schizophrenia, submitted October 19, 2019.

On behalf of LB Pharmaceuticals, Inc., and pursuant to 21 CFR 312.33, we are hereby submitting the IND Annual Report for the reporting period December 5, 2019 – December 4, 2020.

1.13.1 Summary of Nonclinical Studies 2019-2020
1.13.3 Summary of Safety Information 2019-2020
1.13.5 Summary of Manufacturing Changes 2019-2020
1.13.6 Summary of Microbiological Changes 2019-2020
1.13.8 Individual Study Information 2019-2020
1.13.9 General Investigational Plan 2019-2020
1.13.10 Significant Foreign Marketing Developments 2019-2020
1.14.4.1 Investigational Brochure 2019-2020

The submission is compliant with FDA's Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications. The electronic submission is approximately 3 MB. All files were checked and verified to be free of viruses before being sent through the ESG, using *Microsoft System Security Endpoint Protection*.

Please contact me at 646-218-2077 if you have any questions or comments concerning this submission.

Sincerely,

{*See appended electronic signature page*}

Ekta Sheth, MS, BPharm
Sr. Manager, Regulatory Affairs

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Approver: Sheth, Ekta
Senior Manager, Regulatory Affairs
Target Health
Date: 01 Feb 2021
Time: 11:47:47 AM

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

INVESTIGATIONAL NEW DRUG APPLICATION (IND)

(Title 21, Code of Federal Regulations (CFR) Part 312)

Form Approved: OMB No. 0910-0014
Expiration Date: March 31, 2022
See PRA Statement on page 3.

NOTE: No drug/biologic may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40)

1. Name of Sponsor
LB Pharmaceuticals, Inc.

2. Date of Submission *(mm/dd/yyyy)*
02/01/2021

3. Sponsor Address

Address 1 *(Street address, P.O. box, company name c/o)*
575 Madison Avenue

Address 2 *(Apartment, suite, unit, building, floor, etc.)*
10th Floor

City: New York
State/Province/Region: NY
Country: U.S.A.
ZIP or Postal Code: 10022

4. Telephone Number *(Include country code if applicable and area code)*
(646) 588-8175

6A. IND Number *(If previously assigned)*
137581

6B. Select One: ☑ Commercial ☐ Research

5. Name of Drug *(Include all available names: Trade, Generic, Chemical, or Code)*
LB-102

Continuation Page for #5

7A. (Proposed) Indication for Use
For the Treatment of Schizophrenia

Is this indication for a rare disease (prevalence <200,000 in U.S.)? ☐ Yes ☑ No

Does this product have an FDA Orphan Designation for this indication? ☐ Yes ☑ No

If yes, provide the Orphan Designation number for this indication:

Continuation Page for #7

7B. SNOMED CT Indication Disease Term *(Use continuation page for each additional indication and respective coded disease term)*
58214004 |Schizophrenia (disorder)|

8. Phase of Clinical Investigation to be conducted ☑ Phase 1 ☐ Phase 2 ☐ Phase 3 ☐ Other *(Specify)*: _____

9. List numbers of all Investigational New Drug Applications (21 CFR Part 312), New Drug Applications (21 CFR Part 314) , Drug Master Files (21 CFR Part 314.420) , and Biologics License Applications (21 CFR Part 601) referred to in this application.
N/A

10. IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 0000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 0001." Subsequent submissions should be numbered consecutively in the order in which they are submitted..

Serial Number: 0017

11. This submission contains the following *(Select all that apply)*

☐ Initial Investigational New Drug Application (IND)
☐ Request For Reactivation Or Reinstatement
☐ Development Safety Update Report (DSUR)
☐ Response to Clinical Hold
☑ Annual Report
☐ Other *(Specify)*: _____
☐ Response To FDA Request For Information
☐ General Correspondence

Protocol Amendment
☐ New Protocol
☐ Change in Protocol
☐ New Investigator
☐ PMR/PMC Protocol
☐ Human Factors Protocol

Information Amendment
☐ Chemistry/Microbiology
☐ Pharmacology/Toxicology
☐ Clinical/Safety
☐ Statistics
☐ Clinical Pharmacology

Request for
☐ Meeting
☐ Proprietary Name Review
☐ Special Protocol Assessment
☐ Formal Dispute Resolution

IND Safety Report
☐ Initial Written Report
☐ Follow-up to a Written Report

12. For Originals, is the product a combination product (21 CFR 3.2(e))? ☐ Yes ☐ No

Combination Product Type *(See instructions)*

Request for Designation (RFD) Number

13. Select the following only if applicable. *(Justification statement must be submitted with application for any items selected below. Refer to the cited CFR section for further information.)*

Expanded Access Use, 21 CFR 312.300

☐ Emergency Research Exception From Informed Consent Requirements, 21 CFR 312.23 (f)
☐ Charge Request, 21 CFR 312.8
☐ Individual Patient, Non-Emergency 21 CFR 312.310
☐ Individual Patient, Emergency 21 CFR 312.310(d)
☐ Intermediate Size Patient Population, 21 CFR 312.315
☐ Treatment IND or Protocol, 21 CFR 312.320

For FDA Use Only

CBER/DCC Receipt Stamp

DDR Receipt Stamp

Division Assignment

IND Number Assigned

PSC Publishing Services (301) 443-6740 EF

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14. Contents of Application – This application contains the following items *(Select all that apply)*

- [x] 1. Form FDA 1571 *(21 CFR 312.23(a)(1))*
- [ ] *2.* Table of Contents *(21 CFR 312.23(a)(2))*
- [ ] *3.* Introductory statement *(21 CFR 312.23(a)(3))*
- [ ] *4.* General Investigational plan *(21 CFR 312.23(a)(3))*
- [ ] *5.* Investigator's brochure *(21 CFR 312.23(a)(5))*
- [ ] 6. Protocol *(21 CFR 312.23(a)(6))*
  - [ ] *a.* Study protocol *(21 CFR 312.23(a)(6))*
  - [ ] b. Investigator data *(21 CFR 312.23(a)(6)(iii)(b))* or completed Form FDA 1572
  - [ ] c. Facilities data *(21 CFR 312.23(a)(6)(iii)(b))* or completed Form FDA 1572
- *6.* Protocol *(Continued)*
  - [ ] d. Institutional Review Board data (21 CFR 312.23(a)(6)(iii)(b)) or completed Form FDA 1572
- [ ] 7. Chemistry, manufacturing, and control data *(21 CFR 312.23(a)(7))*
  - [ ] Environmental assessment or claim for exclusion *(21 CFR 312.23(a)(7)(iv)(e))*
- [ ] 8. Pharmacology and toxicology data (21 CFR 312.23(a)(8))
- [ ] *9.* Previous human experience *(21 CFR 312.23(a)(9))*
- [ ] *10.* Additional information *(21 CFR 312.23(a)(10))*
- [ ] *11.* Biosimilar User Fee Cover Sheet *(Form FDA 3792)*
- [ ] *12.* Clinical Trials Certification of Compliance *(Form FDA 3674)*

15. Is any part of the clinical study to be conducted by a contract research organization? [x] Yes [ ] No

If Yes, will any sponsor obligations be transferred to the contract research organization? [x] Yes [ ] No

If Yes, provide a statement containing the name and address of the contract research organization, identification of the clinical study, and a listing of the obligations transferred *(use continuation page)*.

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16. Name and Title of the person responsible for monitoring the conduct and progress of the clinical investigations

Anna Eramo, MD, Psychiatrist, Chief Medical Officer

17. Name and Title of the person responsible for review and evaluation of information relevant to the safety of the drug

Anna Eramo, MD, Psychiatrist, Chief Medical Officer

I agree not to begin clinical investigations until 30 days after FDA's receipt of the IND unless I receive earlier notification by FDA that the studies may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold or financial hold. I agree that an Institutional Review Board (IRB) that complies with the requirements set forth in 21 CFR Part 56 will be responsible for initial and continuing review and approval of each of the studies in the proposed clinical investigation. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

18. Name of Sponsor or Sponsor's Authorized Representative

Ekta Sheth, BPharm, MS, Sr. Manager, Regulatory Affairs, Target Health LLC

19. Telephone Number *(Include country code if applicable and area code)*	20. Facsimile (FAX) Number *(Include country code if applicable and area code)*
(212) 681-2100	(212) 681-2105

21. Address

Address 1 *(Street address, P.O. box, company name c/o)*	261 Madison Avenue
Address 2 *(Apartment, suite, unit, building, floor, etc.)*	24th Floor
City	New York
State/Province/Region	New York
Country	U.S.A
ZIP or Postal Code	10016

22. Email Address

esheth@targethealth.com

23. Date of Sponsor's Signature *(mm/dd/yyyy)*

02/01/2021

24. Name of Countersigner

25. Address of Countersigner

Address 1 *(Street address, P.O. box, company name c/o)*	
Address 2 *(Apartment, suite, unit, building, floor, etc.)*	
City	
State/Province/Region	
Country	United States of America
ZIP or Postal Code	

26. Email Address

WARNING : A willfully false statement is a criminal offense (U.S.C. Title 18, Sec. 1001).

27. Signature of Sponsor or Sponsor's Authorized Representative

Ekta Sheth Digitally signed by Ekta Sheth Date: 2021.02.01 11:33:42 -05'00'

Sign

28. Signature of Countersigner

Sign

The information below applies only to requirements of the Paperwork Reduction Act of 1995.

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Department of Health and Human Services
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Office of Operations
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

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FIRST CONTINUATION PAGE FOR ITEM 15 – Information on Contract Research Organization

For each (as applicable below) contract service organization involved in the clinical study, please provide a statement containing the name and address of the contract research organization, identification of the clinical study, and a listing of the obligations transferred.

Contract Service Organization

Target Health LLC
261 Madison Ave, 24th Fl, New York, NY 10016

Target Health will Select qualified monitors (21 CFR Sec. 312.53), Ensure proper monitoring of the investigation (21 CFR Sec. 312.50 and 312.56), Complete and accurate investigator financial records related to the investigation (21 CFR Sec. 312.57), Ensure that the investigation is conducted in accordance with the general investigational plan and protocols contained in the IND (21 CFR Sec. 312.50), Compliance with FDA inspections (21 CFR Sec. 312.68).

Contract Service Organization

Contract Service Organization

Contract Service Organization

Contract Service Organization

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1.13.10 Significant Foreign Marketing Developments

There are no significant foreign marketing developments currently planned for LB 102.

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1.13.9 General Investigational Plan

1.13.9.1 Rationale for the Study

The investigational product LB-102 (structural formula: C18H29N3SO4; IUPAC name: 4-methylamino-*N*-((1-ethyl-2-pyrrolidinyl)methyl)-5-(ethylsulfonyl))-2-methoxybenzamide) proposed by LB Pharmaceuticals, Inc. is indicated for the treatment of Schizophrenia, a disorder affecting 1.1% of the US population (NIMH, 2017). Schizophrenia manifests in delusional behavior, dysfunctional thinking, agitated body movement, social withdrawal, and depression. The course of schizophrenia is highly variable with periods of psychosis and stabilization of varying duration and intensity. Sustained remission of both positive and negative symptoms occurs in a minority of patients even with prolonged antipsychotic therapy. In fact, a study found that a majority of schizophrenia patients stopped their treatment at an early stage due to poor response or psychiatric symptom worsening (Liu-Seifert et al., 2005). Schizophrenia patients suffer a profoundly reduced quality of life and are 8 times more likely to commit suicide than the general population (Harris and Barraclough, 1997). Half of suicides among patients with schizophrenia occur within the first two years of disease onset (Tandon and Jibson, 2003), pointing to the urgency for behavioral and pharmaceutical intervention. However, compliance with long-term medication is a significant problem due to dissatisfaction with antipsychotic side effects, or self-discontinuation of medication as a result of feeling better and no longer perceiving the need for continuous medication as well as impaired insight into illness has been reported as a prevalent feature of schizophrenia. All of these issues contribute to relapse among schizophrenia patients.

Amisulpride, is approved in more than 50 countries worldwide for the treatment of schizophrenia and, in certain countries, for the treatment of dysthymia (IMS, 2015). Amisulpride elicits its activity in part by selectively blocking the human dopaminergic D_2 (Ki 2.8 nM) and D_3 (Ki 3.2 nM) receptors with negligible affinity for the D_1, D_4, and D_5 receptor subtypes (Ki > 1,000 nM), and in part by its activity against the 5-HT_7 receptor (11.5 nM Ki). While amisulpride is a clinically effective drug, it demonstrates poor distribution to the brain. A 2014 study revealed that passive diffusion of amisulpride across a PAMPA membrane, a proxy for the blood-brain barrier, was the lowest of 30 psychiatric drugs tested (Dos Santos Pereira et al., 2014).

LB-102 was created by adding a methyl group to the aniline nitrogen of amisulpride. This change was meant to improve amisulpride by increasing permeability across the blood-brain barrier, potentially decreasing the plasma concentrations needed to achieve efficacy. This would decrease the magnitude and frequency of adverse events typically observed in patients treated with amisulpride. LB-102 was demonstrated to be a selective blocker of the human dopaminergic D_2 and D_3 receptors (the target of all approved schizophrenia drugs to date) and, similar to amisulpride, is also a 5-HT_7 antagonist (which may be important in cognitive aspects of schizophrenia) *in vitro*. In animal models of schizophrenia, LB-102 produced similar or greater responses than amisulpride.

1.13.9.2 Indication(s) to be Studied

LB-102 is indicated for the treatment of Schizophrenia.

1.13.9.3 General Approach in Evaluating the Drug

A Phase 1 clinical study of LB-102 was recently completed. This was a randomized, double-blind, placebo-controlled study designed to evaluate the safety, tolerability, and PK of LB-102 in healthy subjects. The study consisted of two parts: Part A – SAD (single ascending dose) and Part B – MAD (multiple ascending dose): there were 5 cohorts in Part A and 3 cohorts in Part B of this study.

In Part A, eligible subjects were randomized on Day 1 (pre-dose) to placebo (n=2) or LB-102 (n=6) treatment for a total of 40 subjects. Four (4) visits occurred as follows: Screening (Visit 1, Days -28 to -1), Check-in (Visit 2, Day 0), Treatment Evaluation (Visit 3, Days 1-3), and Follow-up (Visit 4, Day 8 and Visit 5, Day 15 [for Cohort 5, Part A only]). Dosage of LB-102 began at 50 mg/day and subsequent groups were administered 10, 100, 200, and 150 mg/day, respectively. In Cohort 1 (Part A), dosing of the first 2 subjects (1 active and 1 placebo) commenced at least 24 hours prior to the remaining 6 subjects. Dosing of the remaining subjects in the cohort proceeded if no safety issues were identified for the first 2 subjects. On Day 1, following a 12-hour overnight fast, subjects received 1 oral dose of placebo or LB-102 at 8 AM (±1 hour). For each cohort, blood samples for PK were collected on Day 1 at pre-dose and at 15, 30, and 45 minutes (±5 min), and 1, 1.5, 2, 3, 4, 6, 8, 12, 16, 24, 32, and 48 hours (±15 min) post-dose, and Day 8 and Day 15. Vital signs were recorded for each subject at Screening, Check-in, Day 1 at pre-dose and at 0.5, 1, 1.5, 2, 4, 6, 8, 12, 24, and 48 hours (±30 min) post-dose, and at the Follow-up visit (Day 8). 12-lead ECG was done on at Screening, Check-in, Day 1 at pre-dose and 1, 2, 3, 4, 5, 6, 8 and 24 hours (±30 min) post-dose. ECG was measured once at each time point for Cohorts 1-4 and in triplicate for Cohort 5. Clinical labs (hematology, chemistry, urinalysis) were assessed at Screening, Check-in, Day 2, and Follow-Up. Hemoglobin A1c (HbA1c) was measured in serum at Screening. Prolactin was measured in serum at Screening, Day 3, Day 8, and Day 15. C-SSRS was assessed at Screening and Day 3. Subjects remained in the clinic from Check-in to Discharge on Day 3 for additional safety assessment and then returned for a Follow-up Visit on Day 8. Subsequent groups followed the same study procedures.

In Part B, eligible subjects were randomized on Day 1 (pre-dose) to placebo (n=2) or LB-102 (n=6) treatment for a total of 24 subjects. Four (4) visits were scheduled for this study: Screening (Visit 1, Days -28 to -1), Check-in (Visit 2, Day 0), Treatment Evaluation (Visit 3, Days 1-9), and Follow-up (Visit 4, Day 15 Dosage of LB-102 was based on the PK observed in a minimum of 2 Part A cohorts. Subjects received 2 doses of placebo or LB-102, first dose at 8:00 AM (±1 hour) and second dose approximately 12 hours later, on Days 1-6 and one dose at 8 AM (±1 hour) on Day 7 for a total of 13 oral doses. The first dose on Day 1 occurred following a 12 hour, overnight fast. For Cohort 6-7, blood samples for PK were collected at multiple timepoints starting on Day 1 at pre-dose and at 15, 30, and 45 minutes (±5 min), and 1, 1.5, 2, 3, 4, 6, 8, 12, and 16 hours (±15 min) post first dose. On Days 2-6, blood samples for PK were collected prior to the first dose. On Day 7 blood samples for PK were collected pre-dose and at 15, 30, and 45 minutes (±5 min), and 1, 1.5, 2, 3, 4, 6, 8, 12, 16, 24, 32, and 48 hours (±15 min) post first dose. For Cohort 8, blood samples for PK were collected at multiple timepoints starting on Day 1 at pre-dose and at 15, 30, and 45 minutes (±5 min), and 1, 1.5, 2, 3, 4, 6, 8, 12, and 16 hours (±15 min) post first dose. On

Days 2-5, blood samples for PK were collected prior to the first dose. On Day 6, blood samples for PK were collected pre-dose, at 15 and 30 minutes (±5 min), and 1, 2, 4, 8, 12, 12.25, 12.5, 13, 14, 16, 18, and 20 hours (±15 min) post dose. On Day 7, blood samples for PK were collected prior to first dose, 24 (Day 8), 32 (Day 8), and 48 (Day 9) hours (±15 min) post Day 7 dose. Vital signs were recorded for each subject at Screening, Check-in, Day 1 at pre-dose and at 0.5, 1, 1.5, 2, 4, 6, 8 and 12 hours (±30 min) post first dose on Day 1, at pre-dose and 2 hours (±30 min) post first dose on Days 2-7, 24 and 48 hours (±30 min) post Day 7 dose, and at Follow-up. 12-lead ECG was done in triplicate at Screening, Check-in, Day 1 at pre-dose and 1, 2, 3, 4, 5, 6, and 8 hours (±30 min) post first dose, prior to first dose on Days 2-7, and on Day 8 (24 hours (±30 min) post-dose Day 7). Clinical labs were assessed at Screening, Check-in, prior to first dose on Day 4, Day 8, and at Follow-up. HbA1c was measured in serum at Screening. Prolactin was measured in serum at Screening, Day 4, Day 9, and Day 15. C-SSRS was assessed at Screening, Day 4, and Day 8. Subjects remained in the clinic from Check-in to Discharge on Day 9 for additional safety assessment and then returned for a Follow-up Visit on Day 15. Subsequent groups followed the same study procedures.

When there were two or more procedures (ECG, vital signs, and PK) scheduled for the same timepoint, the procedures were as close to the time point as possible and in the following order: ECG, vital signs, and then PK blood collection.

The PK profile included maximum plasma concentrations (C_{max}), time to reach C_{max} (T_{max}), area under the plasma concentration-time curve from 0 hours to a specified time (AUC_{0-t}), area under the plasma concentration time curve from 0 hours to 24 hours (AUC_{0-24}), area under the plasma concentration time curve from 0 hours to infinity (AUC_{0-inf}), area under the plasma concentration time curve extrapolated from specified time to infinity as a percentage of total AUC ($AUC_{\%/extrap}$), apparent total clearance of the drug from plasma after oral administration (CL/F), terminal rate constant (λ_z), and elimination half-life ($t_{1/2}$). PK samples were analyzed for all subjects in each cohort prior to dose escalation. These data were used as adjunct information for a safety review, which included a review of AEs, changes in vital signs, physical examination, and clinical laboratory test results.

A Safety Review Committee (SRC) was assembled to review the blinded available study results for a cohort and agree whether the safety profile was sufficiently acceptable to support proceeding with the evaluation of the next higher dose level. The SRC was comprised of the Investigator, Medical Monitor, and a Sponsor Representative (voting members). Other non-voting consultants, including but not limited to, PK or medical expert, statistician, etc. may have supported the SRC on an as needed basis. Blinded data to be reviewed after each cohort included, but was not limited to AEs, physical examinations, vital signs, 12-lead ECGs, clinical laboratory safety tests, and concomitant medications/procedures. Blinded PK analysis occurred at the end of each cohort (Cohorts 1-5) for the SAD study and after each cohort (Cohorts 6-8) for the MAD study.

1.13.9.4 Trials to be Conducted in the Coming Year

A second Phase 1 study (Phase 1b), to be conducted in 2021, will be an open-label, Positron Emission Tomography (PET) study of dopamine receptor occupancy in healthy subjects following a single oral dose of LB-102. Subjects (n=16) will be divided into 4 separate groups of four (4) health adult subjects. Subjects will receive a single oral dose of LB-102 and receptor occupancy of dopamine receptors in the brain will be measured in real-time by PET monitoring of displaced ^{11}C raclopride. Blood levels of LB-102 will also be measured and correlated to dopamine receptor occupancy. This will be an adaptive design study, and dosing in the first cohort at 50 mg will inform dosing in subsequent cohorts.

A Phase 2 study of LB-102 in schizophrenia patients is being planned for 2021. This is anticipated to be a n = 300 patient study lasting four weeks with PANSS as the primary endpoint. Patients will be randomized to one of two doses of LB-102 or placebo.

1.13.9.5 Estimated Number of Patients

For the second phase 1 study (phase 1b) PET studies - A total of 16 subjects will be enrolled with 4 subjects being enrolled in each of 4 cohorts. Each cohort must comprise at least one female and one male subject. Subjects will be considered enrolled at the point they are dosed.

For Phase 2 study, approximately 300 patients will be randomized in the study.

1.13.9.6 Anticipated Risks

The Sponsor does not anticipate any foreseen risks while conducting the clinical trials associated with LB-102. Additionally, all participants have the right to withdraw from the clinical study at any time, as stated in the informed consent form (ICF).

1.13.9.7 References

Danion JM, Rein W, Fleurot O. Improvement of schizophrenic patients with primary negative symptoms treated with amisulpride. Amisulpride Study Group. Am J Psychiatry. 1999 Apr;156(4):610-6.

Dos Santos Pereira JN, Tadjerpisheh S, Abu Abed M, et al. The Poorly Membrane Permeable Antipsychotic Drugs Amisulpride and Sulpride are Substrates of the Organic Cation Transporters from the SLC22 Family. The AAPS Journal. 2014;16(6):1247–58.

Harris EC, Barraclough B. Suicide as an Outcome for Mental Disorders: A Meta-Analysis. Br. J. Psychiatry. 1997;170:205–28.

IMS Health Analyst Services. Interim Delivery December 2015.

Leucht S, Cipriani A, Spineli L, Mavridis D, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. Lancet. 2013;382:951-62.

Liu-Seifert H, Adams DH and Kinon BJ. Discontinuation of treatment of schizophrenic patients is driven by poor symptom response: a pooled post-hoc analysis of four atypical antipsychotic drug. BMC Med. 2005 Dec 23;3:21.

NIH National Institute of Mental Health. Schizophrenia: https://www.nimh.nih.gov/health/statistics/prevalence/schizophrenia.shtml, Accessed on January 31, 2017.

Tandon R, Jibson MD. Suicidal Behavior in Schizophrenia: Diagnosis, Neurobiology, and Treatment Implications. Curr. Opin. Psychiatry. 2003;16(2):193–7.

1.13.8 Individual Study Information

Table 1: Ongoing and Completed Studies

Protocol Number / Title	Clinical Phase	Study Objective	Enrollment Data				Study Status	Study Results
			Planned	Entered	Completed	Discontinued		
LB-102-001 / A Randomized, Double-Blinded, Placebo-Controlled, Single and Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of LB-102 Administered Orally to Healthy Subjects	1	To evaluate the safety, tolerability, and pharmacokinetics (PK) of single (Part A - Single Ascending Dose (SAD)) and multiple (Part B - Multiple Ascending Doses (MAD)) oral doses of LB-102 compared to placebo.	288 screened	64	55	9	Completed	**In Part A (SAD),** LB-102 was rapidly absorbed and LB-102 concentration generally declined from peak in an apparent biphasic manner. Exposure increased in a slightly greater than dose-proportional manner. Apparent clearance appeared to decrease as dose increased. Amisulpride was formed quickly over time after a single dose of LB-102 and generally declined with an approximate biphasic disposition of comparable shape to LB-102 but at approximately 2.5% of LB-102 abundance. The plasma concentrations of amisulpride at lower doses were within several fold of LLOQ making descriptive PK analysis tenuous. In fact, amisulpride was not detected in subjects taking 10 mg LB-102 QD (Cohort 2). In vitro studies suggest equal pharmacological potency between LB-102 and amisulpride, but since amisulpride is present at 2.5% LB-102 concentration, it thus represents a minor active metabolite (defined as either less than 10% parent concentration or less than 10% of total pharmacological activity).

Table 1: Ongoing and Completed Studies (Continued)

Protocol Number / Title	Clinical Phase	Study Objective	Enrollment Data				Study Status	Study Results
			Planned	Entered	Completed	Discontinued		
								In Part B (MAD), trough concentrations of LB-102 and amisulpride plateaued before the morning dose on Day 4. After multiple doses, there was slight to moderate accumulation of LB-102 across dose levels. Amisulpride had a higher accumulation (R_{Cmax} and R_{AUC}) than LB-102 across dose levels. Exposure to LB-102 increased in a dose proportional manner. Apparent clearance at steady state to LB-102 appeared to be similar as dose increased.

1.14.4.1 Investigational Brochure

The Investigator's Brochure, Edition 2.0, was updated during the reporting period, December 05, 2019 – December 04, 2020 (SN 0013).

1.13.5 Summary of Manufacturing Changes

There were no manufacturing changes made to the drug product during the reporting period.

1.13.6 Summary of Microbiological Changes

No microbiological changes occurred during this reporting period.

1.13.1 Summary of Nonclinical Studies

Table 1: Nonclinical Studies Completed/Ongoing During the Reporting Period

Study Number	Title	Status
Completed Studies		
2591-006	Report Amendment for Validation of an LC-MS/MS Assay for LB- 102 and Amisulpride in Dog Plasma with K2EDTA	Final – 12/23/19
180920.MCQ	Effect of LB-102 on Cloned hERG Potassium Channels Expressed in Human Embryonic Kidney Cells	Final – 12/10/19
Initiated Studies		
2591-015	A Metabolite Profiling and Identification Study of LB-102 by Oral Gavage in Dogs	Initiated dosing 11/17/20
2591-016	An In Vivo Micronucleus Study of LB-102 by Oral Gavage in Rats	Initiated dosing 12/1/20
2591-017	A 26-Week Study of LB-102 by Oral Gavage in Rats with a 28-Day Recovery Period	Initiated dosing 12/3/20
2591-018	A 39-Week Study of LB-102 by Oral Gavage in Dogs with a 28-Day Recovery Period	Initiated dosing 11/19/20

Two nonclinical studies were completed during the December 5, 2019 to December 4, 2020 reporting period.

The first was an amendment to the bioanalytical validation report for dog plasma. The amended report contained extended long-term frozen stability: 129 days for LB-102 and 111 days for amisulpride at -70°C.

The second was the finalization of the hERG report. LB-102 exhibited an IC_{50} for inhibition of the hERG potassium channel of 16.7 µM.

For the other studies listed in the table above, dosing has initiated, but no data are available.

1.13.3 Summary of Safety Information

LB-102 was generally well-tolerated with all TEAEs either mild (37) or moderate (6) severity. Out of the 64 subjects, 28 subjects (50 mg QD, N=4; 10 mg QD, N=2; 100 mg QD, N=3; 200 mg QD, N=3; 150 mg QD, N=1; 50 mg BID, N=2; 100 mg BID, N=3; 75 mg BID, N=5; Placebo, N=5) experienced at least one TEAE, with a total of 43 TEAEs. Out of the 43 TEAEs, 29 (50 mg QD, 3; 10 mg QD, 1; 100 mg QD, 3; 200 mg QD, 5; 150 mg QD, 1; 50 mg BID, 2; 100 mg BID, 5; 75 mg BID, 8; Placebo, 1) were considered possibly, probably, or definitely related to treatment.

Of the TEAEs definitely related to study drug, there were 11 cases of elevated prolactin (≥100 µg/L; 50 mg QD, N=3; 10 mg QD, N=1; 100 mg QD, N=1; 150 mg QD, N=1; 50 mg BID, N=2; 100 mg BID, N=1; 75 mg BID, N=2), 4 cases of moderate dystonia (200 mg QD, N=1; 100 mg BID, N=2; 75 mg BID, N=1), and 1 case of mild ECG QTcF prolongation (458 msec, 200 mg LB-102 QD) that were all resolved with either no course of action (prolactin increase and QTcF interval prolongation) or concomitant medications (dystonia). Due to 2 TEAEs in the same system organ class (acute dystonic reaction), treatment was halted in all subjects taking 100 mg LB-102 BID (Cohort 7) and the 2 subjects in Cohort 7 taking placebo. As a result, the SRC recommended reducing the dose for Cohort 8 to 75 mg LB-102 BID. Of TEAEs probably or possibly related to study drug, there were 4 cases of nausea (100 mg LB-102 QD, N=1; 200 mg LB-102, N=1; 100 mg LB-102 BID, N=1; 75 mg LB-102 BID, N=1), 1 case of vomiting (100 mg LB-102 BID), urticaria (100 mg LB-102 QD), gastroesophageal disease (200 mg LB-102), insomnia (75 mg LB-102 BID), dizziness (75 mg LB-102 BID), and somnolence (75 mg LB-102 BID).

Vital signs and physical examination results were largely unchanged from baseline. Other than mild increases in prolactin, chemistry laboratory results were also largely unchanged throughout study treatment. C-SSRS did not change during study treatment.

1.13.3.1 Most Frequent and Serious Adverse Events by Body System

There were no deaths or other serious AEs. There were 4 cases of dystonia, 1 case of prolonged QTcF interval and 11 cases of elevated prolactin.

1.13.3.2 Summary of IND Safety Reports Submitted

Clinical Study Report LB-102-001 was submitted during the reporting period (SN 0014).

1.13.3.3 List of Subjects who Died During the Investigation

No subjects died during the investigation.

1.13.3.4 List of Subjects who Dropped Out During the Investigation

No TEAE led to study discontinuation. Three (3) subjects receiving 100 mg LB-102 BID (Cohort 7) withdrew consent from the study for personal/family or work issues, and 2 out of these 3 subjects experienced an acute dystonic reaction but withdrew consent prior to reporting their TEAE and the remaining subjects (N=3 LB-102; N=2 Placebo) in this cohort discontinued drug administration based on a stopping criterion being met. One (1) subject receiving 75 mg LB-102 BID (Cohort 8) experienced acute dystonic reaction on Day 3, and voluntarily withdrew consent the following day.