To: Medpace Clinical Pharmacology Unit

From: Zachary Prensky, CEO - LB Pharmaceuticals

Date: June 03, 2020

RE: Clarification Memo #8

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

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The intent of this protocol clarification memo is to provide clarification for the LB-102-001 protocol (Protocol Version 5, 18 May 2020). All items listed below will be incorporated into the next amendment. The protocol amendment will be sent after it is filed with FDA.

Section 1 – Study Design, Section 5.1 – Study Design, and Section 8.5.1 - Safety Review Committee (SRC)

Original Wording

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

Revised Wording

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

Section 1 – Study Design and Section 6.3 – Treatment Administration

<u>Original Wording</u>

Part A	
Cohort	***Treatment***
1 (n=8)[a]	*LB-102 50 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
2 (n=8)[b]	*LB-102 10 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
3 (n=8)[b]	*LB-102 100 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
4 (n=8)[b]	*LB-102 200 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
5 (n=8)[b]	*LB-102 150 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
Part B	
6 (n=8)	*LB-102 (n=6) 50 mg BID (100 mg/day) x 6 days (Days 1-6) and QD x 1 day (Day 7)* *or* *Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)*
7 (n=8)	*LB-102 (n=6) Y* mg BID x 6 days (Days 1-6) and QD x 1 day (Day 7)* *or* *Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)*
8 (n=8)	*LB-102 (n=6) Y* mg BID x 6 days (Days 1-6) and QD x 1 day (Day 7)* *or* *Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)*

Revised Wording

Part A	
Cohort	***Treatment***
1 (n=8)[a]	*LB-102 50 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
2 (n=8)[b]	*LB-102 10 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
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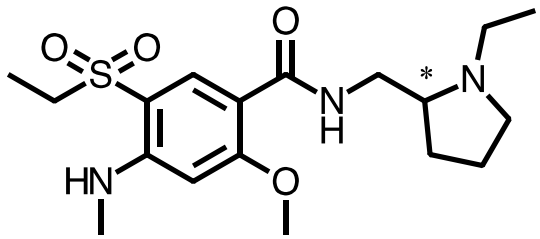
5 (n=8)[b]	*LB-102 150 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
Part B	
6 (n=8)	*LB-102 (n=6) 50 mg BID (100 mg/day) x 6 days (Days 1-6) and QD x 1 day (Day 7)* *or* *Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)*
7 (n=8)	*LB-102 (n=6)* ***100*** *mg BID* ***(200 mg/day)*** *x 6 days (Days 1-6) and QD x 1 day (Day 7)* *or* *Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)*
8 (n=8)	*LB-102 (n=6) Y* mg BID x 6 days (Days 1-6) and QD x 1 day (Day 7)* *or* *Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)*

Section 14.1 – Appendix 1: Clinical Pharmacology Summary Table

<u>Original Wording</u>

Table 1: Clinical Pharmacology Summary Table

<table>
<tr><th colspan="2">General Information</th></tr>
<tr><td>Chemical Structure and Major Physical and Chemical Properties</td><td>


Molecular Weight: 383.51
<table>
<tr><td>Description</td><td colspan="5">White to off-white powder</td></tr>
<tr><td>pKa</td><td colspan="5">9.36</td></tr>
<tr><td>Partition Coefficient (LogP)</td><td colspan="5">1.72 (pH 7)</td></tr>
<tr><td>Aqueous Solubility</td><td>Vehicle</td><td>HPLC Area of Sample (225 nm)</td><td>Sample Concentration (mg/mL)</td><td>Calculated Solution Concentration (mg/mL)</td><td>Comment</td></tr>
<tr><td></td><td>30% DMF 70% pH 4.7 MES</td><td>2769</td><td>0.44</td><td>44.0</td><td>100:1 dilution, pH of buffer is unchanged</td></tr>
<tr><td></td><td>pH 4.7 MES Buffer</td><td>3770</td><td>0.614</td><td>61.4</td><td>100:1 dilution, pH of buffer is unchanged</td></tr>
<tr><td></td><td>pH 5 HCl</td><td>4990</td><td>0.839</td><td>83.9</td><td>100:1 dilution, pH of buffer is unchanged</td></tr>
<tr><td></td><td>pH 6 phosphate buffer</td><td>3827</td><td>0.625</td><td>625</td><td>1000:1 dilution, pH of buffer is unchanged</td></tr>
<tr><td></td><td>pH 5 acetate buffer</td><td>Not Determined</td><td>>800</td><td>>800</td><td>pH of solution becomes 6.5</td></tr>
</table>
</td></tr>
<tr><td>Indication (for this IND)</td><td>For the Treatment of Schizophrenia.</td></tr>
<tr><td>Route and Formulation Type (for this IND)</td><td>Oral Capsule.</td></tr>
<tr><td>Planned Strengths (for this IND)</td><td>LB-102 consists of API in a Size 2 white opaque/white opaque hard gelatin capsule in dosage strengths of 25 mg, 50 mg, 75 mg, and 100 mg.</td></tr>
<tr><td>Planned Dose Levels (for this IND)</td><td>For Part A (Single Ascending Dose Study) there were 5 dose levels: 50, 10, 100, 200, and 150 mg QD.
For Part B (Multiple Ascending Doses Study) there will be 3 dose levels (BID), starting with 50 mg (100 mg/day). The remaining doses will be determined by the SRC depending on the safety profile and clinical observations of the previous Cohort.</td></tr>
</table>

<table>
<tr><td>Mechanism of Action (for this Indication)</td><td>The proposed mechanism of action for LB-102 is through dopamine D2/D3 receptor antagonism.</td></tr>
<tr><td colspan="2">Dose and AEs</td></tr>
<tr><td>Therapeutic Dose and Exposure (for this IND)</td><td>
<table>
<tr><td colspan="2">Part A</td></tr>
<tr><td>Cohort</td><td>Treatment</td></tr>
<tr><td>1 (n=8)[a]</td><td>LB-102 50 mg (n=6) or Matching Placebo (n=2) QD x 1 day</td></tr>
<tr><td>2 (n=8)[b]</td><td>LB-102 10 mg (n=6) or Matching Placebo (n=2) QD x 1 day</td></tr>
<tr><td>3 (n=8)[b]</td><td>LB-102 100 mg (n=6) or Matching Placebo (n=2) QD x 1 day</td></tr>
<tr><td>4 (n=8)[b]</td><td>LB-102 200 mg (n=6) or Matching Placebo (n=2) QD x 1 day</td></tr>
<tr><td>5 (n=8)[b]</td><td>LB-102 150 mg (n=6) or Matching Placebo (n=2) QD x 1 day</td></tr>
<tr><td colspan="2">Part B</td></tr>
<tr><td>6 (n=8)</td><td>LB-102 (n=6) 50 mg BID (100 mg/day) x 6 days (Days 1-6) and QD x 1 day (Day 7)
or
Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)</td></tr>
<tr><td>7 (n=8)</td><td>LB-102 (n=6) Y* mg BID x 6 days (Days 1-6) and QD x 1 day (Day 7)
Or
Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)</td></tr>
<tr><td>8 (n=8)</td><td>LB-102 (n=6) Y* mg BID x 6 days (Days 1-6) and QD x 1 day (Day 7)
Or
Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)</td></tr>
</table>
a – In Cohort 1 (Part A), dosing of the first 2 subjects (1 active and 1 placebo) will commence at least 24 hours prior to the remaining 6 subjects.
b – For Cohorts 2-5, the doses may be reduced based on the PK results of Cohort 1 (Refer to Section 5.1).
Y* - Dose will be determined by the SRC depending on the safety profile and clinical observations of the previous Cohort.
QD = Once daily; BID = Twice daily
<u>Treatment Exposure:</u>
Part A: 1 day
Part B: 7 days
</td></tr>
<tr><td>Maximum Tolerated Dose</td><td><u>Rats</u>
• In the 14-day repeat dose phase study, the maximum tolerated dose was determined to be 200 mg/kg/day
<u>Dogs</u>
• In the single-dose phase of the dog range-finding study, the maximum tolerated dose was determined to be 25 mg/kg/day
• In the 14-day repeat-dose phase study, the maximum tolerated dose was determined to be 5 mg/kg/day</td></tr>
<tr><td>Principal Adverse Events</td><td>Prolactin elevation (≥ 100 ng/mL)</td></tr>
<tr><td colspan="2">PK Features</td></tr>
</table>

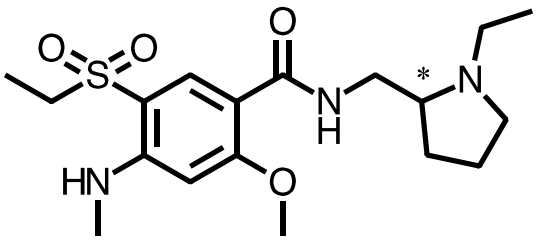
Dose/Exposure Range Tested in Clinic (Data from this IND and/or Elsewhere)	*Single Dose*	*50 mg, 10 mg, 100 mg, 200 mg, 150 mg*
	Multiple Dose	*N/A*
Range of Linear PK	*At least to 200 mg (highest dose examined to date)*	
Accumulation at Steady State	*Repeat dose PK model suggests 40% of Cmax with b.i.d. dosing*	
Metabolites	*LB-101 approximately 2.5%*	
Absorption	*Absolute/Relative Bioavailability*	*N/A*
	Mean Tmax	*50 mg – 3.000 h* *10 mg – 3.000 h* *100 mg – 2.833 h* *200 mg – 2.083 h* *150 mg – 3.167 h*
Distribution	*Vd/F or Vd*	*N/A*
	% bound in plasma	*N/A*
	Blood / plasma partition ratio	*N/A*
Elimination	*Route*	*Oral (PO)*
	Mean Terminal t½	*50 mg – 12.311 h* *10 mg – 13.675 h* *100 mg – 14.656 h* *200 mg – 12.835 h* *150 mg – 12.620 h*
	Mean CL/F or CL	*50 mg – 31.624 L/h* *10 mg – 42.323 L/h* *100 mg – 36.346 L/h* *200 mg – 28.901 L/h* *150 mg – 32.964 L/h*
Metabolism	*• by CYP450 ☐ Yes ☐ No ☒ NA, if yes, specify* *• by Phase 2 enzymes ☐ Yes ☐ No ☒ NA* *• by other enzyme systems ☐ Yes ☐ No ☒ NA, if yes, specify* *• inhibits CYP450 ☒ Yes ☐ No ☐ NA, if yes, specify and provide K_i and/orIC_{50}. A Cytochrome P450 Inhibition Assay demonstrated that LB-102 slightly inhibits CYP2C8 (IC_{50} = 75.5 µM).* *• inhibits Phase II enzymes ☐ Yes ☐ No ☒ NA, if yes specify and provide K_i and/or IC_{50}.* *• induces CYP450 ☐ Yes ☐ No ☒ NA, if yes specify*	
Transporters	*by major transporters ☐ Yes ☐ No ☒ NA, if yes, specify* *• inhibits major transporters ☐ Yes ☐ No ☒ NA, if yes, specify and provide Ki and/or IC50.* *• induces major transporters ☐ Yes ☐ No ☒ NA, if yes specify*	
Intrinsic Factors	*Age*	*N/A*
		N/A
	Sex	*N/A*
	Race	*N/A*
	Hepatic Impairment	*N/A*
	Renal Impairment	*N/A*
	Poor Metabolizers	*N/A*
Extrinsic Factors	*Drug interactions*	*N/A*

	Food Effects	*N/A*
	Alcohol Effects (Oral MR formulation only)	*N/A*
PD Features		
PD Studies: e.g., *QT Effect* *Driving Test* *Receptor Occupancy* *Sleeping Test* *Other Safety Evaluation*	*Part A (Single Ascending Dose)* *Cohort 1 - 50 mg LB-102:* • *Three (3) mild, Grade 1 AEs (elevated prolactin, ≥100 ng/mL) that were experienced by 3 subjects. All 3 prolactin elevations were asymptomatic. The 3 AEs were considered definitely related to LB-102 in Cohort 1. All 3 AEs resolved by Day 8 (Follow-Up Visit).* *Cohort 2 – 10 mg:* • *One (1) mild, Grade 1 AE (elevated prolactin, > 100 ng/mL) was experience by 1 subject. The prolactin elevation was asymptomatic. The AE was considered definitely related to LB-102 in Cohort 2. The AE resolved by Day 8.* *Cohort 3 – 100 mg:* • *One (1) mild, Grade 1 AE (elevated prolactin, > 100 ng/mL) was experienced by 1 subject. The prolactin elevation was asymptomatic. The AE was considered definitely related to LB-102 in Cohort 3. The AE resolved by Day 8.* *Cohort 4 – 200 mg:* • *One (1) mild, Grade 1 AE (QTcF prolongation of > 450 ms was noted, 2 hours post-dose on Day 1) was experienced by 1 subject. The AE was considered definitely related to LB-102 in Cohort 4. The AE resolved by 3 hours post-dose on Day 1. The overall maximum QTcF prolongation for the subject was 43 msec from baseline.* • *One (1) moderate, Grade 2 AE (acute dystonic reaction). The acute dystonic reaction was definitely related to the study drug in Cohort 4. The AE resolved on the same day it was experienced (Day 1) with no recurrence. Subject was treated with concomitant medication for the symptoms.* *Cohort 5 – 150 mg:* • *One (1) mild, Grade 1 AE (elevated prolactin, > 100 ng/mL) was experienced by 1 subject. The subject was asymptomatic. The AE was considered definitely related to LB-102 in Cohort 5. The AE resolved by Day 15 Follow-Up Visit.*
E-R Studies: e.g.: Important E-R Relationships	*N/A*
Other Studies	
e.g., Genotype	*N/A*

Revised Wording

Table 1: Clinical Pharmacology Summary Table

General Information	
Chemical Structure and Major Physical and Chemical Properties	



***Molecular Weight**: 383.51*

Description	*White to off-white powder*
pKa	*9.36*
Partition Coefficient (LogP)	*1.72 (pH 7)*

Aqueous Solubility

Vehicle	***HPLC Area of Sample (225 nm)***	***Sample Concentration (mg/mL)***	***Calculated Solution Concentration (mg/mL)***	***Comment***
30% DMF 70% pH 4.7 MES	*2769*	*0.44*	*44.0*	*100:1 dilution, pH of buffer is unchanged*
pH 4.7 MES Buffer	*3770*	*0.614*	*61.4*	*100:1 dilution, pH of buffer is unchanged*
pH 5 HCl	*4990*	*0.839*	*83.9*	*100:1 dilution, pH of buffer is unchanged*
pH 6 phosphate buffer	*3827*	*0.625*	*625*	*1000:1 dilution, pH of buffer is unchanged*
pH 5 acetate buffer	*Not Determined*	*>800*	*>800*	*pH of solution becomes 6.5*

Indication (for this IND)	*For the Treatment of Schizophrenia.*
Route and Formulation Type (for this IND)	*Oral Capsule.*
Planned Strengths (for this IND)	*LB-102 consists of API in a Size 2 white opaque/white opaque hard gelatin capsule in dosage strengths of 25 mg, 50 mg, 75 mg, and 100 mg.*
Planned Dose Levels (for this IND)	*For Part A (Single Ascending Dose Study) there were 5 dose levels: 50, 10, 100, 200, and 150 mg QD.* *For Part B (Multiple Ascending Doses Study) there will be 3 dose levels (BID), starting with 50 mg (100 mg/day) **for Cohort 6 and 100 mg (200 mg/day) for Cohort 7**. The remaining dose **for Cohort 8** will be determined by the SRC depending on the safety profile and clinical observations of the previous Cohorts.*
Mechanism of Action (for this Indication)	*The proposed mechanism of action for LB-102 is through dopamine D2/D3 receptor antagonism.*

Dose and AEs

Therapeutic Dose and Exposure (for this IND)	***Part A***	
	Cohort	***Treatment***

	1 (n=8)[a]	*LB-102 50 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
	2 (n=8)[b]	*LB-102 10 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
	3 (n=8)[b]	*LB-102 100 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
	4 (n=8)[b]	*LB-102 200 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
	5 (n=8)[b]	*LB-102 150 mg (n=6) or Matching Placebo (n=2) QD x 1 day*
	Part B	
	6 (n=8)	*LB-102 (n=6) 50 mg BID (100 mg/day) x 6 days (Days 1-6) and QD x 1 day (Day 7)* *or* *Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)*
	7 (n=8)	*LB-102 (n=6)* ***100*** *mg BID* ***(200 mg/day)*** *x 6 days (Days 1-6) and QD x 1 day (Day 7)* *Or* *Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)*
	8 (n=8)	*LB-102 (n=6) Y* mg BID x 6 days (Days 1-6) and QD x 1 day (Day 7)* *Or* *Matching Placebo (n=2) BID x 6 days (Days 1-6) and QD x 1 day (Day 7)*
	a – In Cohort 1 (Part A), dosing of the first 2 subjects (1 active and 1 placebo) will commence at least 24 hours prior to the remaining 6 subjects. *b – For Cohorts 2-5, the doses may be reduced based on the PK results of Cohort 1 (Refer to Section 5.1).* *Y* - Dose will be determined by the SRC depending on the safety profile and clinical observations of the previous Cohort.* *QD = Once daily; BID = Twice daily* ***Treatment Exposure:*** *Part A: 1 day* *Part B: 7 days*	
Maximum Tolerated Dose	***Rats*** • *In the 14-day repeat dose phase study, the maximum tolerated dose was determined to be 200 mg/kg/day* ***Dogs*** • *In the single-dose phase of the dog range-finding study, the maximum tolerated dose was determined to be 25 mg/kg/day* • *In the 14-day repeat-dose phase study, the maximum tolerated dose was determined to be 5 mg/kg/day*	
Principal Adverse Events	*Prolactin elevation (≥ 100 ng/mL)*	
PK Features		
Dose/Exposure Range Tested in Clinic (Data from this IND and/or Elsewhere)	*Single Dose*	*50 mg, 10 mg, 100 mg, 200 mg, 150 mg*
	Multiple Dose	***50 mg BID (100 mg/day)***
Range of Linear PK	*At least to 200 mg (highest dose examined to date)*	
Accumulation at Steady State	*Repeat dose PK model suggests 40% of Cmax with b.i.d. dosing*	
Metabolites	*LB-101 approximately 2.5%*	
Absorption	*Absolute/Relative Bioavailability*	*N/A*

	Mean Tmax	*50 mg – 3.000 h* *10 mg – 3.000 h* *100 mg – 2.833 h* *200 mg – 2.083 h* *150 mg – 3.167 h* ***50 mg BID*** • ***Day 1 – 2.250 h*** • ***Day 7 – 2.333 h***
Distribution	*Vd/F or Vd*	*N/A*
	% bound in plasma	*N/A*
	Blood / plasma partition ratio	*N/A*
Elimination	*Route*	*Oral (PO)*
	Mean Terminal t½	*50 mg – 12.311 h* *10 mg – 13.675 h* *100 mg – 14.656 h* *200 mg – 12.835 h* *150 mg – 12.620 h* ***50 mg BID*** • ***Day 1 – 4.962 h*** • ***Day 7 – 14.088 h***
	Mean CL/F or CL	*50 mg – 31.624 L/h* *10 mg – 42.323 L/h* *100 mg – 36.346 L/h* *200 mg – 28.901 L/h* *150 mg – 32.964 L/h*
Metabolism	*• by CYP450 ☐ Yes ☐ No ☒ NA, if yes, specify* *• by Phase 2 enzymes ☐ Yes ☐ No ☒ NA* *• by other enzyme systems ☐ Yes ☐ No ☒ NA, if yes, specify* *• inhibits CYP450 ☒ Yes ☐ No ☐ NA, if yes, specify and provide K_i and/orIC_{50}. A Cytochrome P450 Inhibition Assay demonstrated that LB-102 slightly inhibits CYP2C8 (IC_{50} = 75.5 μM).* *• inhibits Phase II enzymes ☐ Yes ☐ No ☒ NA, if yes specify and provide K_i and/or IC_{50}.* *• induces CYP450 ☐ Yes ☐ No ☒ NA, if yes specify*	
Transporters	*by major transporters ☐ Yes ☐ No ☒ NA, if yes, specify* *• inhibits major transporters ☐ Yes ☐ No ☒ NA, if yes, specify and provide Ki and/or IC50.* *• induces major transporters ☐ Yes ☐ No ☒ NA, if yes specify*	
Intrinsic Factors	*Age*	*N/A*
		N/A
	Sex	*N/A*
	Race	*N/A*
	Hepatic Impairment	*N/A*
	Renal Impairment	*N/A*
	Poor Metabolizers	*N/A*

Extrinsic Factors	*Drug interactions*	*N/A*
	Food Effects	*N/A*
	Alcohol Effects *(Oral MR formulation only)*	*N/A*
PD Features		
PD Studies: e.g., *QT Effect* *Driving Test* *Receptor Occupancy* *Sleeping Test* *Other Safety Evaluation*	*Part A (Single Ascending Dose)* *Cohort 1 - 50 mg LB-102:* • *Three (3) mild, Grade 1 AEs (elevated prolactin, ≥ 100 ng/mL) that were experienced by 3 subjects. All 3 prolactin elevations were asymptomatic. The 3 AEs were considered definitely related to LB-102 in Cohort 1. All 3 AEs resolved by Day 8 (Follow-Up Visit).* *Cohort 2 – 10 mg:* • *One (1) mild, Grade 1 AE (elevated prolactin, ≥ 100 ng/mL) was experience by 1 subject. The prolactin elevation was asymptomatic. The AE was considered definitely related to LB-102 in Cohort 2. The AE resolved by Day 8.* *Cohort 3 – 100 mg:* • *One (1) mild, Grade 1 AE (elevated prolactin, ≥ 100 ng/mL) was experienced by 1 subject. The prolactin elevation was asymptomatic. The AE was considered definitely related to LB-102 in Cohort 3. The AE resolved by Day 8.* *Cohort 4 – 200 mg:* • *One (1) mild, Grade 1 AE (QTcF prolongation of > 450 ms was noted, 2 hours post-dose on Day 1) was experienced by 1 subject. The AE was considered definitely related to LB-102 in Cohort 4. The AE resolved by 3 hours post-dose on Day 1. The overall maximum QTcF prolongation for the subject was 43 msec from baseline.* • *One (1) moderate, Grade 2 AE (acute dystonic reaction). The acute dystonic reaction was definitely related to the study drug in Cohort 4. The AE resolved on the same day it was experienced (Day 1) with no recurrence. Subject was treated with concomitant medication for the symptoms.* *Cohort 5 – 150 mg:* • *One (1) mild, Grade 1 AE (elevated prolactin, ≥ 100 ng/mL) was experienced by 1 subject. The subject was asymptomatic. The AE was considered definitely related to LB-102 in Cohort 5. The AE resolved by Day 15 Follow-Up Visit.* ***Cohort 6 – 50 mg BID (100 mg/day)*** • ***Two (2) mild, Grade 1 AEs (elevated prolactin, ≥ 100 ng/mL were experienced by 2 subjects. Both prolactin elevations were asymptomatic. The 2 AEs were considered definitely related to LB-102 in Cohort 6. Both AEs resolved by Day 15 (Follow-Up Visit).***
E-R Studies: e.g.: Important E-R Relationships	*N/A*	
Other Studies		
e.g., Genotype	*N/A*	

Zachary Prensky		6/3/2020
Zachary Prensky, CEO	Signature	Date