UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 1, 2021

Longboard Pharmaceuticals, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**1-40192**	**84-5009619**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
4275 Executive Square, Suite 950 La Jolla, CA		**92037**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (619) 592-9775

N/A
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.0001 per share	LBPH	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

Included as Exhibit 99.1 to this Form 8-K is a corporate presentation dated December 2021 that is incorporated herein by reference. We intend to utilize this presentation and its contents in various meetings with securities analysts, investors and others, including in connection with the Evercore ISI 4th Annual HealthCONx Virtual Conference, commencing on December 1, 2021.

The information in this Current Report on Form 8-K, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits. (d) Exhibits.

Exhibit No.	Description
99.1	Longboard Pharmaceuticals Corporate Presentation dated December 2021
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Longboard Pharmaceuticals, Inc.

Date: December 1, 2021

By: */s/ Kevin R. Lind*
Kevin R. Lind
President and Chief Executive Officer

Exhibit 99.1

LONGBOARD PHARMACEUTICALS

Corporate Presentation

December 2021

Forward-Looking Statements

This presentation contains forward-looking statements about Longboard Pharmaceuticals, Inc. ("we," "Longboard" or the "Company"), including statements regarding: our future results of operations and financial position; business strategy; the timing, costs and conduct of our preclinical studies and clinical trials for our product candidates; the timing and likelihood of regulatory filings and approvals for our product candidates; our intellectual property; our ability to commercialize our product candidates, if approved; and other statements that are not historical facts, including statements that may include words such as "will", "may", "can", "intend", "plan", "expect", "believe", "potential" and similar words. For such statements, we claim the protection of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to: our limited operating history; net losses; our expectation that we will incur net losses for the foreseeable future, and that we may never be profitable; our need for additional funding and related risks for our business, product development programs and future commercialization activities; the timing and success of clinical trials we conduct; the ability to obtain and maintain regulatory approval of our product candidates; the ability to commercialize our product candidates; our ability to compete in the marketplace; risks regarding our license and dependencies on others; our ability to obtain and maintain intellectual property protection and freedom to operate for our product candidates; our ability to manage our growth; and other risks and factors disclosed in our filings with the U.S. Securities and Exchange Commission. We operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. The forward-looking events and circumstances discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Except as required by law, we assume no responsibility for the accuracy and completeness of the forward-looking statements, and we undertake no obligation to update any forward-looking statements after the date of this presentation to conform these statements to actual results or to changes in our expectations.

Certain information contained in this presentation and statements made orally during this presentation relate to or are based on studies, publications, surveys and other data obtained from third-party sources and Longboard's own internal estimates and research. While Longboard believes these third-party studies, publications, surveys and other data to be reliable as of the date of this presentation, it has not independently verified, and makes no representations as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources.

This presentation discusses product candidates that have not yet been approved for marketing by the U.S. Food and Drug Administration.

Investment Thesis

Three drug candidates internally developed by Arena which represents a culmination of >20 yrs of world-class GPCR research:

- Targeting large market opportunities
- Broad clinical applicability across multiple indications
- Well understood mechanisms of action
- Retain rights to all major markets in therapeutic areas of focus

Program / MOA	Therapeutic Area	IND-Enabling	Ph 1	Ph 2	Ph 3	Key Milestones
LP352 5-HT2c Superagonist	DEEs and other refractory epilepsies					✓ Completion of Ph 1 MAD study • Initiate Ph 1b/2a – Q1 2022
LP143 CB2 Agonist	ALS and other neurodegenerative diseases					• Additional preclinical validation • IND submission – Q1 2022
LP659 S1P Receptor Modulator	Multiple neurodegenerative diseases					• Additional preclinical validation • IND submission – H2 2022

Additional earlier discovery stage compounds in development

Definitions: DEEs = developmental and epileptic encephalopathies; ALS =amyotrophic lateral sclerosis; CB2 = cannabinoid type 2 (CB2) receptor; S1P = sphingosine 1-phosphate (S1P) receptor modulators

Leadership Team

EO

Kevin Lind

- **23+** years experience in healthcare investing in special situations and pharmaceuticals; as well as executive leadership in life sciences

ARENA PHARMACEUTICALS
TPG–AXON CAPITAL
TPG
LEHMAN BROTHERS

Chief Medical Officer

Phil Perera, M.D

- **35+** years clinical research leadership, including research, development and approval of small molecule drugs in a variety of CNS & pain disorders, as well as hospital management and practice

Sage Therapeutics™
Dart NeuroScience
Jazz Pharmaceuticals
gsk GlaxoSmithKline
Pfizer

Chief Financial Officer

Brandi Roberts

- **25+** years of public accounting and finance experience, including pharmaceutical, medical tech, life sciences; CFO of multiple public companies

LINEAGE CELL THERAPEUTICS
MAST THERAPEUTICS, INC.
Pfizer
REVA

VP, Head of Operations

Chad Orevillo

- **25+** years of experience in pharmaceutical clinical development and operations at both large and small pharmaceutical companies

ARENA PHARMACEUTICALS
Pearl
MERCK
NOVARTIS

Independent Directors

Vince Aurentz

ARENA PHARMACEUTICALS
EMD SERONO
HEMOSHEAR THERAPEUTICS
CSC
EPIRUS
QUINTILES

Corinne Le Goff, Pharm D.

moderna
Roche
AMGEN
Pacific Council ON INTERNATIONAL POLICY
SANOFI
Pfizer

Casey Lynch

CORTEXYME
NIO NEUROTECHNOLOGY INDUSTRY ORGANIZATION
ASPIRA
CLSA California Life Sciences Association
NEUROINSIGHTS

Phillip Schneider

IDEC Pharmaceuticals Corporation
KPMG
PFENEX
AUSPEX PHARMACEUTICALS
GEN-PROBE
ARS PHARMA
ARENA PHARMACEUTICALS

Paul Sekhri

egenesis ENGINEERING HOPE
LYCERA
Cerimon Pharmaceuticals
Pharming
SANOFI
TPG
NOVARTIS
IPSEN
teva
BiomX
Veeva
ARIAD

Jane Tiller, MBChB, FRCPsych

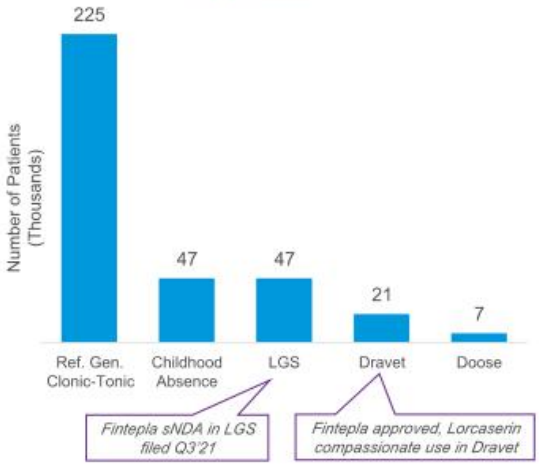
Neumora
BlackThorn THERAPEUTICS
Bristol Myers Squibb
Cephalon

LP352

Oral, Centrally Acting 5-HT2c Receptor Superagonist Targeting Seizures Associated with Multiple Refractory Epilepsies

LP352, A Centrally Acting 5-HT2c Superagonist Targeting Multiple Epileptic Indications with Significant Unmet Need

The 5-HT2c Pathway Has Been Implicated in Multiple DEEs



LP352 Design Features*

- Designed to be a next-generation (new chemical series) of lorcaserin
- In preclinical studies LP352 has shown to be highly selective to 5-HT2c; no observable impact on 2a or 2b
  - 2a can be associated with psychogenic effects
  - 2b can be associated with pulmonary arterial hypertension (PAH) and valvular heart disease (VHD)

LP352 Status

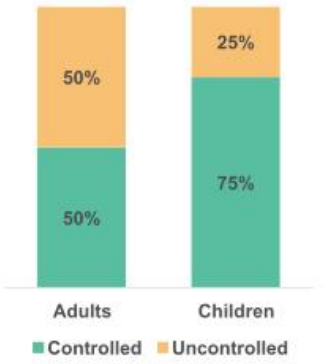
- Ph 1 (including SAD & MAD portions) trial completed
- **Ph 1b/2a expected to initiate Q1 2022**

Strong IP Position Potentially Through 2041**

*Arena designed LP352 to be a differentiated drug candidate; the design features listed above is the intended profile, but there is no guarantee continuing clinical or non-clinical studies will corroborate these features
**Composition of matter through 2036 with potential for PTE & PTA

There is a Large Unsatisfied Patient Population in Epilepsy

Epilepsy is **uncontrolled** for ~25% of children[1] and up to 50% of adults[2]



~50% of all patients have unknown etiology[3]

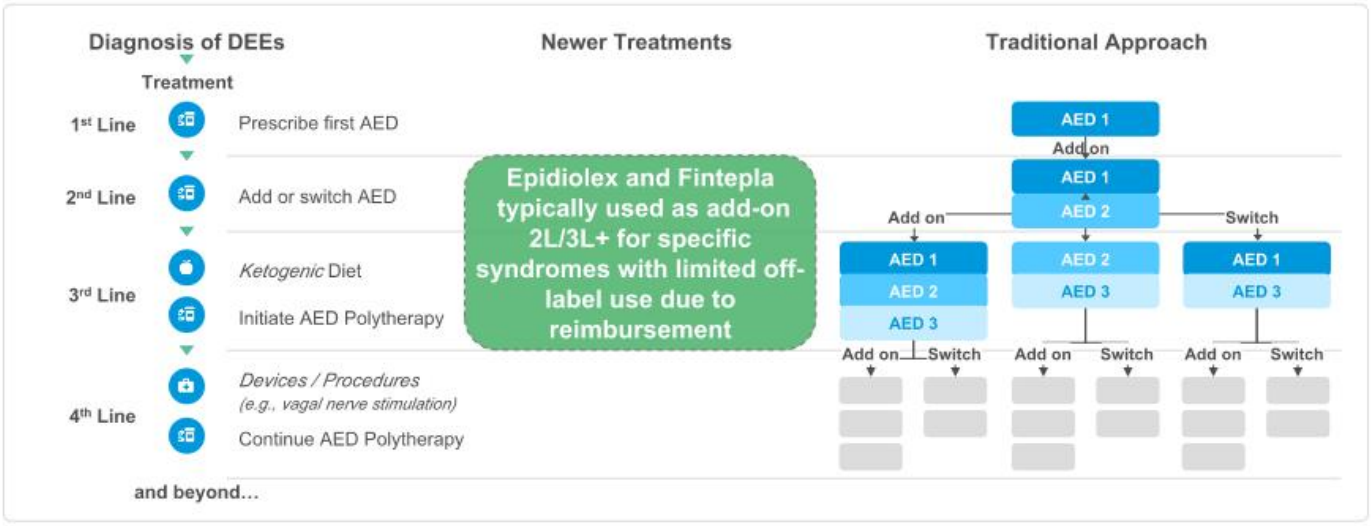
It has been estimated that between 35% and 50% of new onset epilepsy in children is of unknown etiology and the remainder is genetic, structural or metabolic[4]

Developmental and Epileptic Encephalopathy (DEE) is a group of severe epilepsies characterized by seizures, often drug-resistant, and encephalopathy

Over
25 Syndromes
Described

(1) Tian, et al. MMWR 2018;67:437-442. (2) Epilepsy Foundation, Research RoundTable for Epilepsy 2020. (3) Beghi. Neuroepidemiology. 2020;54(2):185-191. (4) Wirrell, et al. Epilepsy Res. 2011;95(1-2):110-8. Sokka A,Epilepsia Open. 2017;2(1):76-83

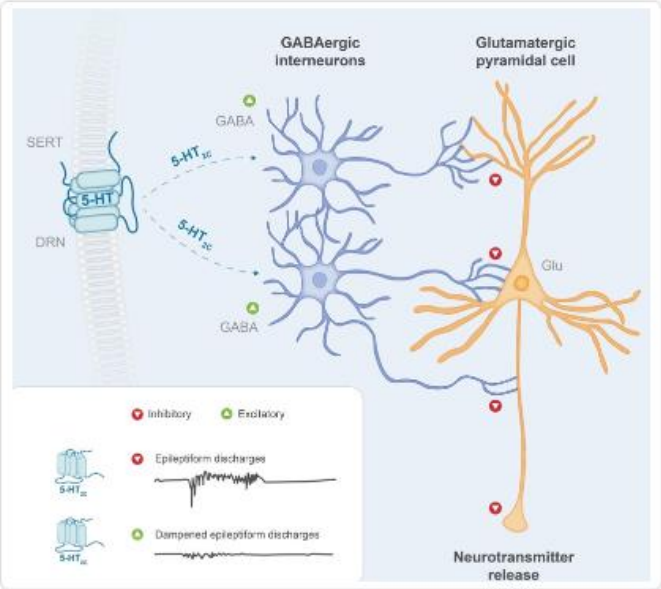
Treatment Paradigm for DEEs is Characterized by Initial Short-Term Trial of Monotherapy, Followed by Polytherapy Strategies



Despite numerous available therapies, there remains a significant unmet need for refractory patients

Definitions: AED = Anti-epileptic drugs

Role of 5-HT2c Receptors in Epilepsy



- 5-HT2c modulation of hippocampal pyramidal GABAergic neurons suppresses hyperexcitability
- 5-HT2c KO mice display spontaneous seizures and decreased threshold for proconvulsant stimuli
- *m*-CPP (5-HT2c) increases threshold for PTZ- and electroshock induced myoclonic and tonic seizures; effect blocked by 5-HT2c antagonist
- In a genetic model of DS, 5-HT2c agonist decreased seizure-like behavior and epileptiform electrical activity in *scn1Lab-/-* mutant zebrafish

Source: Gharedaghi MH et al., Exp Brain Res. 2014; Bagdy G et al., J Neurochemistry. 2007; Strac DS et al., Front Neurosci. 2016; Sourbron J et al., ACS Chem Neuroscience. 2016; Tecott LH et al, Nature. 1995; Upton N et al, Eur J Pharmacol. 1998; Orban G et al., CNS Neurosci Ther. 2014; Schoonjans A et al., Eur J Neurol. 2017; DS, Dravet syndrome; GABA, gamma aminobutyric acid; KO, knock-out; mCPP, m-chlorophenyl-piperazine; PTZ, pentylenetetrazole; TLE, temporal lobe epilepsy

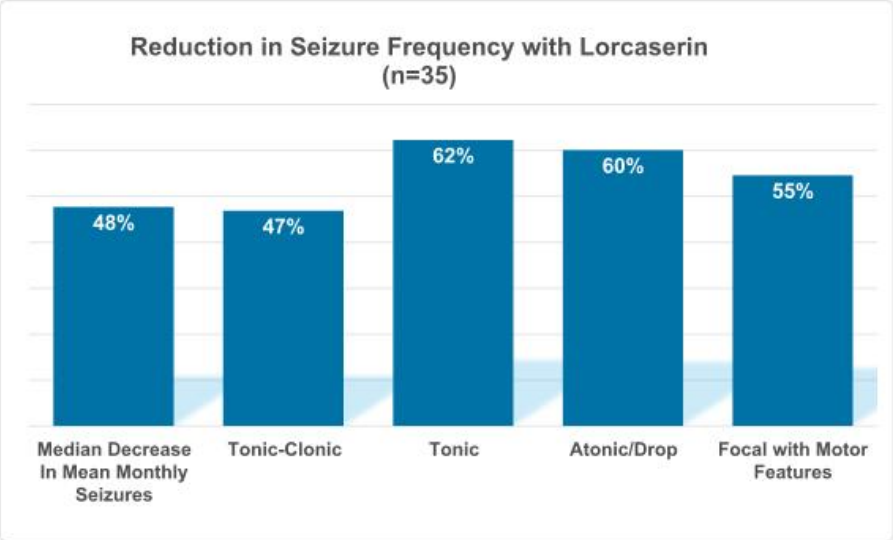
5-HT2c Agonists Have Shown Real World Evidence in Epilepsy, However Significant Unmet Need Remains

	FINTEPLA® DS (fenfluramine, ZX008)	Lorcaserin
History	Pulled from market in 1997 because of high incidence of cardiac valvular abnormalities found in patients (originally marketed as appetite suppressant) • Norfenfluramine (active metabolite) implicated in cause of valvular heart disease (VHD) and pulmonary arterial hypertension (PAH)	Pulled from market March 2020 for numerical, not significant, increase in malignancies in patients treated for obesity; lorcaserin (n=462) vs. placebo group (n=423) difference of only 39 participants (0.33%) • Risk / Benefit low in obesity • Population predisposed to cancer • Despite market removal, FDA authorized evaluation in Dravet syndrome and compassionate use
Clinical Evidence	Successful Ph 3 in Dravet syndrome: — 54.0% (95% CI, 35.6%-67.2%; P < 0.001) greater reduction in mean monthly convulsive seizure frequency vs placebo	Multi-center retrospective chart-review (n=35): — 48% reduction in mean monthly motor seizures — 50% of patients remaining on lorcaserin after 15 months — Durability to remain on treatment
Safety Considerations	• Boxed warning for VHD and PAH • Echocardiograms required pre, during and post dosing • Available only through restricted drug distribution program, under a risk evaluation and mitigation strategy (REMS) program	• TBD for Dravet syndrome
Status	• Approved in treatment of seizures associated with DS Q2 2020 • Positive Ph 3 topline data in LGS Q1 2020; sNDA filed Q3 2021	• Eisai in a Ph 3 program in DS (n=58)

Critical need for highly selective and potent agonist of 5-HT2c that mitigates refractory seizures without significant risks of present drugs

Real World Clinical Evidence of 5-HT2c Agonism Efficacy with Lorcaserin

- 35 refractory patients ranging from 3 - 40 years old (including DS, LGS, treatment resistant focal and generalized seizures)
- Failed at least 5 and up to 9+ previous AED medications
- 47.7% median percentage reduction in mean monthly frequency of motor seizures from baseline
- 15 patients (42%) had a >50% reduction in motor seizures



After 15 months, 50% of patients remained on lorcaserin supporting durability of response

Tolete, et al. Neurology 2018;91:637-839

Lorcaserin Single-Site Cohort at Children's Hospital (Aurora, CO)

Patient	1	2	3	4	5
Age	10	18	10	7	14
Weight (kg)	28	46	23	24	35
Dose	.25	.27	.19	.32	.31
Prior AED's	CLZ, CZP, KD, LMT, LBT, PRM, OXC, RUF, TPX, VPA	CBZ, CBD, CLZ, CLB, CZP, FBM, LMT, LVT, PRM, PHB, TPM, VPA, CC, KD, VNS	ESM, FBM, LMT, LVT, MSM, VPA, VMP, ZNM, KD	CZP, ESM, LVT, LZP, STP, TPM, ZNM, KD	CBZ, FBM, GBP, LCM, LMT, LVT, OXC, PHB, PRED, RUF
Concurrent AEDs	CLB, STP, VPA	CZP, STP, ZNM	KD, TPM, VPA	BRO, CBD, CLB, VPA	CLB, TPX, VPA
Prior seizure type / frequency	• FS: 50/day • GTC clusters: 1/mon	• MS: numerous daily • PS+GTC: 10/mon	• MS: Daily • GTC seizures: 100/month	• AS: 12/h • FS: 3-5/wk	• MS: constant through day • GTC seizures: 1-2/wk
Seizure frequency after 3 months trt	• **Seizure free initial 3wks** • Cluster seizures then seizure free for 2wks	• Seizure free for 2wks • PS+GTC: 1/mon • MS: occasional • **90% reduction in GTC**	• GTC seizures: 46/mon • MS: daily • **> 50% reduction in GTC/mon**	• NCS: 1/mon • **1-2 seizure free days/wk** • AS or PS: 3/Mon	• MS: initially reduced in morning then increased to constant - late afternoon • GTC: 1-2/wk
Seizure frequency after trt. following first 3 months	Gradual increase with return to BL frequency	• MS: 1-2/wk • PS+GTC: 1-2/mon	Gradual decrease to 16/mon before returning to BL	NCS: 1/mon	Unchanged. Tapered off with no change in frequency
Duration on trt.	12 mon (still on trt.)	12 mon (still on trt.)	14 mon, stopped to participate in FFA study	13 mon	9 mon
Reported side effects	none	none	Vomiting, decreased appetite	Decreased appetite	Decreased appetite

Seizure reductions and ability to remain on treatment was demonstrated in all 5 participants

Griffin A, BRAIN 2017: 140; 669–683
AS = atonic seizures; FS = focal seizures; GTC = generalized tonic clonic seizures; MS = myoclonic seizures; NCS = non-convulsive status;

Fenfluramine Approved for DS Associated Seizures, but Removed from Market for Weight Loss in 1997 After Link to VHD and PAH

Fenfluramine lacks sensitivity: potent 5-HT2b agonism implicated in cardiac side effects

Heart Disease > News >

Lasting Damage From Fen-Phen Drug?

Study Shows Lingering Heart Valve Problems in Former Users of Banned Obesity Drugs Fenfluramine and Dexfenfluramine

By Miranda Hitti

Nov. 5, 2008 -- Two banned obesity drugs may have lingering effects on the heart, according to a new study.

The study shows that heart valve problems linked to the banned obesity drugs fenfluramine and/or dexfenfluramine typically last years after stopping those drugs.

Retrospective Analysis Fenfluramine Treatment in Dravet

Pt	Age	Dose Daily (mg/kg)	No. of Echos Performed	Previous Echo	Most Recent Echo (2016)
1	30	.12	6	2012: slightly thickened AML without dysfunction. 2014: Normal	Normal
2	41	.26	9	2015: trace mitral regurg; no valvular heart disease	No valvular heart disease; mild LV dysfunction (grade 1)
3	31	.27	4	2010-2015: stable slight thickened aortic and tricuspid leaves w/out dysfunction	Stable slight thickened aortic and tricuspid leaves w/out dysfunction
4	26	.33	7	2013-2015: stable slight thickened AML & tricuspid leaves w/out dysfunction	Stable slight thickened AML + tricuspid leaves w/out dysfunction
5	23	.27	11	2014: slight thickened AML & tricuspid leaves w/out dysfunction	Normal
6	28	.20	7	Normal at all exams	Trace mitral regurg
9	19	.29	7	Normal at all exams	Trace mitral regurg
10	21	.24	7	2013: slight thickened AML w/out dysfunction 2014&2015: Normal	Trace mitral regurg
11	20	.19	6	2010,2013 slight thickened AML w/out dysfunction. 2014: Normal	Trace mitral regurg
12	9	.42	9	Normal at all exams	Normal

A.-S. Schoonjans et al., Current Medical Research and Opinion, 2017 VOL. 33, NO. 10, 1773–1781

Limitations of FINTEPLA®

FINTEPLA is Non-Selective

FINTEPLA is a 5-HT2 agonist with activity on the 5-HT2b receptor subtype, therefore, can cause off-target cardiovascular adverse events

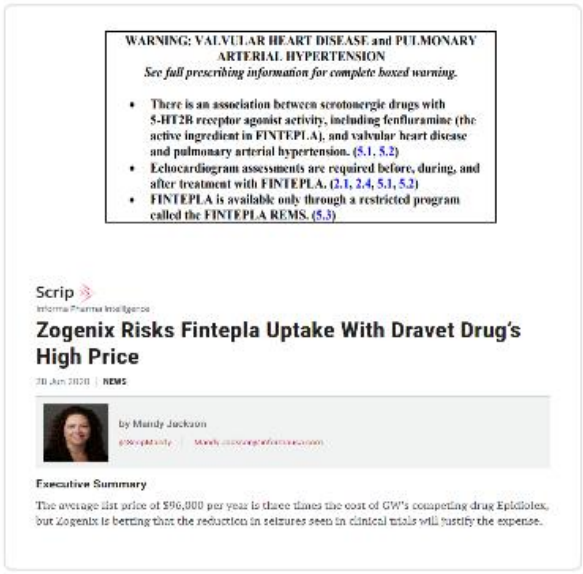
And Carries Fenfluramine's Stigma

Black box warning and Risk Evaluation and Mitigation Strategy (REMS) program requires echo before, during and after treatment

With a High Price

Average list price is high at $96,000/year and can reach up to $180,000/year at higher doses

In comparison, Epidiolex at a significantly lower price $32,500/year, is also approved for DS



WARNING: VALVULAR HEART DISEASE and PULMONARY ARTERIAL HYPERTENSION

See full prescribing information for complete boxed warning.

- **There is an association between serotonergic drugs with 5-HT2B receptor agonist activity, including fenfluramine (the active ingredient in FINTEPLA), and valvular heart disease and pulmonary arterial hypertension. (5.1, 5.2)**
- **Echocardiogram assessments are required before, during, and after treatment with FINTEPLA. (2.1, 2.4, 5.1, 5.2)**
- **FINTEPLA is available only through a restricted program called the FINTEPLA REMS. (5.3)**

Scrip

Zogenix Risks Fintepla Uptake With Dravet Drug's High Price

28 Jun 2020 | NEWS

by Mandy Jackson

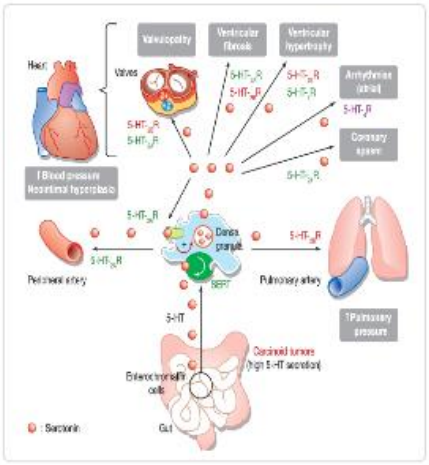
Executive Summary

The average list price of $96,000 per year is three times the cost of GW's competing drug Epidiolex, but Zogenix is betting that the reduction in seizures seen in clinical trials will justify the expense.

https://www.ncbi.nlm.nih.gov/books/NBK349321/
https://odp.idaho.gov/wp-content/uploads/sites/114/2018/11/Epidiolex-Legislative-Fact-sheet_11-7-18.pdf

LP352 Designed to be a Next-Generation 5-HT2c with Greater Selectivity and Specificity

	Serotonin Receptor Subtype	EC_{50}, nM	Ki, nM	Selectivity 2c vs 2b	Selectivity 2c vs 2a	Noted Side Effects
LP352 5-HT2c Superagonist	**5-HT2c**	**~120**	**~50**	**>200x**	**>200x**	Headache, Nausea, Weight Loss
	5-HT2b	>10,000	>10,000			
	5-HT2a	>10,000	>10,000			
Nordexfenfluramine (an active metabolite of fenfluramine) [1]	5-HT2c	72.4	10.4	0.94x	11.5x	Headache, Nausea, Weight Loss
	5-HT2b	25.7	9.8			Valvular Heart Disease and Pulmonary Arterial Hypertension
	5-HT2a	1778	120.2			Insomnia
Lorcaserin [2]	5-HT2c	39	13	11.3x	7.1x	Headache, Nausea, Weight Loss
	5-HT2b	2380	147			
	5-HT2a	553	92			Insomnia



LP352 selectivity may limit off-target effects associated with currently available non-selective AEDs

1 Third party study previously commissioned by Arena, 2 BELVIQ FDA approved prescribing information 06/2012
Note: The above table is for illustrative purposes only and is not a head-to-head comparison. Differences exist between in vitro study designs and methodologies, and caution should be exercised when comparing data across studies.

LP352 Ph 1 Trial – Favorable Safety, Tolerability, Pharmacokinetics and Pharmacodynamics Observed

Randomized, double-blind, placebo-controlled, 4-part trial in healthy adult males and females (N=83)

Single ascending dose

Single-dose food effect

(N=40)

Pharmacokinetics

- Target plasma exposure (C_{min}) based on prolactin PK/PD
- No clinically meaningful effect of food on $AUC_{0\text{-}inf}$ and C_{max}

Safety & Tolerability

- Majority of AEs were mild to moderate (most common was headache)
- AEs generally consistent with expected CNS effects and expected effects of serotonergic drugs
- No SAEs reported

Multiple ascending dose

Dose titration

(N=43)

Pharmacokinetics

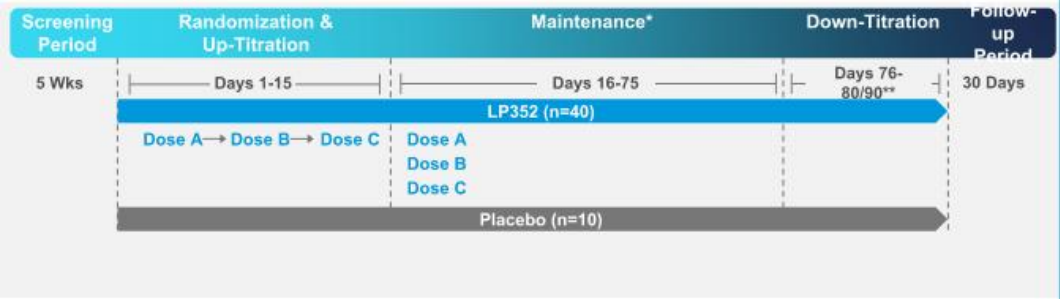
- Central 5-HT2c receptor engagement demonstrated by dose- and exposure-dependent increases of prolactin
- Dose-dependent increases in exposure (C_{max} and AUC_{tau})

Safety & Tolerability

- Majority of AEs were mild to moderate (most common was headache)
- AEs generally consistent with expected CNS effects and expected effects of serotonergic drugs
- At the maximum planned dose, a single SAE of anxiety was reported two days after last dose of study drug and subsequently resolved

Ph 1b/2a trial expected to initiate in Q1 2022

LP352 Ph 1b/2a PACIFIC Study in Patients with DEEs



A double-blind, placebo-controlled study to assess the safety, tolerability and pharmacokinetics of LP352 and

Key Efficacy Signals:

- **Evaluate reduction in seizures across a broad group of epilepsies**
- **Identify potential indications for pivotal studies**
- **Analyze concentration response to understand dosing in different seizure types and disorders**

Basic Information:

Sites: ~25 sites in North America

Ages: ≥ 18 to ≤65 years old with potential to add adolescents at a future date

Key Inclusion Criteria:

- Developmental and epileptic encephalopathies (several syndromes) with ≥ 4 motor seizures per month in 3 mos. prior to screening and ≥ 4 motor seizures in the month of screening

Key Exclusion Criteria:

- Use of stiripentol, fenfluramine, & lorcaserin

Initiating in Q1 2022; Expected Completion: 2H 2023

* Maintenance Dose of LP352 (TID): Dose A, Dose B, Dose C or placebo TID
** Up to a 15-day down-titration/taper period (reducing dose every 5 days) depending on the last maintenance dose
Pending feedback from regulatory agencies

LP352 Summary

Addressable and unsatisfied orphan disease opportunity

Clinical Trial and Real-World Evidence supports significant potential of 5-HT2c agonism in managing refractory seizure disorders

Designed to be more selective and specific than other 5-HT2c agonists

Strong IP potentially out to 2041 in the U.S.

- **LP352's potential for receptor selectivity and specificity position it as an attractive compound to evaluate for the treatment of DEEs**
- **Completed Ph 1 SAD/MAD trials**
- **Next steps: Ph 1b/2a trial expected to start Q1 2022**

LP143

Centrally Acting Full Agonist to the Cannabinoid Type 2 (CB2) Receptor Targeting a Broad Range of Neurodegenerative Diseases

LP143 Summary

Potential to Redefine Treatment of Neurodegenerative Diseases

CB2 Evidence in CNS Diseases:

- Microglial cells are critical for neuron homeostasis - In neurodegenerative disease, microglial cells activate triggering a shift from neuroprotective to proinflammatory phenotypes
- Inflammatory processes in non-neuronal cells have shown to play an important role in driving motor neuron degeneration
- CB2 receptors primarily located on microglia, with some expression in astrocytes and neurons
- Preclinical data indicate that CB2 agonism has the potential to restore the neuroprotective phenotype of microglial cells
- Preclinical support exists for indications including:
  - ALS – Longboard initial focus
  - Alzheimer's
  - Parkinson's
  - Huntington's

LP143:

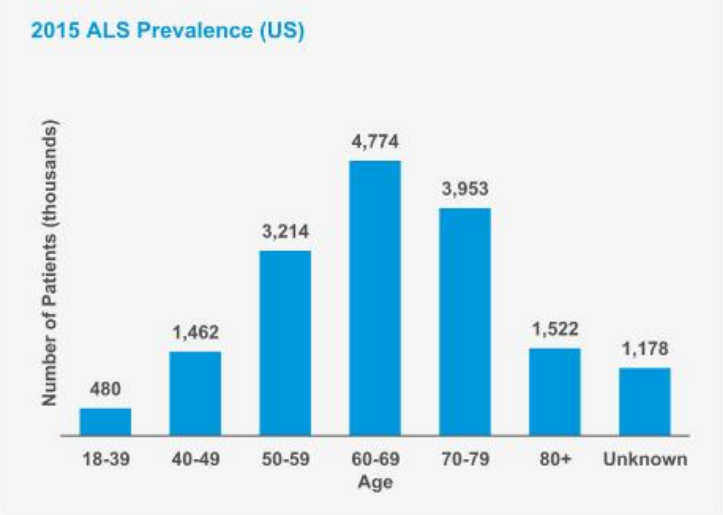
Designed to be a centrally acting full CB2 agonist with the following preclinical observations and design features:

- High brain-to-plasma ratio
- Demonstrated to be 1000x more selective for CB2 than CB1 in preclinical models; Selectivity for CB2 potentially reduces risk of psychoactive effects and abuse liability
- High oral bioavailability
- Designed to internalize the CB2 receptor / no tachyphylaxis

ALS is an Orphan Motor Neuron Disease with Poor Prognosis

Average time from diagnosis to paralysis and death from respiratory failure is 2-5 years

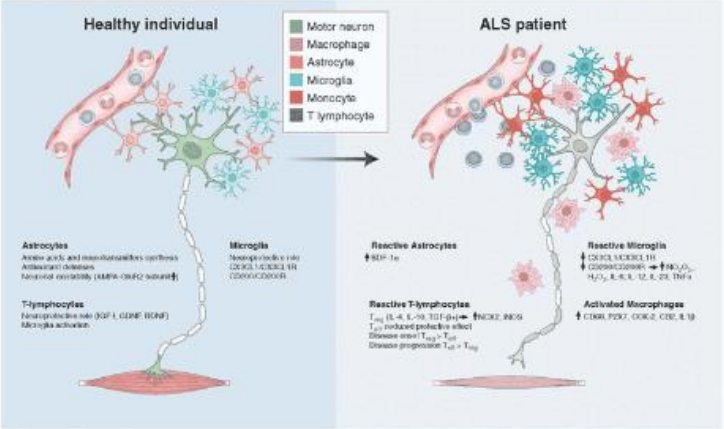
- **Progressive neurodegenerative disease** that affects upper and lower motor neurons (MNs)
- Characterized by **rapid progression** of muscle wasting and weakness. Patients typically present with weakness, spasticity, cachexia, and/or slurred speech
- Incidence 2 per 100,000 (most diagnosed 55-65 years)
- US National ALS Registry identified 16.6K people living with ALS, and 29K estimated in EU as of 2015
- Approved treatments provide limited benefit - No significant benefit in survival curves



Mehta P, Kaye W, Raymond J, et al. Prevalence of Amyotrophic Lateral Sclerosis —United States, 2015. MMWR Morb Mortal Wkly Rep 2018;67:1285–1289. DOI:http://dx.doi.org/10.15585/mmwr.mm6746a1External

Neuroinflammation Mediated by Microglial Activation Plays an Important Role in ALS Progression

- Inflammatory processes in non-neuronal cells have been shown to play an important role in driving motor neuron degeneration
- Studies of ALS animal models show that microglial cells **initially** have a **neuroprotective** phenotype that promote tissue repair and enhance motor neuron survival in the early, slowly progressive stages of the disease
- At the later, **more rapidly progressing disease** stage, microglial cells **shift to a neuroinflammatory phenotype** that is toxic to motor neurons



Cross-talk between motor neurons, astrocytes, and immune cells (including microglia, T lymphocytes, and macrophages) in a healthy individual (a) and an ALS patient (b)

Rizzo, F., Riboldi, G., Salani, S. et al. Cell. Mol. Life Sci. (2014) 71: 999. https://doi.org/10.1007/s00018-013-1480-4

Increased CB2 Receptor Expression in Brain of ALS Patients

Human ALS motor cortex – increase in CB2 receptors (Fig 1)**, but no changes in CB1 receptors or monoacylglycerol lipase (MAGL) and Fatty Acid Amide Hydrolase (FAAH) enzymes** (Fig 2)

Figure 1

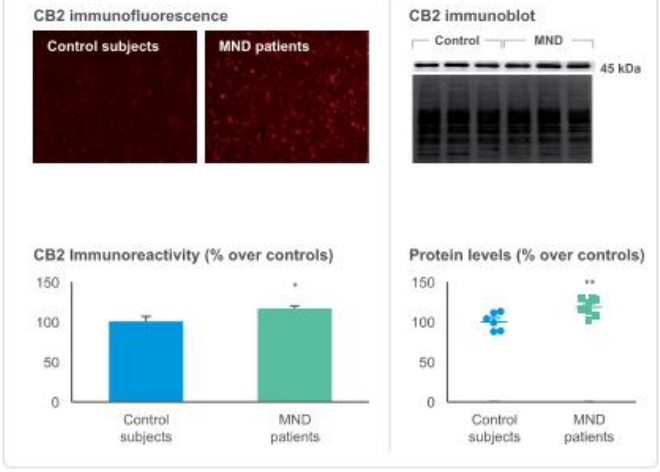
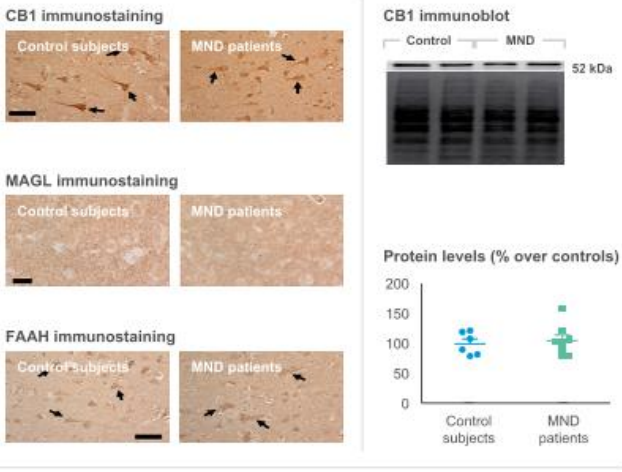


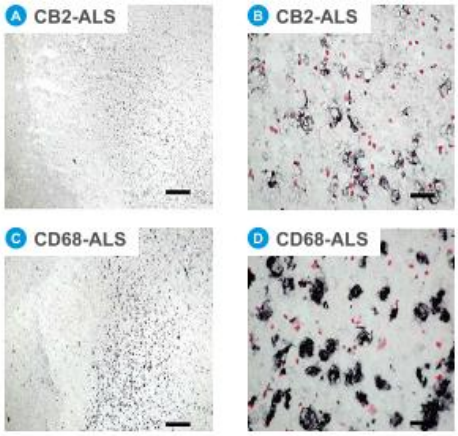
Figure 2



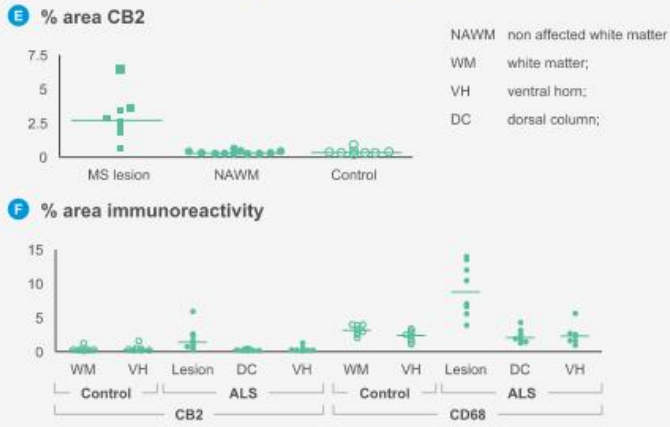
MND = Motor Neuron Disease
Espejo-Porras et al., 2018, https://doi.org/10.1080/21678421.2018.1425454

Increased CB2 Receptor Expression in Spinal Cord of ALS Patients

ALS spinal cord (A-D)



CB2 receptors are increased in lesion areas with microglial cells (CD68 marker) (E-F)



Yiangou et al., 2006, https://doi.org/10.1186/1471-2377-6-12.

Preclinical Data Indicate that CB2 Agonism Has the Potential to Restore the Neuroprotective Phenotype of Microglial Cells

- CB2 activation has shown **beneficial effects in animal models** of ALS:
  - Reduced microglial mediated neuroinflammation, excitotoxicity and oxidative cell damage
  - Inhibited release of pro-inflammatory cytokines
  - Inhibited glutamate release
- Neuroinflammation has also been suppressed in Alzheimer's animal models where it is associated with improvements in neuronal plasticity and memory

Study Reviewed Evidence Supporting Use of Cannabinoids to Treat ALS

Joana Fernandes, PhD

Feb. 2017

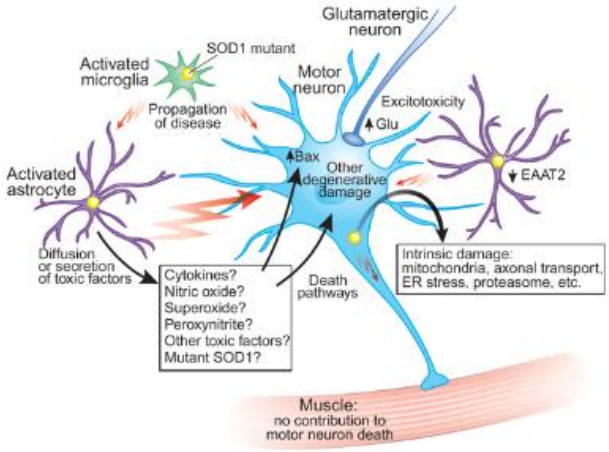
ALS NEWS TODAY

"The spinal cord of ALS patients has been shown to present motor neuron damage triggered by immune system's cells (microglia/macrophages) that express increased levels of the CB2 receptor. So all these data show how editing CB2-mediated processes could change ALS progression and how much the endocannabinoid system is potentially involved in reducing neuroinflammation, excitotoxicity and oxidative cell damage."

https://alsnew stoday.com/2017/02/28/can-cannabinoids-be-a-potential-therapeutic-tool-in-amyotrophic-lateral-sclerosis/Giacoppo and Mazzon 2016, https://doi.org/10.4103/1673-5374.197125

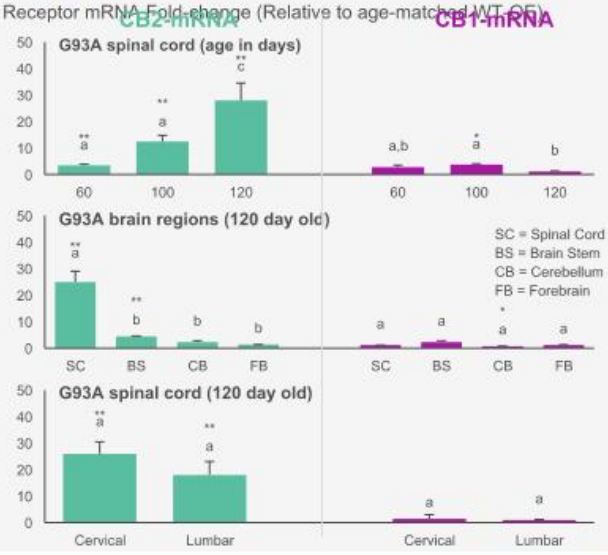
Increased CB2 Receptor Expression in Experimental Model of ALS (hSOD1^{G93A} mice)

- Transgenic mice overexpressing human mutated SOD-1 enzyme
- Validated ALS model



hSOD1^{G93A} - Increase in CB2, but not CB1 receptors

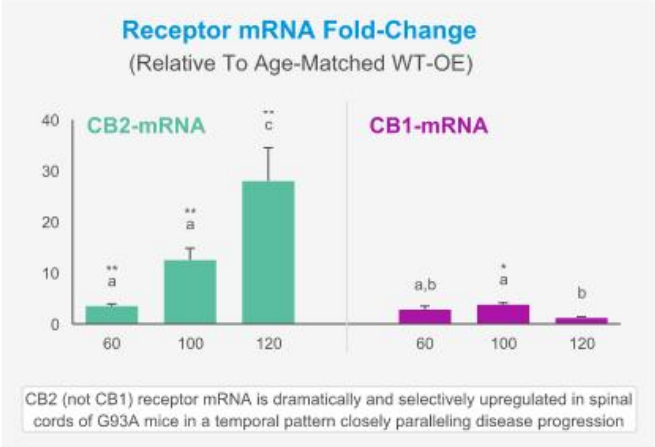
Receptor mRNA Fold-change (Relative to age-matched WT-OE)



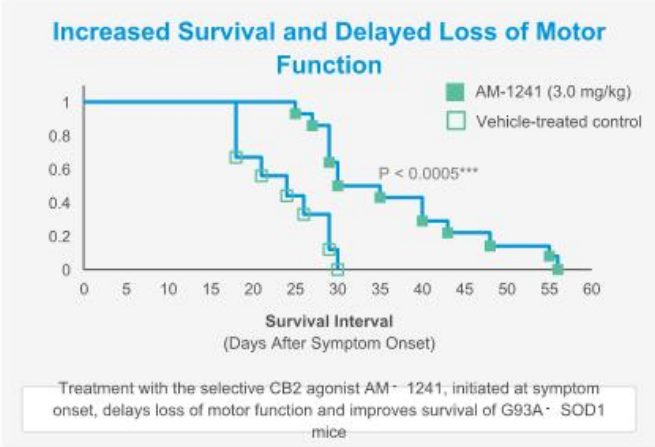
Shoemaker et al., 2007, https://doi.org/10.1111/j.1471-4159.2006.04346.x; http://lougehrigs.tumblr.com/post/22791452671/mutant-sod1-caused-intrinsic-damage-to-motor

CB2 Receptor was Upregulated and Treatment with CB2 Receptor Agonist Prolonged Survival in Model of ALS

CB2 receptor agonist AM1241 has demonstrated **delayed loss of motor function and improved survival** in an experimental mouse model of ALS (hSOD1G93A)



CB2 (not CB1) receptor mRNA is dramatically and selectively upregulated in spinal cords of G93A mice in a temporal pattern closely paralleling disease progression



Treatment with the selective CB2 agonist AM‑1241, initiated at symptom onset, delays loss of motor function and improves survival of G93A‑SOD1 mice

Kim et al., 2006, https://doi.org/10.1016/j.ejphar.2006.05.025; J Neurochem.2007 Apr;101(1):87-98 10.1111/j.1471-4159.2006.04346

LP143 Summary

CB2 pathway involved in multiple neuroinflammatory orphan disease state opportunities including ALS

Centrally acting full agonist of the CB2 receptor with high brain to plasma ratio and high oral bioavailability

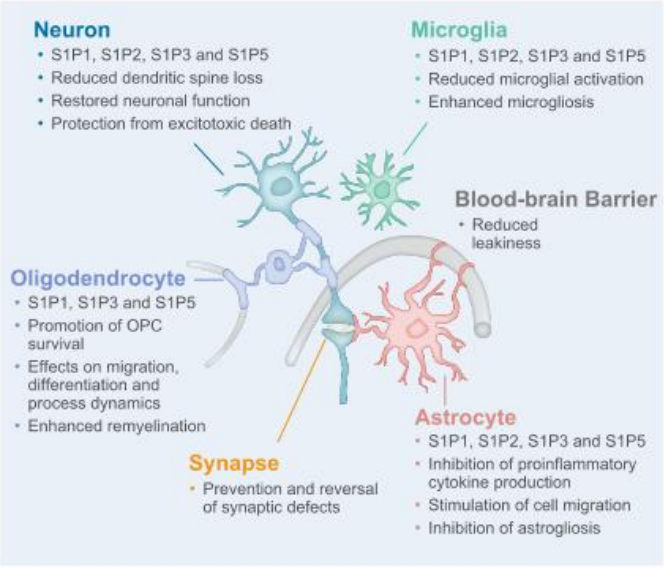
Selective CB2 receptor agonist delayed loss of motor function and improved survival in preclinical ALS model

- **LP143: Centrally acting CB2 agonist, has the potential to redefine multiple neurodegenerative diseases**
- **Next steps: Ongoing preclinical & IND-enabling work, IND submission expected Q1 2022**

LP659

Centrally Acting Sphingosine-1-Phosphate (S1P) Receptor Modulator Targeting a Range of Neurodegenerative Diseases

LP659 Potential to Redefine Treatment of Multiple Grievous, Underserved Neurodegenerative Diseases



LP659

- Designed to be a centrally acting S1P receptor modulator, addressing a wide range of neurodegenerative diseases
- High oral bioavailability with direct impact on CNS glial cell S1P receptors
- Rapid onset and offset of action
- S1P1 selectivity with no impact on S1P2 or 3 in preclinical models

S1PRM Potential Indications and Rationale

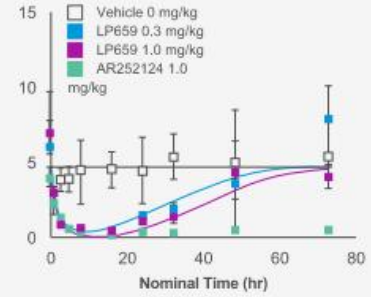
- S1P1, 5 are expressed in the CNS across the microglial, neuron, astrocyte and oligodendrocyte cells
- S1P receptor modulation may play a role in various neurodegenerative diseases including MS, Parkinson's, Rett syndrome, Epilepsy, Huntington's, ALS, etc.
- S1P receptor modulators have generated billions of dollars of revenues in MS

Fingolimod as a Treatment in Neurologic Disorders Beyond Multiple Sclerosis

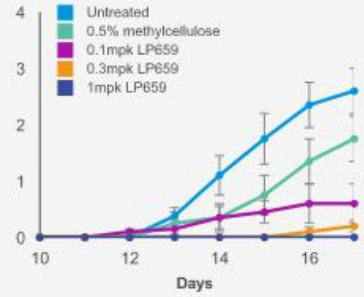
LP659 Favorable Efficacy and Safety Results Observed in Preclinical MOG-EAE Model

- MOG-EAE is a widely accepted model of demyelinating disease (ex. MS)
- Pretreatment of LP659 reduced incidence and disease severity of MOG-EAE in murine model
- LP659 rapidly reduced circulating lymphocytes, which returned to baseline after clearance of LP659
- No notable impact observed on heart rate, mean arterial pressure or body temperature (30 mg/kg)

Lymphocyte Reduction (PO, single dose)
(Lymphocytes (cells 10^3/µl))



Mean disease score: MOG-EAE Model
(Prophylactic, n=12 mice/grp, PO, QD from day 3)



Dose-dependent decrease in disease progression based upon clinical scoring (0-5) after disease induction

All PK/PD studies in male Sprague-Dawley rats. Data on file.MOG-EAE, myelin oligodendrocyte glycoprotein-induced experimental autoimmune encephalomyelitis; MS, multiple sclerosis

LP659 Summary

Designed to provide centrally acting S1P receptor modulation, with no impact on S1P2 or 3

High brain to plasma ratio suggests LP659 has the potential to address a wide range of neurodegenerative diseases

Oral bioavailability with rapid onset and offset of action

- **LP659: Designed to be a centrally acting S1P receptor modulator with potential to transform the treatment of numerous neurodegenerative diseases**
- **Next steps: Ongoing preclinical & IND-enabling work, IND submission expected 2H 2022**

Financial Summary & Key Milestones

Financial Summary

Cash, Cash Equivalents & Investments

$112.6 million

As of September 30, 2021

Shares Outstanding*

17.2 million

As of November 2, 2021

YTD Sep-21 Operating Expenses

$19.0 million

- R&D - $13.4 million
- G&A - $5.6 million

Completed and Expected Key Milestones

* Includes voting and non-voting common shares outstanding, as well as 348,450 shares that are subject to repurchase

LONGBOARD PHARMACEUTICALS

Nasdaq: LBPH