



acertherapeutics

**Developing Therapeutics for the Treatment of
Serious Rare and Life-Threatening Diseases with
Significant Unmet Medical Needs**



Corporate Presentation

July 2020

Nasdaq: ACER

Forward-looking Statements

This presentation contains “forward-looking statements” that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this presentation regarding strategy, future operations, timelines, future financial position, future revenues, projected expenses, regulatory submissions, actions or approvals, cash position, liquidity, prospects, plans and objectives of management are forward-looking statements. Examples of such statements include, but are not limited to, statements relating to expectations regarding our capital resources; the potential for emetine, EDSIVO™ (celiprolol), ACER-001 and osanetant to safely and effectively treat diseases and to be approved for marketing; the commercial or market opportunity of any of our product candidates in any target indication and any territory; the adequacy of our capital to support our future operations and our ability to successfully initiate and complete clinical trials and regulatory submissions; our progress toward possible approval for EDSIVO™ in light of the Complete Response Letter we received June 2019 and the Formal Dispute Resolution Request response letter received March 2020; the ability to protect our intellectual property rights; our strategy and business focus; and the development, expected timeline and commercial potential of any of our product candidates. We may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in the forward-looking statements and you should not place undue reliance on these forward-looking statements. Such statements are based on management’s current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors, including, without limitation, risks and uncertainties associated with the ability to project future cash utilization and reserves needed for contingent future liabilities and business operations, the availability of sufficient resources to meet our business objectives and operational requirements, the fact that the results of earlier studies and trials may not be predictive of future clinical trial results, the protection and market exclusivity provided by our intellectual property, the substantial costs and diversion of management’s attention and resources which could result from pending securities litigation, risks related to the drug development and the regulatory approval process, including the timing of regulatory actions, and the impact of competitive products and technological changes. We disclaim any intent or obligation to update these forward-looking statements to reflect events or circumstances that exist after the date on which they were made. You should review additional disclosures we make in our filings with the Securities and Exchange Commission, including our Quarterly Reports on Form 10-Q and our Annual Report on Form 10-K. You may access these documents for no charge at <http://www.sec.gov>.

Corporate Overview

Acer Therapeutics is a pharmaceutical company that acquires, develops and seeks to commercialize therapies for serious rare and life-threatening diseases with significant unmet medical needs

- Headquartered: **Newton, MA**
- Headcount: **19**
- Founded: **December 2013**
- Public: **September 2017**
- Cash: **\$7.0M** as of March 31, 2020
 - Expected to have sufficient capital to fund current operations into Q4 2020, excluding:
 - Planned emetine clinical trial
 - Support for EDSIVO™ development and precommercial activities

Leadership Team

<p>Chris Schelling CEO & Founder</p>	<ul style="list-style-type: none"> • 20 years; strategic commercial development & orphan 	
<p>Harry Palmin Chief Operating & Financial Officer</p>	<ul style="list-style-type: none"> • 25 years; corporate & finance experience 	
<p>Matt Seibt Chief Commercial Officer</p>	<ul style="list-style-type: none"> • 22 years; sales, market access & product launch 	
<p>John Klopp Chief Technical Officer</p>	<ul style="list-style-type: none"> • 18 years; orphan manufacturing & commercialization 	
<p>Don Joseph, JD Chief Legal Officer & Secretary</p>	<ul style="list-style-type: none"> • 25 years; general counsel & senior management 	
<p>Renee Carroll VP, Regulatory Affairs</p>	<ul style="list-style-type: none"> • 25 years; regulatory affairs in all phases of development 	
<p>Nancy Duarte-Lonnroth VP, Quality</p>	<ul style="list-style-type: none"> • 20 years; quality assurance, control and management 	

Investment Highlights

- Acer's pipeline includes four clinical-stage product candidates:
 - **Emetine** for the treatment of COVID-19
 - **EDSIVO™** (celiprolol) for the treatment of vascular Ehlers-Danlos syndrome (vEDS) in patients with a confirmed type III collagen (COL3A1) mutation
 - **ACER-001** (a taste-masked, immediate release formulation of sodium phenylbutyrate) for the treatment of various inborn errors of metabolism, including urea cycle disorders (UCDs) and Maple Syrup Urine Disease (MSUD)
 - **Osanetant** for the treatment of induced Vasomotor Symptoms (iVMS) where Hormone Replacement Therapy (HRT) is likely contraindicated
- Product candidates are believed to present a comparatively de-risked profile, having one or more of:
 - Favorable safety profile; clinical proof-of-concept data; mechanistic differentiation
 - Potential expedited paths for development through specific FDA-established programs
- Multiple anticipated key regulatory milestones:

✓ Emetine NCATS collaboration signed; discussions w/FDA ongoing:	Q2 2020
• Emetine IND submission:	Q3 2020
• Emetine Phase 2/3 trial initiation*§:	Q3 2020
• Osanetant IND submission:	Q4 2020
• Osanetant initiate Phase 1/2*§:	H1 2021
• ACER-001 (UCD) NDA submission**§:	H1 2021
- Expected to have sufficient capital into Q4 2020, excluding support for the planned emetine trial and EDSIVO™ development and precommercial activities

Clinical Pipeline

Program / Indication	Novel MOA / Unique Characteristics	Preclinical	Phase 1	Phase 2	Phase 3	
Emetine Hydrochloride						
COVID-19	Third party studies have shown broad-acting antiviral inhibition					
EDSIVO™ (celiprolol)						
vascular Ehlers-Danlos syndrome (COL3A1+)	Induces vascular dilatation and smooth muscle relaxation					
ACER-001 (taste-masked, immediate-release form of sodium phenylbutyrate)						
Urea Cycle Disorders	Taste-masked formulation; evaluating bioequivalence to BUPHENYL®					
Maple Syrup Urine Disease	Inhibition of BCKD kinase to increase BCAA metabolism					
Osanetant						
Induced Vasomotor Symptoms (iVMS)	Neurokinin 3 Receptor Antagonist					

*Initiation of Phase 2/3 trial subject to successful IND submission and clearance, and sufficient capital resources to fund the program

**Response received March 2020 denying appeal of the Complete Response Letter but describing possible paths forward for Acer to explore that could provide the substantial evidence of effectiveness needed to support a potential resubmission of the EDSIVO™ NDA

***Pivotal bioavailability and bioequivalence (BE) trial

Emetine Overview

Disease Overview

- **Global pandemic with no currently approved therapeutic options for COVID-19 outpatients**
- Highly contagious and spread via respiratory droplets, direct contact, and if aerosolized, airborne routes
- Approximately 12 million cases and 550,000+ deaths worldwide (as of 7/8/2020)

Mechanism of Action

- **Host-targeting therapy with potent antiviral activity**
- Restores cellular stress response, inhibiting viral replication
- Believed to be the only drug in development exploiting this MOA

Product Profile

- **Broad-acting antiviral in development for patients with COVID-19; potential application against other viruses**
- Acer, in collaboration with NCATS, is believed to be the only company developing emetine as a potential COVID-19 treatment
- Used previously in humans as an antiprotozoal, emetic, and antiviral agent
- Potential benefit against other viruses: Dengue, Zika, Ebola, MERS, SARS

The Opportunity

- **Ongoing discussions with FDA following pre-IND feedback; targeting Phase 2/3 trial initiation in Q3[§]**
- Proposed trial will evaluate emetine in high-risk, symptomatic adult patients with COVID-19 infection not requiring hospitalization
- Pursuing several financing options, including federally-funded research and grants
- Acer to oversee supply and contract manufacture of emetine

[§]Subject additional capital

^{*}Subject to successful IND submission and clearance



Emetine: History

- Emetine is one of the main alkaloids found in ipecacuanha (ipecac) root
- Clinically, emetine hydrochloride was originally marketed in the U.S. as a topical anti-infective in dental applications (ca 1890s by Eli Lilly and Company)
- Later, emetine hydrochloride for injection gained market adoption as a specific treatment for amebic infections and was used for this purpose through the 1980s in the U.S. until its market displacement by metronidazole
 - On WHO's Essential Medicines List until ~1980
- An oral formulation, syrup of ipecac, also contains emetine as one of its active ingredients
- Substantial clinical experience with emetine and emetine-containing products exists because of their introduction in the U.S. prior to the 1938 Food, Drug, and Cosmetic Act, and especially the development of an over-the-counter monograph for syrup of ipecac
- Its broad antiviral activity has only been discovered in the past decade



Emetine: Broad & Potent Antiviral Activity

- Clinically, emetine has been used to treat approximately 700 patients (including pediatrics) with viral hepatitis¹ and varicella-zoster virus²
- The antiviral activity of emetine in various *in vitro/in vivo* models is provided below:

Virus Type	Antiviral Activity*	Reference
SARS-CoV-2 (Caco-2)	IC₅₀ = 0.47 µM	Bojkova et al. Proteomics of SARS-CoV-2-infected host cells reveals therapy targets. Nature https://doi.org/10.1038/s41586-020-2332-7 (2020).
SARS-CoV-2 (Vero-E6)	EC₅₀ = 0.46 µM**	Choy et al. Antiviral Research. 2020 Apr 3; pre-proof https://doi.org/10.1016/j.antiviral.2020.104786
SARS-CoV-2 (Vero-E6)	EC₅₀ < 0.01 µM	lanevski et al. 2020 May. Antiviral options against SARS-CoV-2 infection. doi.org/10.1101/2020.05.12.091165
HCoV-OC43	EC₅₀ = 0.30 / CC₅₀ = 2.69	Shen et al. J Virol. 2019 May 29;93(12). pii: e00023-19. doi: 10.1128/JVI.00023-19.
HCoV-NL63	EC₅₀ = 1.43 / CC₅₀ = 3.63	
MERS-CoV	EC₅₀ = 0.34 / CC₅₀ = 3.08	
MHV-A59	EC₅₀ = 0.12 / CC₅₀ = 3.51	
MERS-CoV	EC₅₀ = 0.014	
SARS-CoV	EC₅₀ = 0.051	Dyall et al. Antimicrob Agents Chemother. 2014 Aug;58(8):4885-93. doi: 10.1128/AAC.03036-14.
ZIKV-MR766	IC₅₀ = 9.15e-009	Yang et al. Cell Discov. 2018 Jun 5;4:31. doi: 10.1038/s41421-018-0034-1.
ZIKV-FSS13025	IC₅₀ = 1.072e-008	
ZIKV-PRVABC59	IC₅₀ = 9.591e-009	
EBOV-Vero E6	IC₅₀ = 16.9 nM	
HSV-2	EC₅₀ = 0.03 / CC₅₀ = 1.12	Andersen et al. Viruses. 2019 Oct 18;11(10). pii: E964. doi: 10.3390/v11100964.
HMPV	EC₅₀ = 0.14 / CC₅₀ = 1	
HIV M184V	EC₅₀ = 0.012 – 0.03	Chaves Valadao et al. Molecules. 2015 Jun 22;20(6):11474-89. doi: 10.3390/molecules200611474.
HCMV	EC₅₀ = 40 nM / CC₅₀ = 8 µM	Mukhopadhyay et al. PLoS Pathog. 2016 Jun 23;12(6):e1005717. doi: 10.1371/journal.ppat.1005717.

EC₅₀ = concentration of a drug that gives half-maximal response. IC₅₀ = concentration of an inhibitor where the response is reduced by half. CC₅₀ = 50% cytotoxic concentration

*EC₅₀ / CC₅₀ values = µM (unless otherwise noted)

**For reference, the EC₅₀ of remdesivir is 23.15 µM at MOI 0.02; paper demonstrates that a combination of remdesivir and emetine shows synergy



Emetine: Uniquely Suited for COVID-19

Nanomolar potency in SARS-CoV-2 in vitro models

- $IC_{50} = 0.47 \mu M^1$
- $EC_{50} = <0.01 \mu M^2$
- Synergy between remdesivir and emetine was observed:
 - Combination: remdesivir ($EC_{50} = 6.25 \mu M$) plus emetine ($EC_{50} = 0.195 \mu M$) may achieve 64.9% inhibition in SARS-CoV-2 viral yield³
 - Single agent: remdesivir ($EC_{50} = 23.15 \mu M$) and emetine ($EC_{50} = 0.46 \mu M$)³

High and long duration lung tissue concentrations⁴

- EC_{50} concentrations of emetine >1,800x higher in the lungs
- Plasma $t_{1/2} = 65-163$ hours
- Tissue $t_{1/2} \geq 30$ days

Clinical experience with parenteral emetine

- 600+ patients with viral hepatitis treated⁵
- 90 patients with herpes zoster treated⁶



1 Bojkova, D. et al. Proteomics of SARS-CoV-2-infected host cells reveals therapy targets. Nature <https://doi.org/10.1038/s41586-020-2332-7> (2020).

2 Ianevski et al. 2020 May. Antiviral options against SARS-CoV-2 infection. doi.org/10.1101/2020.05.12.091165.

3 Choy et al. *Antiviral Res.* 2020 Jun; 178: 104786.

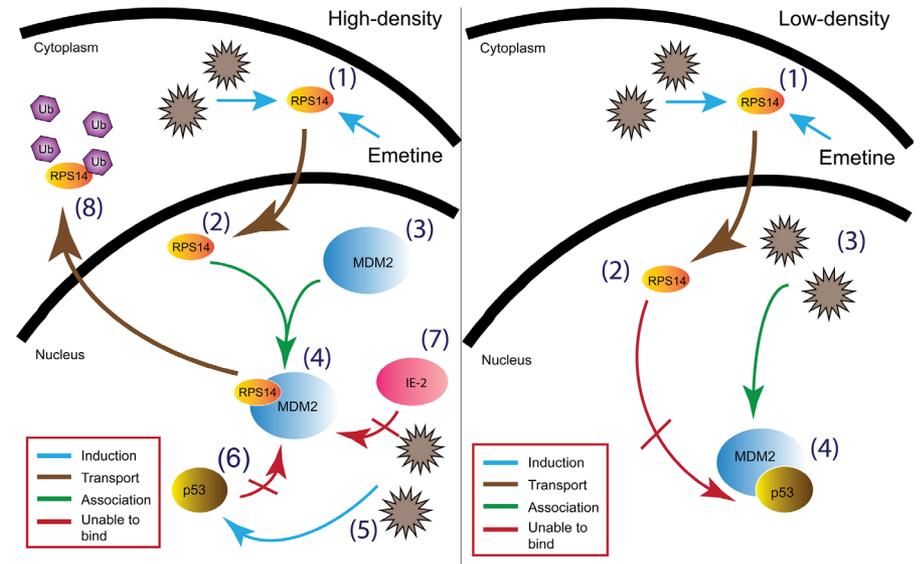
4 Asano et al. *European Journal of Drug Metabolism and Pharmacokinetics* volume 27, pages17–27(2002).

5 Del Puerto et al. *Pren. méd. argent.*, 55: 818, 1968.

6 Annamalai et al. *Emetine Hydrochloride in the Treatment of Herpes Zoster.* 1968.

Emetine: Unique Mechanism of Action

- Viral infections have developed evolutionary mechanisms for inhibiting the cellular stress response and promote ribosome biogenesis to facilitate viral replication
- **Binding of emetine with RPS14 restores the cellular stress response, which results in blocking ribosome biogenesis and translation-elongation of viral mRNA in infected cells**
- Emetine does not inhibit viral replication in null RPS14 cells
- Viral resistance believed to be extremely unlikely given unique MOA



In high-density infected cells (A) emetine induces (1) nuclear translocation of RPS14 (2) followed by RPS14 binding to MDM2 (3 & 4) resulting in disruption of the interaction between MDM2-p53 (6) and MDM2- viral IE2 (5 & 7), and by RPS14 ubiquitination and degradation (8). In low-density infected cells (B) although emetine induces (1) nuclear translocation of RPS14 (2), it is unable to interact with MDM2 (4) which is already bound to p53 to facilitate virus replication (3).

Emetine: Safety

- Patients treated with 1 mg/kg/day emetine daily via SC injection for 10 days (cumulative dose 650 mg) did not experience any notable toxicity¹
- Electrocardiographic abnormalities are seen, but not often associated with significant cardiac symptoms^{2,3,4}
 - T wave inversion (TWI) is the first to appear and the last to disappear
 - Q-T interval prolongation
 - The average time required for complete return of the tracing to normal is ~six weeks
- At higher cumulative doses (e.g. ≥ 650 mg): hypotension, tachycardia, cardiomyopathy, myocarditis, precordial pain, gallop rhythm (on auscultation), dyspnea, cardiac dilatation, congestive failure, and death have been reported⁵
- Toxicity with emetine appears to be cumulative-dose related and independent of schedule^{1,6}
- Complete reversibility of cardiac adverse effects⁶

1 Mastrangelo et al. Cancer 31:1170-1175.

2 Banerjea et al J Assoc Physicians India 14:349-364.

3 Ramachandran et al. Ceylon Med J 18:138-143.

4 Moertel et al. Cancer Chemother Rep 58:229-232, 1974.

5 Bleasel et al. Pharmaceuticals 2020, 13, 51.

6 Siddiqui et al. Cancer Chemother Rep 57:423-428, 1973.



Emetine: Proposed Clinical Trial*

- **Title:** A Phase 2/3 Randomized, Blinded, Placebo-Controlled Clinical Study to Evaluate the Safety and Activity of Emetine Hydrochloride Injection, USP (ACER-2820) in High Risk, Symptomatic Adults with Confirmed SARS-CoV-2 Infection Not Requiring Hospitalization
- **Inclusion**
 - COVID-19+
 - Mildly symptomatic, high risk adults
 - Not requiring hospitalization (outpatient)
 - Part A: 45 patients (PK / safety / efficacy)
 - Part B: 105 patients (efficacy / safety)
 - Part C: 300 patients (efficacy / safety)
- **Endpoints**
 - Clinical endpoints (rate of hospitalization, mortality)
 - Viral load/shedding assessments (quantitative) by nasopharyngeal, saliva/mouthwash and rectal swabs
 - Exploratory laboratory endpoints (antibodies, cytokines, chemokines, D-dimer, ferritin)
- **Doses**
 - Administer subcutaneously (SC) at low doses
 - Arm 1: Single Dose 120 mg x 1 day
 - Arm 2: Multiple Dose 30 mg x 4 days



Emetine: Regulatory Path

- Acer submitted Pre-Investigational New Drug (Type B) expedited (PIND 149290) briefing package on April 14, 2020
- Initial written responses received from Division of Antivirals (DAV) on April 29, 2020 – requested additional PIND information:
 - Systematic Literature Database Search & Integrated Summary
 - Characterize pharmacokinetics (PK) of subcutaneous (SC) administration of emetine in Part A of study
- Provided additional information to FDA on June 24, 2020
- Assuming FDA supports moving forward, Acer aims to submit IND Q3 2020
 - Targeting IND clearance Q3 2020



EDSIVO™ Overview

Disease Overview

- **No approved therapeutic options for vEDS patients**
- Autosomal dominant connective tissue disorder of collagen synthesis caused by mutations in the COL3A1 gene for type III procollagen
- Characterized by arterial aneurysms, dissections and/or ruptures
- Median survival in the U.S. is estimated to be 51 years of age

Mechanism of Action

- **EDSIVO™ has a unique pharmacological profile**
- β 2 and β 3 adrenergic receptor agonist; selective β 1 and α 2 adrenergic receptor antagonist; activates endothelial Nitric Oxide Synthase (eNOS)
- EDSIVO's™ potential beneficial effects in vEDS thought to be through vascular dilatation and smooth muscle relaxation, thereby reducing the mechanical stress on collagen fibers within the arterial wall

Product Profile

- **BBEST Clinical Trial: 64% reduction in risk of arterial events observed¹**
- Statistically-significant improvement in event-free survival (EFS) compared to control in vEDS patients (n=53)¹

The Opportunity

- **FDRR response appeal denied; exploring possible paths forward**
- Evaluating possible next steps with the goal of resubmission of the EDSIVO™ NDA
- Neither resubmission nor the prospect of approval of EDSIVO™ NDA is assured

EDSIVO™: Regulatory Timeline

- **June 2019:** Received CRL from FDA
 - CRL stated it will be necessary to conduct an adequate and well-controlled trial to determine whether celiprolol reduces the risk of clinical events in patients with vEDS
- **December 2019:** Submitted Formal Dispute Resolution Request (FDRR) to the Office of New Drugs (OND)
- **March 2020:** Received OND FDRR response
 - Denied appeal of CRL
 - OND described possible paths forward for Acer to explore that could provide substantial evidence of effectiveness needed to support a potential resubmission of NDA
 - Evaluating possible next steps with the goal of EDSIVO™ NDA resubmission (neither resubmission nor approval is assured)
- Updates to be provided as appropriate and the company may discontinue the process at any point where risk/benefit no longer justifies continued resources

FDA: Substantial Evidence of Effectiveness

THE QUANTITY OF CLINICAL EVIDENCE TO ESTABLISH EFFECTIVENESS

Level of Persuasiveness ↑

Two adequate and well-controlled clinical investigations²

- In many situations FDA requires two adequate and well-controlled trials to establish effectiveness
- This reflects the need for substantiation of experimental results

One adequate and well-controlled investigation plus confirmatory evidence²

- Under certain circumstances and consistent with FDAMA, FDA can conclude that one adequate and well-controlled clinical investigation plus confirmatory evidence is sufficient to establish effectiveness

One adequate and well-controlled investigation¹

- FDA can accept a single adequate and well-controlled trial when the results are highly persuasive such that the single trial provides support comparable to that from two adequate and well controlled studies

Vascular Ehlers-Danlos Syndrome (vEDS)

- Ehlers-Danlos syndrome (EDS) is a group of hereditary disorders of connective tissue
- vEDS (EDS type IV) is the severe subtype:
 - Characterized by aneurysms, dissections and/or ruptures
 - Vascular
 - Hollow Organs (e.g. gastrointestinal, uterine)
 - Autosomal dominant (50%); spontaneous mutations (50%)
 - Diagnosed by clinical symptoms and confirmed by presence of mutations in the COL3A1 gene
 - Events occur in 25% of patients before the age of 20, and 90% by the age of 40
 - Median age of death is estimated to be 51 years¹
- No approved therapeutic options for vEDS
 - Current treatment is focused on surgical intervention

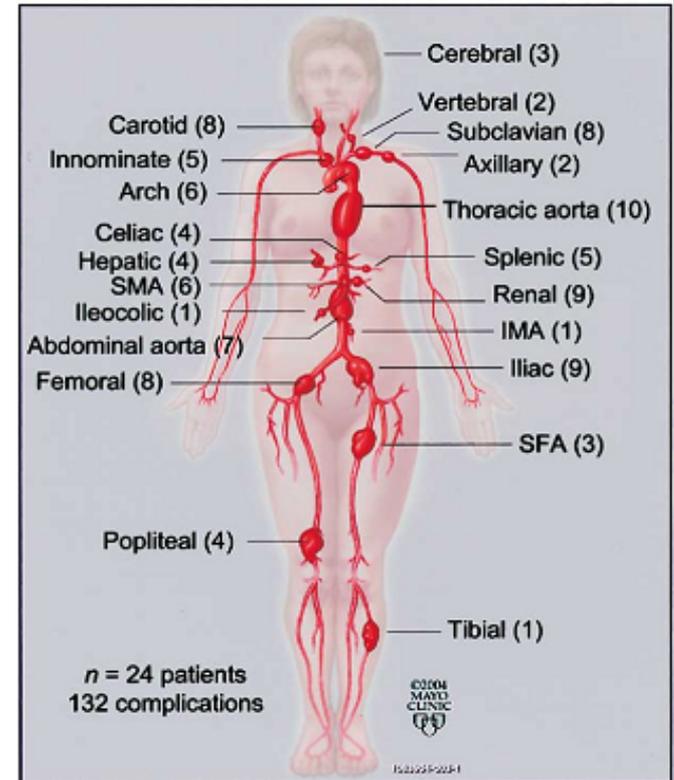
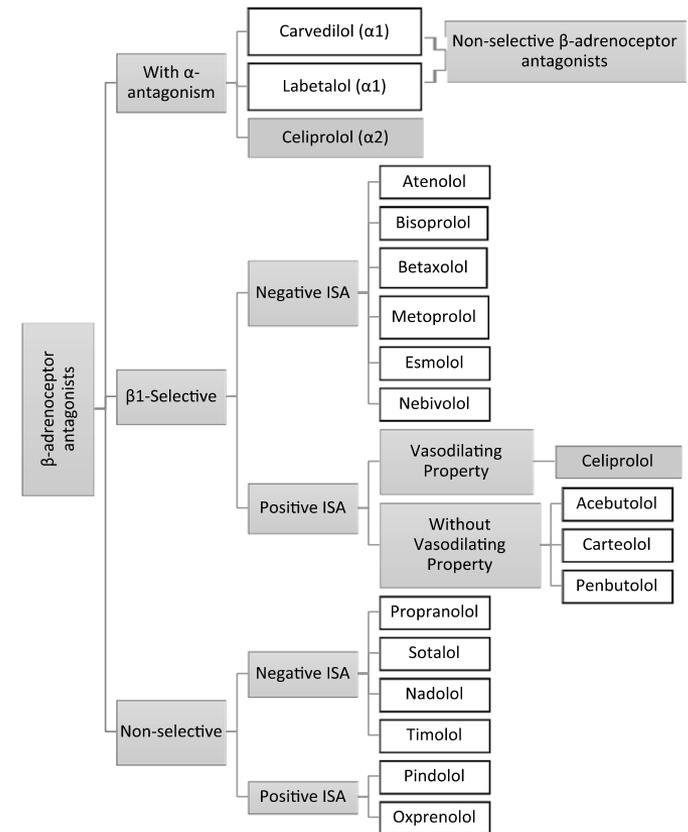


Fig. 3 Distribution of 132 vascular complications in 24 patients with a clinical diagnosis of EDS type IV. J Vasc Surg 2005;42:98-106.

Unique Mechanism of Action

- EDSIVO™ has a unique pharmacological profile:
 - β_2 and β_3 adrenergic receptor agonist
 - Selective β_1 and α_2 adrenergic receptor antagonist
 - Intrinsic sympathomimetic activity (ISA+)
 - Lacks non-specific membrane effects
 - Activates endothelial Nitric Oxide Synthase (eNOS)*
- Void of blood pressure lowering in normotensive people
 - Most vEDS patients are normotensive, thus the potential beneficial effect of celiprolol is unlikely to be through blood pressure lowering (β_1 antagonism)
- EDSIVO's™ mechanism of action in vEDS patients is thought to be through vascular dilatation and smooth muscle relaxation, thereby reducing the mechanical stress on collagen fibers within the arterial wall



BBEST Trial: COL3A1+ Subpopulation

Efficacy:

- 76% reduction in the risk of fatal or nonfatal cardiac or arterial events in COL3A1+ EDSIVO™ patients vs. control group over mean follow-up of 47 months
- 75% reduction in risk of primary (cardiac or arterial events) and secondary (intestinal or uterine rupture) events in COL3A1+ EDSIVO™ patients vs. control group

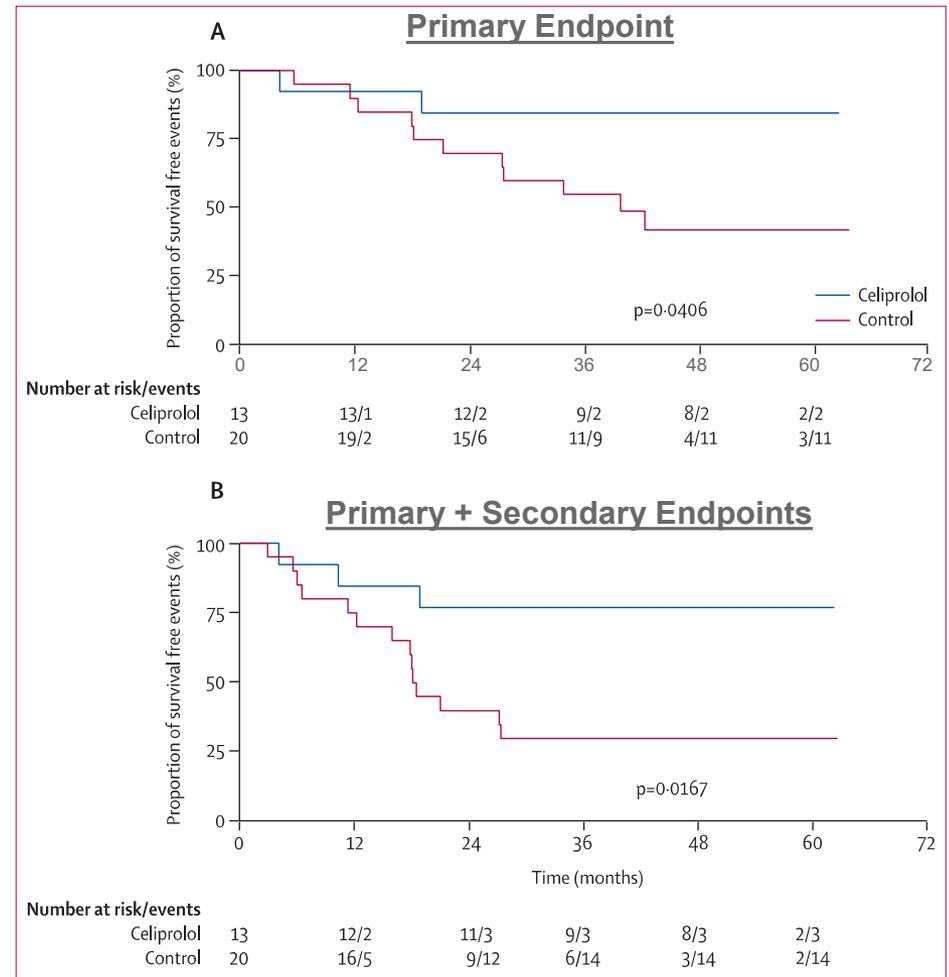


Figure 3: Kaplan-Meier curves of event-free survival in 33 patients with positive COL3A1 mutation
Primary endpoint (A). Primary and secondary endpoints (B).

ACER-001: Overview

Mechanism of Action

- **Small molecule with unique MOAs in various disorders**
- **UCDs:** NaPB is a prodrug of phenylacetate, a NH₄⁺ scavenger
- **MSUD:** NaPB is an allosteric inhibitor of BCKD kinase

Disease Overview

- **UCDs:** A group of metabolic genetic diseases that lead to toxic build-up of NH₄⁺
- **UCDs:** Currently treated with RAVICTI[®], BUPHENYL[®], AMMONUL[®], and a highly-restricted diet
- **MSUD:** A metabolic genetic disease that leads to toxic build-up of leucine and other branched-chain amino acids
- **MSUD:** Currently managed with a highly-restricted diet; poor compliance

Product Profile

- **A taste-masked, immediate release formulation of sodium phenylbutyrate**
- **UCDs:** Trial showed ACER-001 bioequivalence to BUPHENYL[®] in healthy volunteers
- ACER-001 in fasted state achieved >2x C_{max} of PBA in food effect study
- **MSUD:** POC study¹ suggests ~60% of patients have 30% reduction in Leucine

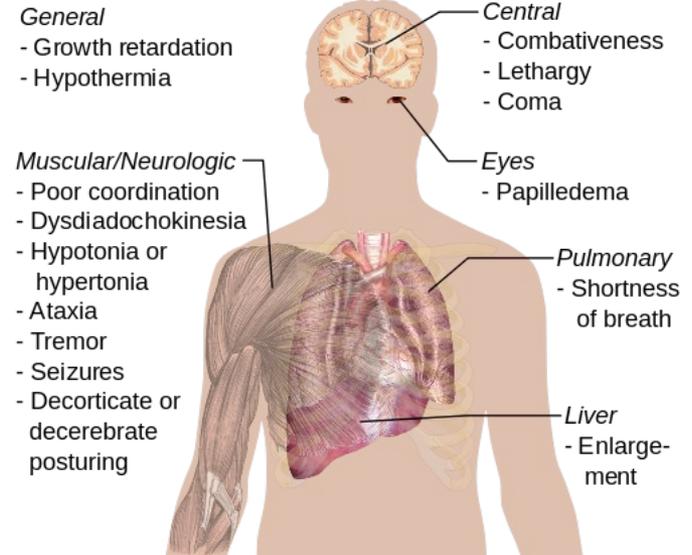
The Opportunity

- **Anticipate NDA submission for UCD H1 2021*[§]**
- **UCDs:** >2,000 patients in the U.S.; ~700 patients treated with sodium / glycerol phenylbutyrate
- **MSUD:** ~800 eligible patients in the U.S.
- Advantageous orphan pricing with robust program to support patient access and reimbursement

UCDs: Clinical Manifestations

- Newborns with severe urea cycle disorders become catastrophically ill with symptoms that mimic sepsis -- failure to feed, lethargy, respiratory distress, seizures and ultimately coma
- Children and adults with milder (or partial) urea cycle enzyme deficiencies may go years without a diagnosis, until a trigger -- a high protein meal, viral illness, excessive exercise or calorie deficiency -- causes excessive ammonia to be produced in the body, resulting in critical elevations of blood ammonia levels
- For individuals with OTC deficiency, typical neuropsychological complications include developmental delay, learning disabilities, intellectual disability, attention deficit hyperactivity disorder (ADHD), and executive function deficits

Symptoms of Hyperammonemia



Reproduced from:
http://upload.wikimedia.org/wikipedia/commons/7/76/Symptoms_of_hyperammonemia.svg.

Phenylbutyrate: Mechanism of Action

Nitrogen scavenger therapy

- Alternative pathway treatment diverts nitrogen from the urea cycle to alternate routes of excretion
- Both Ravicti® and Buphenyl® metabolize to phenylbutyrate (PBA), a prodrug of phenylacetate (PAA)
- **PAA is the active moiety** – it combines with glutamine, producing phenylacetylglutamine
- Phenylacetylglutamine (PAGN) is excreted by the kidneys

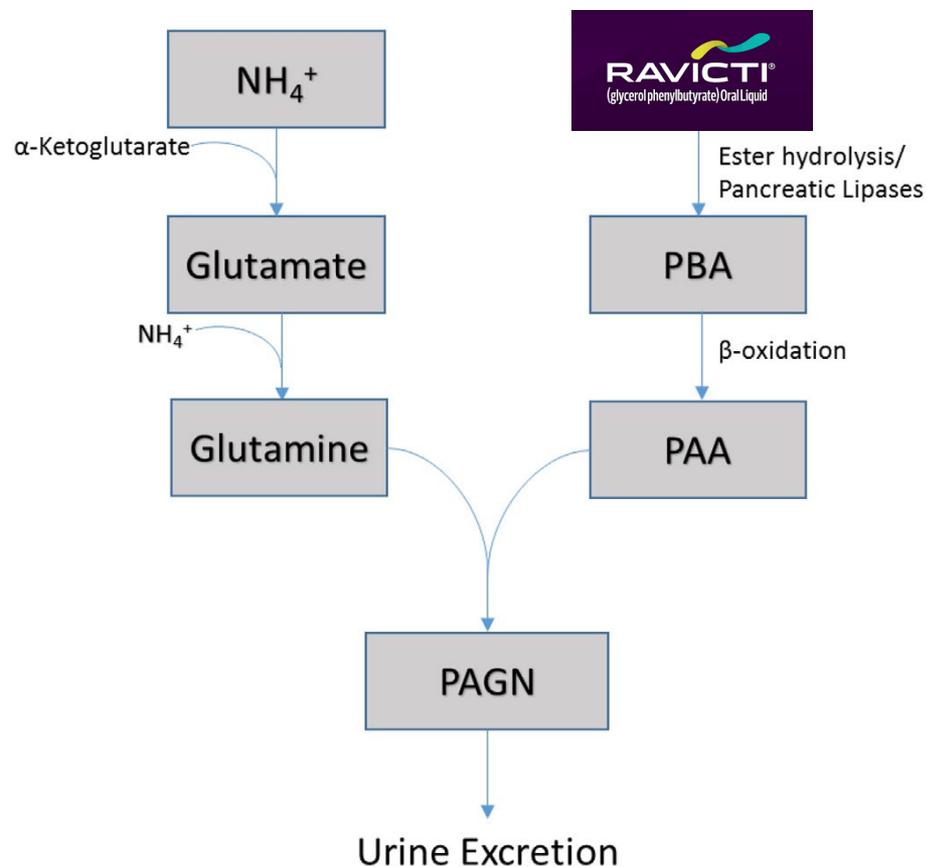


Fig. 1. Metabolizing pathway and mechanism of action of GPB. GPB (glycerol phenylbutyrate); PAA (phenylacetic acid); PBA (phenylbutyric acid); PAGN (phenylacetylglutamine).

UCDs: Unmet Need

- **BUPHENYL®:** Foul odor and foul/bitter taste; considered unpalatable*
 - 64% of patients reported it is difficult to take because of taste
 - Physicians reported that 25-33% of patients were prescribed less than target dose due to tolerability
 - Only 25% of patients indicated that they never miss a dose
 - 46% of patients reported taste as the reason for discontinuation*

- **RAVICTI®:** Mostly Tasteless/Odorless
 - Pricing has risen to levels considered challenging
 - Reports of difficult access, unaffordability, and forced switches back to sodium phenylbutyrate
 - For example: BUPHENYL® and RAVICTI® both recently removed from CVS/Caremark formulary for JPMorgan Chase plan members, effective 8/1/2019**
 - Patient groups and physicians have called for a taste-masked, affordable and accessible treatment***

*Shchelochkov et al., Barriers to drug adherence in the treatment of urea cycle disorders: Assessment of patient, caregiver, and provider perspectives. *Molecular Genetics and Metabolism Reports* 8 (2016) 43-47.

**https://www.caremark.com/portal/asset/Formulary_Drug_Removals_JPMC.pdf

***Acer Market Research

NaPB: Food Effect

BUPHENYL® (sodium phenylbutyrate) Tablets **BUPHENYL® (sodium phenylbutyrate) Powder**¹

[bu'fen-əl]
(sodium phenylbutyrate)

Rx Only

Absorption:

Peak plasma levels of phenylbutyrate occur within 1 hour after a single dose of 5 grams of sodium phenylbutyrate tablet with a C_{max} of 218 µg/mL under fasting conditions; peak plasma levels of phenylbutyrate occur within 1 hour after a single dose of 5 grams of sodium phenylbutyrate powder with a C_{max} of 195 µg/mL under fasting conditions. The effect of food on phenylbutyrate's absorption is unknown.

BUPHENYL® Powder is indicated for oral use (via mouth, gastrostomy, or nasogastric tube) only. The powder is to be mixed with food (solid or liquid), for immediate use.

HIGHLIGHTS OF PRESCRIBING INFORMATION²

These highlights do not include all the information needed to use RAVICTI safely and effectively. See full prescribing information for RAVICTI.

RAVICTI™ (glycerol phenylbutyrate) oral liquid
Initial U.S. Approval: 1996

Instruct patients to take RAVICTI with food and to administer directly into the mouth via oral syringe or dosing cup.

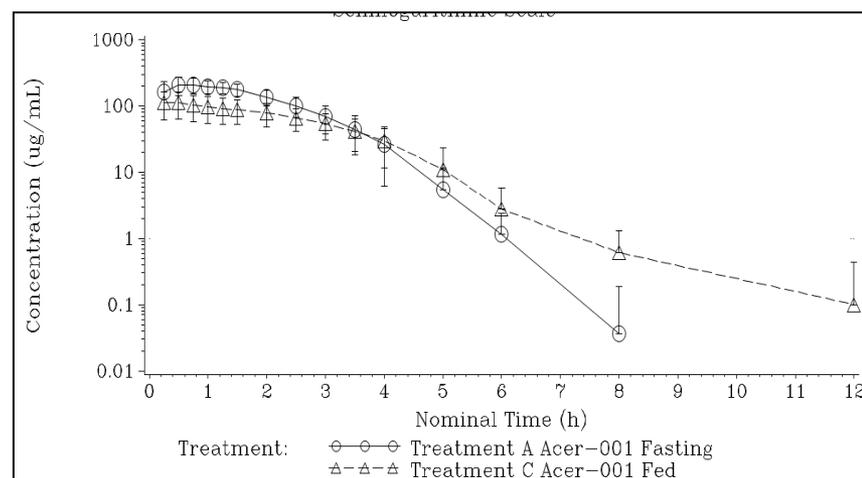
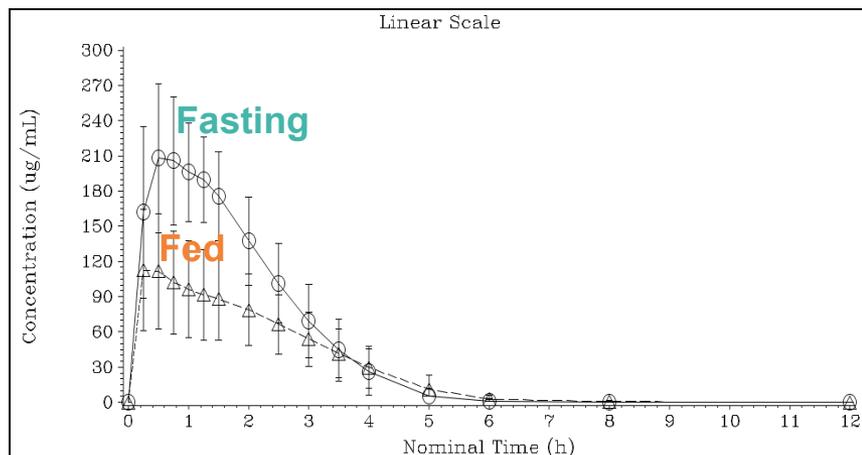
From Ravicti Patent (US8642012B2):

(T)he pharmacokinetic (PK) and pharmacodynamic (PD) properties of HPN-100 are indistinguishable in the fed or fasted states.

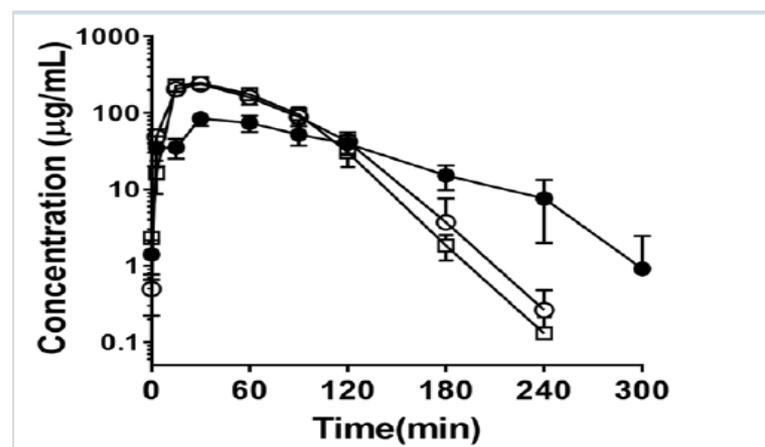
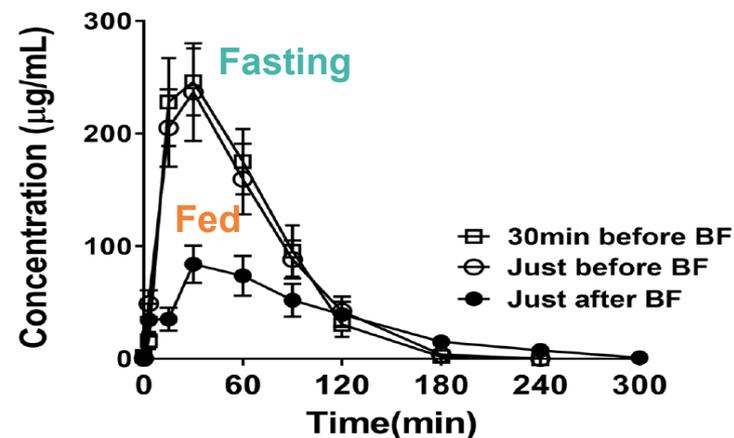
NaPB: Food Effect

Maximum concentration (C_{max}) ~2x higher under fasted conditions

ACER-001¹

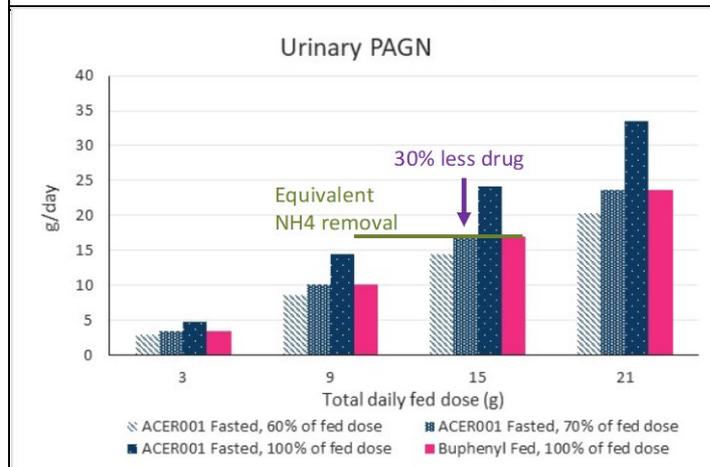
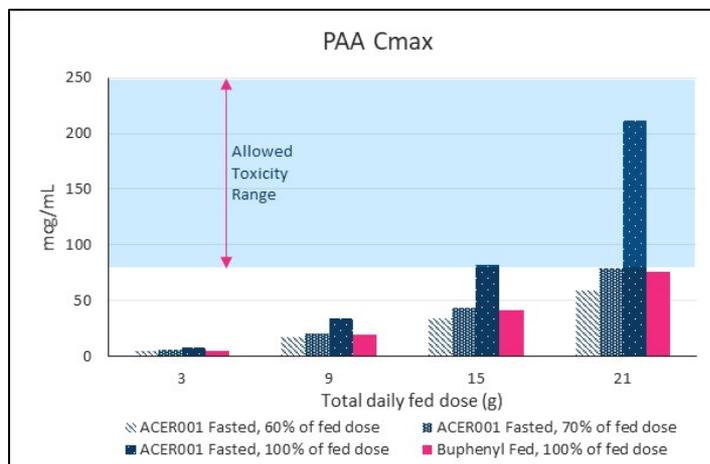


NaPB²

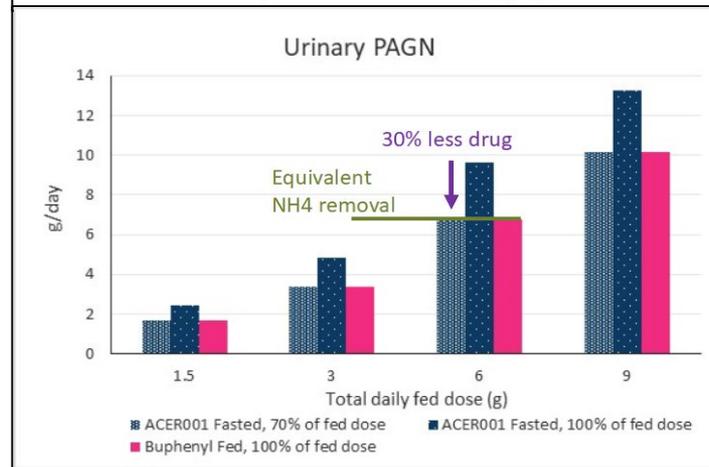
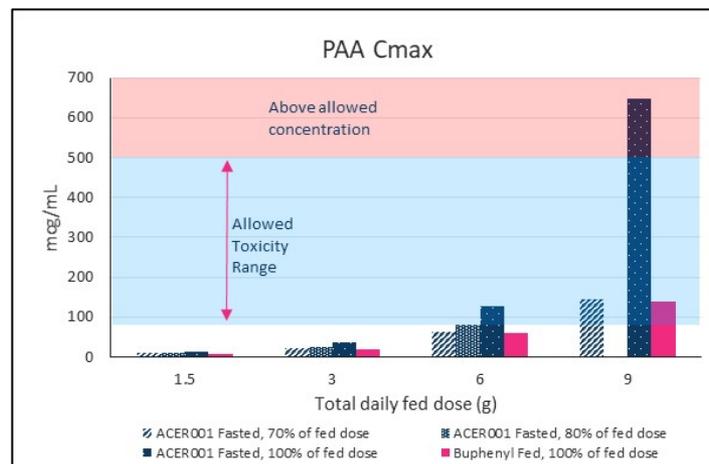


PK: Rosa & Co. In Silico Model

Adult Virtual Patient



Child Virtual Patient



PAA
(Safety^{1,2,3})

uPAGN
(Efficacy)

- ACER-001 in a fasted state required ~30% less PBA to achieve comparable therapeutic benefit in a fed state
- Model predicted 43% increase in urinary PAGN levels (negative correlation with blood ammonia AUC)

PK: Summary

- Dosing and Administration for Buphenyl, Ravicti and Pheburane are all instructed to be given with food
 - There is a significant food effect with NaPB
 - The pharmacokinetic (PK) and pharmacodynamic (PD) properties of Ravicti are indistinguishable in the fed or fasted states¹
- This means that all approved forms of phenylbutyrate have been dosed and administered in a suboptimal manner for decades
- Dosing under fasted conditions (likely 10 minutes prior to a meal) should increase exposure, and theoretically improve ammonia control / outcomes in UCD patients
- 2x the C_{max} of PBA may also improve efficacy in other disorders (where PBA is the active moiety), such as MSUD and PFIC²
- ACER-001's taste-masked formulation should improve palatability / tolerability of the drug when administered fasted (likely 10 minutes prior to a meal)

UCDs: Clinical & Regulatory Path

- **Pivotal bioavailability and bioequivalence (BE) trial:**
 - Single-center, single-blind, randomized, single-dose crossover study to demonstrate bioequivalence of the optimal formulation of ACER-001 compared to BUPHENYL® in 36 healthy adult subjects
 - ✓ Successfully completed in Q1 2020; bioequivalence established to RLD
- **Taste Assessment trials:**
 - Taste assessment of three different formulations of ACER-001 (multi-particulate powder) assessed relative to BUPHENYL® (powder) between 5 and 10 minutes using certified taste-testers
 - ✓ Successfully completed and informed selection of optimal formulation of ACER-001
 - Taste assessment of ACER-001 to characterize extent of taste masking between 0 and 5 minutes after reconstitution
 - Goal: to support taste masking claims / administration guidelines in label
- **Clinical Program:** proposing to FDA to conduct an expanded access program (EAP) to collect data to assess PK/PD (dosing / efficacy) and safety predicted from in silico model:
 - Lower dose / equivalent exposure
 - Equivalent dose / improved ammonia control
- **NDA:** Anticipate submission H1 2021^{\$} pending successful outcome of additional nonclinical work and long-term stability data (may vary depending on feedback from FDA re: EAP)

ACER-001: Differentiation

Phenylbutyrate Formulations			
	ACER-001 ¹ (Investigational)	RAVICTI [®]	BUPHENYL [®]
Efficacy / Safety in UCDs	✓✓ ²	✓	✓
Palatability / Compliance	✓	✓	✗ ³
Pricing (Per Patient Per Year)	TBD, likely near BUPHENYL	\$158k-\$1.2M ⁴	\$204k-\$402k ⁴
Formulation	Multi-Particulate (Sachet)	Oil (Tablespoons)	Powder/Tablets (up to 40 tablets/day)

1 Subject to FDA approval

2 Projected efficacy/safety from in silico model

3 Molecular Genetics & Metabolism Reports 8 (2016) 43-47.

4 Ravicti & Buphenyl pppy is based on patient weight and WAC price

ACER-001: IP / Exclusivities

- IP:
 - Filed formulation and method of use patent application for UCDs (filed Oct. 2016)
 - Issued patents (US/EP): “Methods of modulation of branched chain acids and uses thereof” [US PATENT NO. 10,092,532]
 - In addition, we continue to pursue new patents and exclusivity possibilities, based on our development plans and product attributes
- Exclusivities:
 - UCDs: Potential 3 years market exclusivity from FDA approval for administration without food
 - MSUD: Granted U.S. Orphan Drug Designation: 7 years market exclusivity from FDA approval
 - Pediatric exclusivity: +6 months added (if pediatric indication study approved)

Osanetant: Overview

Mechanism of Action

- **Osanetant is a selective, non-peptide tachykinin NK3 receptor antagonist**
- NK3R is the main receptor for neurokinin B (NKB), a tachykinin peptide primarily found in the arcuate nucleus (ARC) of the hypothalamus

Disease Overview

- **iVMS: Induced Vasomotor Symptoms where Hormone Replacement Therapy (HRT) is likely contraindicated**
 - Induced vasomotor symptoms (iVMS) are well documented with the use of hormonal cancer therapies and certain surgical procedures
 - Symptoms such as hot flashes can appear immediately and be severe
 - Traditional HRTs are usually contraindicated

Product Profile

- **Clinical and laboratory safety results are available from 21 completed Phase 1 and 2 studies (325 healthy subjects and 665 patients were treated with osanetant)**
- Oral bioavailability, readily crosses the blood-brain barrier

The Opportunity

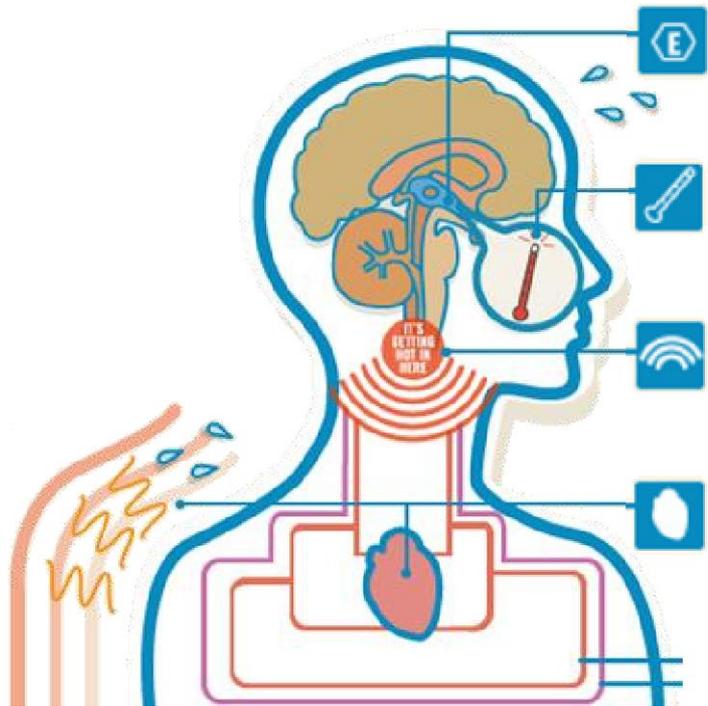
- **Acer licensed worldwide rights to osanetant from Sanofi in December 2018**
- Anticipate submitting IND in Q4 2020
- Currently no other NK3R antagonists in development in iVMS space

History

- Acer acquired worldwide rights to osanetant from Sanofi in December 2018
- Osanetant (SR142801) was the first selective non-peptide tachykinin NK3 receptor antagonist evaluated as a potential treatment for schizophrenia
- Clinical and laboratory safety results are available from 21 completed Phase 1 and 2 studies in which 325 healthy subjects and 665 schizophrenic patients were treated with osanetant
- No major safety concerns identified from these studies after single-dose and repeated-dose administration of up to 400 mg QD for up to 21 days, and 200 mg QD for up to 6 weeks for schizophrenia
- In March 2005, Sanofi-Aventis discontinued the development of osanetant for schizophrenia citing 'lack of efficacy compared with placebo' in this indication as a major reason for this decision

Vasomotor Symptoms (VMS): Overview

- VMS, typically comprised of hot flashes and night sweats, are associated with decreases in reproductive hormones commonly associated with menopause (e.g. MR-VMS)



A diminished amount of hormones, such as estrogen, affects the hypothalamus



This confuses the hypothalamus and makes it read “too hot”



The brain responds by relaying an alert to cool off



The body then tries to cool off by beginning to perspire

- While VMS associated with menopause can often be treated with hormone replacement therapy (HRT), there are patients who experience VMS who are not in menopause and for whom HRT is likely contraindicated

Induced Vasomotor Symptoms (iVMS)

Women who are BRCA+ and have prophylactic bilateral salpingo-oophorectomy (PBSO)

- 67% of women have symptoms of menopause such as hot flashes⁵
- Up to 35% complain of “extremely bothersome” symptoms up to two years after their surgery⁶

Men with HR+ Prostate Cancer (CaP) receiving Leuprolide

- 80% of men experience hot flashes³
- 15-27% of patients consider hot flashes the most distressing side effect
- 30-40% experienced moderate-to-severe symptoms
- 20% discontinued or disrupted treatment

Women with HR+ Breast Cancer (CaB) receiving Tamoxifen

- 84% of women experienced hot flashes¹
- 80% experienced night sweats
- 60% experienced severe symptoms
- Symptoms persisted throughout 5 years of treatment and were mainly attributed to tamoxifen
- After 4.5 years, 46% of women had discontinued tamoxifen²

¹Moon, Z. et al., JOURNAL OF PSYCHOSOMATIC OBSTETRICS & GYNECOLOGY, 2017 VOL. 38, NO. 3, 226–235.

²Nichols, H, et al., JNCI J Natl Cancer Inst, 2015, 1–8.

³Challapalli, A, et al., Clinical and Translational Radiation Oncology 10 (2018) 29–35.

⁴Abildgaard, J, et al., JNCI Cancer Spectrum, 2018, Vol. 0, No. 0.

⁵L. Johnson, et al. American Society for Reproductive Medicine, 2014 Vol 102 No. 3, Supplement, e249.

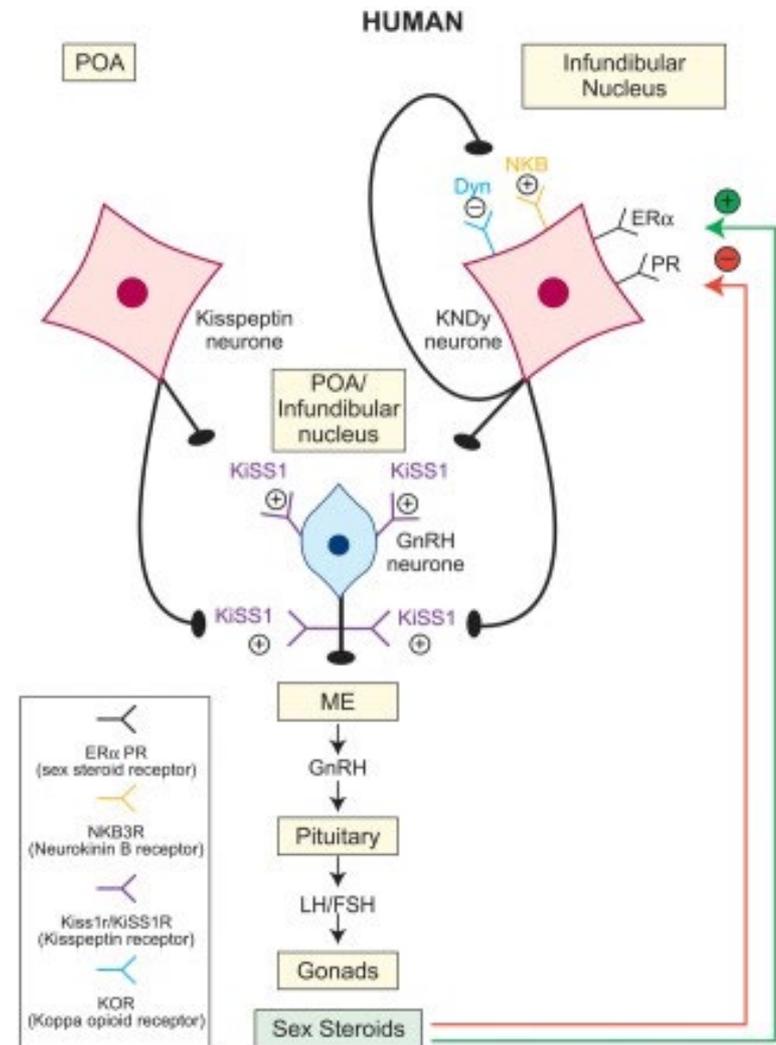
⁶Griffiths, E, et al: The Obstetrician & Gynaecologist, 2005: 7:23-27.

iVMS: The Unmet Need

- Induced vasomotor symptoms (iVMS) are well documented with the use of hormonal cancer therapies and certain surgical procedures
- Symptoms such as hot flashes can appear immediately and be severe
- Traditional HRTs are usually contraindicated
- Non-adherence to cancer therapy can be associated with side effects which increases the mortality risk or shortens the time to recurrence
- A non-hormonal treatment for iVMS is needed to help ensure breast or prostate cancer patients can start and stay on critical hormonal cancer therapy and BRCA2 post-PBSO can obtain help with significantly impactful and limiting iVMS

NK3 Receptor (Neurokinin B)

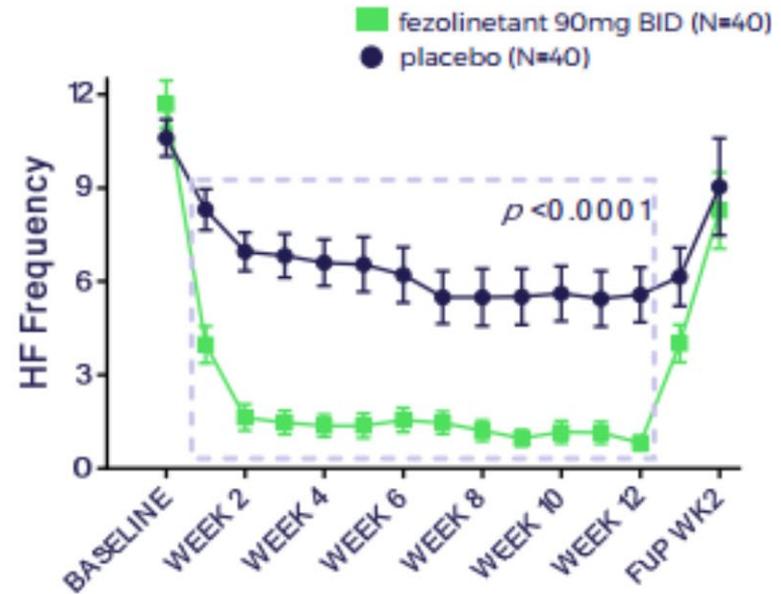
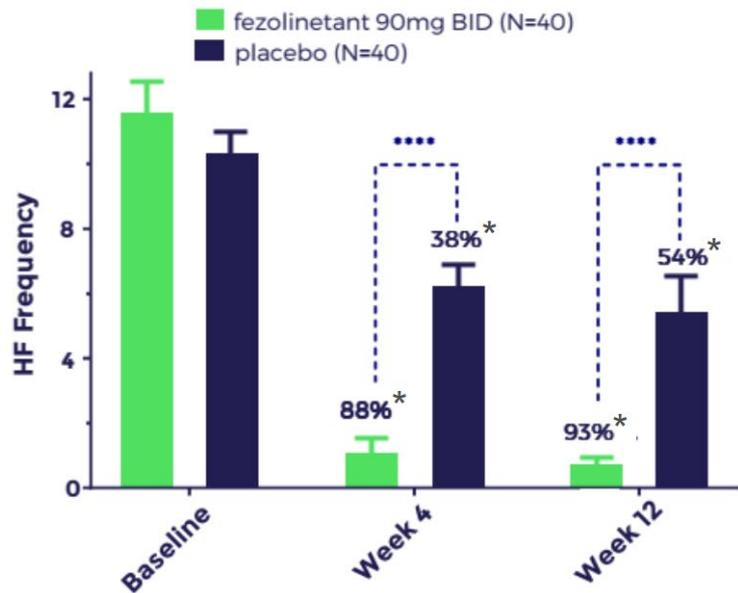
- Neurokinin B (NKB) belongs to a group of neuropeptides, called tachykinins or neurokinins, that includes substance-P (SP), neurokinin A (NKA), and two N-terminally extended forms of NKA, neuropeptide g and neuropeptide K
- The biological effects of tachykinins are mediated through specific receptors denoted NK1, NK2, and NK3
- NKB is the preferred endogenous ligand of tachykinin NK3 receptors
- The tachykinin NK3 receptors are located primarily in the brain, while a few receptors are also present in the peripheral nervous system (intestines, placenta)



NK3R Antagonist Clinical POC in VMS

- Fezolinetant is a NK3R antagonist being developed by Astellas for moderate-to-severe VMS

Average Daily Hot Flash Frequency Reported as per FDA Guidance



At Week 4:

- fezolinetant group: 14/40 patients have ZERO hot flash
- placebo group: 2/40 patients have ZERO hot flash

NK3R Antagonist Clinical POC in VMS

- Pavinetant (MLE4901) was a NK3R antagonist that was discontinued by Millendo for the treatment of polycystic ovary syndrome and menopausal hot flashes

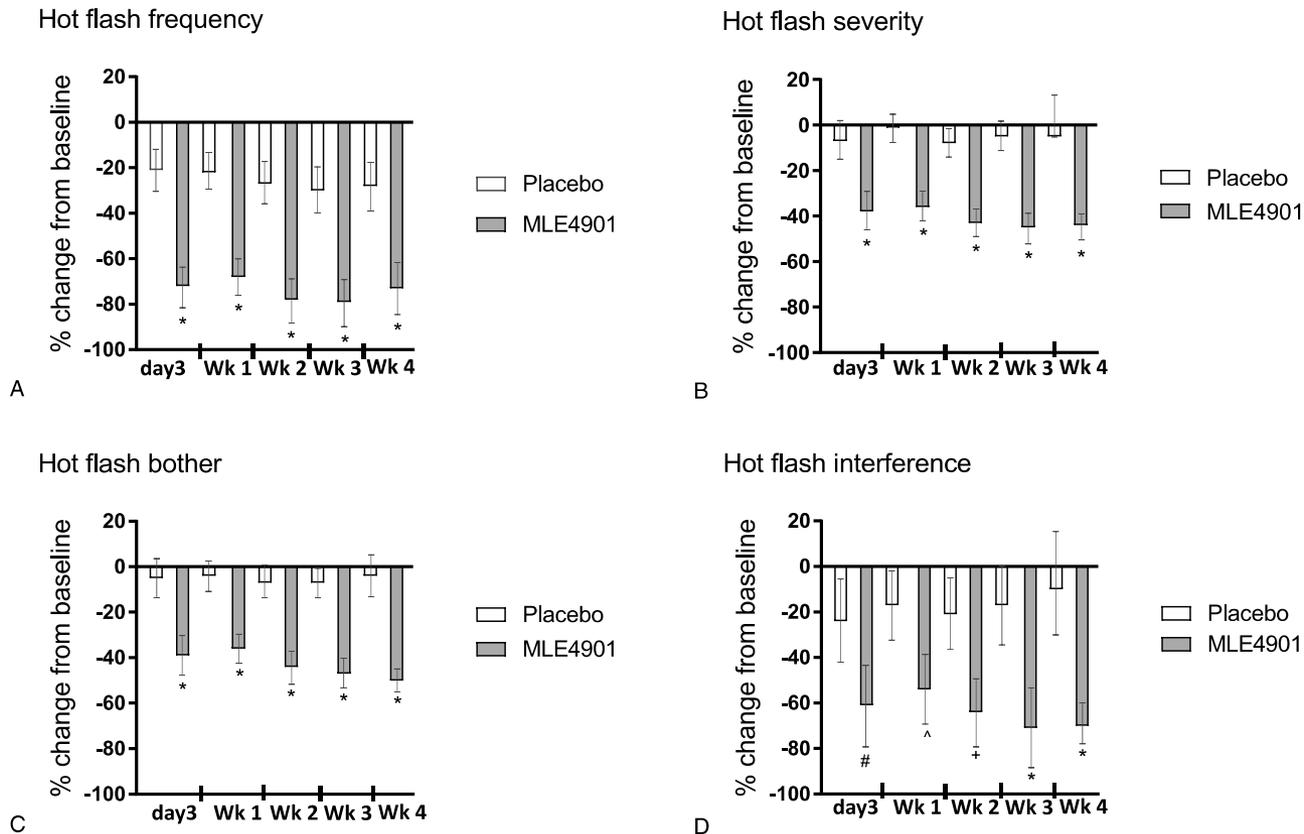


FIG. 2. Hot flash frequency (A), severity (B), bother (C), and interference (D) outcomes: results are presented as percentage change with 95% CIs from baseline at each time point during the treatment period (ie, on day 3 of treatment, and then weekly mean total for each week (wk) of the 4-week treatment period for both placebo (white) and MLE4901 (gray). Minimum $n = 33$; maximum $n = 37$. * $P < 0.0001$, # $P = 0.0006$, ^ $P = 0.0011$, + $P = 0.0001$. Week 4 data adapted from Prague et al, *Lancet*, 2017¹⁸.

Osanetant: Clinical Development Plan

- Acer is partnering with leading universities to design & conduct clinical trials to evaluate osanetant in various patient populations with iVMS
- These include patients with medically or surgically iVMS (may include any/all of the following):
 - Women who are BRCA+ and have had a PBSO
 - Men with HR+ Prostate Cancer receiving leuprolide
 - Women with HR+ Breast Cancer receiving tamoxifen
- The initial Phase 1/2 BRCA+ trial would evaluate:
 - PK/PD and Safety, including physiologic PD
 - Identify the optimal dosing strategy to advance into further efficacy studies in minimizing the iVMS symptoms
 - Subject to additional capital

Osanetant: Exclusivity / Timelines

- Osanetant would be a New Chemical Entity (NCE) in the US, and as such would be eligible for five years' market exclusivity from potential FDA approval
- Additional exclusivity (e.g. Orphan Drug Designation) will depend upon indication(s) and development pathway chosen
- Anticipate IND submission in Q4 2020
- Aim to initiate Phase 1/2 trial in H1 2021, subject to additional capital

Financial Overview

- Cash
 - \$7.0M as of March 31, 2020
 - Expected to have sufficient capital into Q4 2020, excluding support for the planned emetine trial and EDSIVO™ development and precommercial activities
- Capitalization as of April 30, 2020
 - 10.2M shares of common stock outstanding
 - 11.6M shares of common stock fully diluted
- \$87M invested through August 2018

Summary

- Acer's pipeline includes four clinical-stage product candidates:
 - **Emetine** for the treatment of COVID-19
 - **EDSIVO™** (celiprolol) for the treatment of vascular Ehlers-Danlos syndrome (vEDS) in patients with a confirmed type III collagen (COL3A1) mutation
 - **ACER-001** (a taste-masked, immediate release formulation of sodium phenylbutyrate) for the treatment of various inborn errors of metabolism, including urea cycle disorders (UCDs) and Maple Syrup Urine Disease (MSUD)
 - **Osanetant** for the treatment of induced Vasomotor Symptoms (iVMS) where Hormone Replacement Therapy (HRT) is likely contraindicated
- Product candidates are believed to present a comparatively de-risked profile, having one or more of:
 - Favorable safety profile; clinical proof-of-concept data; mechanistic differentiation
 - Potential expedited paths for development through specific FDA-established programs
- Multiple anticipated key regulatory milestones:

✓ Emetine NCATS collaboration signed; discussions w/FDA ongoing:	Q2 2020
• Emetine IND submission:	Q3 2020
• Emetine Phase 2/3 trial initiation*§:	Q3 2020
• Osanetant IND submission:	Q4 2020
• Osanetant initiate Phase 1/2*§:	H1 2021
• ACER-001 (UCD) NDA submission**§:	H1 2021
- Expected to have sufficient capital into Q4 2020, excluding support for the planned emetine trial and EDSIVO™ development and precommercial activities



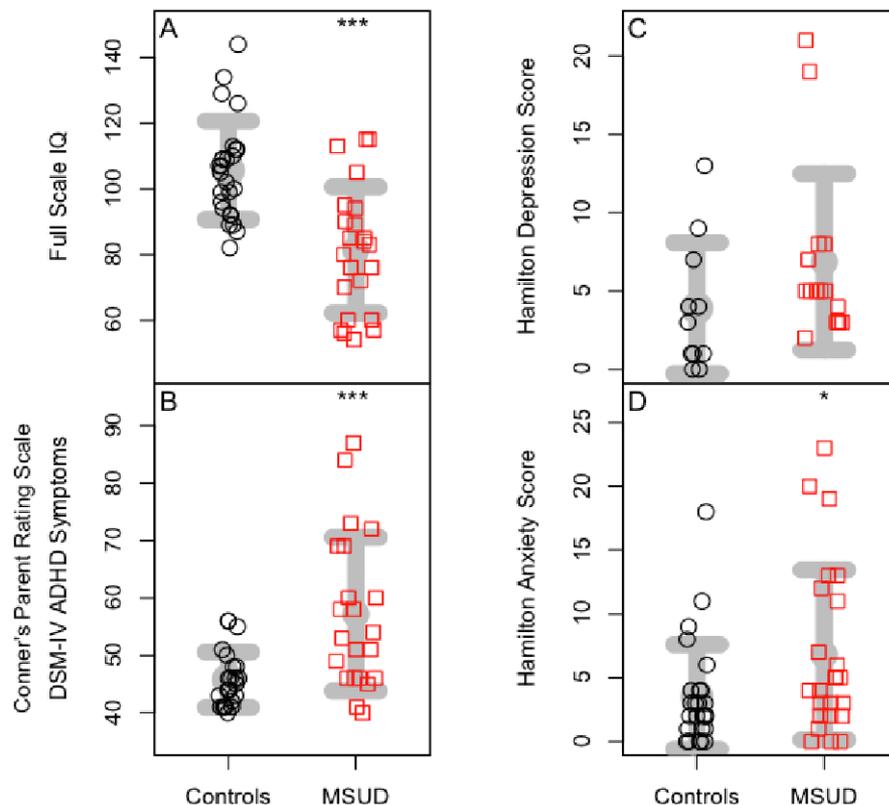
acertherapeutics

Reference Slides



Maple Syrup Urine Disease (MSUD)

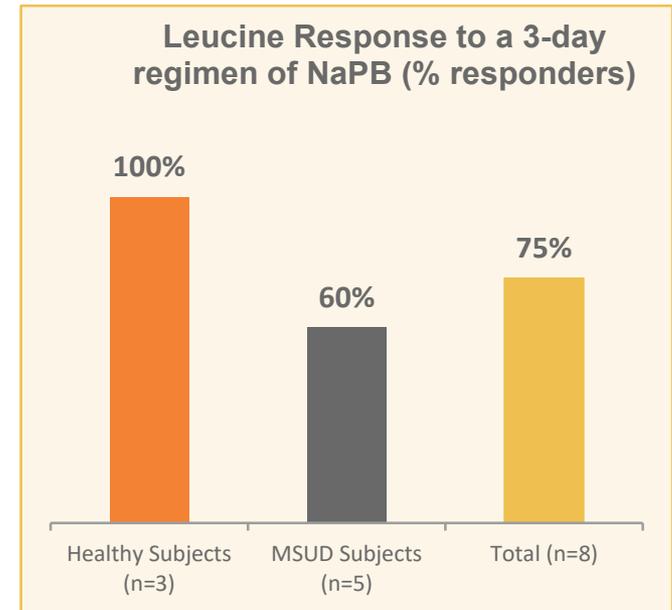
- MSUD is an inborn error of Branched-chain Amino Acid (BCAA) – leucine, isoleucine, valine – metabolism
 - Caused by deficiency of the mitochondrial Branched-chain Keto Acid Dehydrogenase complex (BCKDC)
 - ~800 patients in U.S., ~3,000 patients worldwide
 - MSUD Family Support Group has >500 patients
 - Part of newborn screening in U.S., UK, Germany
- High leucine levels lead to chronic and acute neurological damage
 - Lower IQ
 - Mental impairment (poor cognitive function)
 - Social impairment (poor executive function)
 - Metabolic decompensation (seizures and coma)
- A highly-restricted diet is the primary treatment
 - Consists of BCAA-free synthetic foods and formula
 - Very few foods have low BCAAs (fruits & vegetables)
 - Balancing act: enough BCAAs for growth & development



indicates p < 0.05, *** p < 0.001 compared to the control group*

MSUD: Clinical POC Study

- Design: Open label pilot study¹ at Baylor College of Medicine – 3 healthy and 5 MSUD subjects with late onset disease
 - 3 days of steady-state protein diet*; then 3 days of NaPB + diet*
 - BCAAs and BCKAs determined at day 3 of each study period (4 time points)
- Results: NaPB showed a statistically significant reduction of leucine in all 3 healthy subjects ($p < 0.05$) and 3 out of 5 MSUD patients ($p < 0.05$ in responders)
 - ~30% reduction (28-34%) in leucine in MSUD responders
 - Clinicians view >20-30% ↓ as clinically meaningful**
- Comments: Despite the short treatment duration (3 days) NaPB showed statistically significant (intra-subject) reduction in leucine in 75% of the subjects



Brunetti-Pierri et al., Hum Mol Genet. 2011 February 15; 20(4): 631–640

¹Brunetti-Pierri et al., Hum Mol Genet. 2011 February 15; 20(4): 631–640.

*All subjects received a constant protein intake of 0.6 g/kg/day as combination of BCAA-free formula and whole protein

**Acer commissioned market research

MSUD: Market Opportunity

- About 1,000 MSUD patients in the U.S., ~3,000 WW*
 - 20-25% MSUD patients in U.S. are Mennonite; incidence up to 1/380
 - Ashkenazi Jewish population; incidence of 1/26,000
- No treatments currently approved for MSUD
- Early treatment may help reduce the rate of neuropsychological comorbidities and optimize growth**
- MSUD specialists recognize NaPB's potential effectiveness, yet tolerability is a concern***
- Plan to initiate Phase 2 trial in MSUD in 2021§

*<https://www.ncbi.nlm.nih.gov/books/NBK1319/>

**Molecular Genetics and Metabolism Reports 15 (2018).

***Acer Therapeutics: US Market Research – 2014.

§Subject to additional capital