



**acer**therapeutics

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



**Corporate Presentation**

May 2020

Nasdaq: ACER

# Forward-looking Statements

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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: **18**
- Founded: **December 2013**
- Public: **September 2017**
- Cash: **\$12.1M** as of December 31, 2019
  - Expected to have sufficient capital to fund current operations into Q4 2020, excluding:
    - Planned emetine clinical trial
    - Support for EDSIVO™ development and precommercial activities

# Executive Leadership Team

<p>Chris Schelling <b>CEO &amp; Founder</b></p>	<ul style="list-style-type: none"> <li>• 20 years; strategic commercial development &amp; orphan</li> </ul>	
<p>Will Andrews, MD <b>Chief Medical Officer</b></p>	<ul style="list-style-type: none"> <li>• 20 years; clinical development, medical affairs &amp; orphan</li> <li>• M.D. Yale University School of Medicine</li> </ul>	
<p>Harry Palmin <b>Chief Operating &amp; Financial Officer</b></p>	<ul style="list-style-type: none"> <li>• 25 years; corporate &amp; finance experience</li> </ul>	
<p>Matt Seibt <b>Chief Commercial Officer</b></p>	<ul style="list-style-type: none"> <li>• 22 years; sales, market access &amp; product launch</li> </ul>	
<p>John Klopp <b>Chief Technical Officer</b></p>	<ul style="list-style-type: none"> <li>• 18 years; orphan manufacturing &amp; commercialization</li> </ul>	
<p>Don Joseph, JD <b>Chief Legal Officer &amp; Secretary</b></p>	<ul style="list-style-type: none"> <li>• 25 years; general counsel &amp; senior management</li> <li>• J.D. University of Texas School of Law</li> </ul>	

# 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:	<b>Q2 2020</b>
• Emetine Phase 2/3 trial initiation* <sup>§</sup> :	<b>Q3 2020</b>
• Osanetant IND submission:	<b>Q4 2020</b>
• Osanetant initiate Phase 1/2 <sup>§</sup> :	<b>Q1 2021</b>
• ACER-001 (UCD) NDA submission** <sup>§</sup> :	<b>Q1 2021</b>
- 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	Development Status
<b>Emetine Hydrochloride</b>		
<b>COVID-19</b>	Unique MOA; restores cellular stress response	<b>Phase 2/3*</b>
<b>EDSIVO™ (celiprolol)</b>		
<b>vascular Ehlers-Danlos syndrome (COL3A1+)</b>	Induces vascular dilatation and smooth muscle relaxation	<b>TBD**</b>
<b>ACER-001 (taste-masked, immediate-release form of sodium phenylbutyrate)</b>		
<b>Urea Cycle Disorders</b>	Taste-masked formulation; evaluating bioequivalence to BUPHENYL® ***	<b>Pre-NDA</b>
<b>Maple Syrup Urine Disease</b>	Inhibition of BCKD kinase to increase BCAA metabolism	<b>Phase 2</b>
<b>Osanetant</b>		
<b>Induced Vasomotor Symptoms (iVMS)</b>	Neurokinin 3 Receptor Antagonist	<b>Phase 1/2*</b>

\*Initiation subject to successful IND submission and clearance

\*\*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 4.1 million cases and 280,000+ deaths worldwide (as of 5/11/20)

## Mechanism of Action

- **Potent antiviral activity through modulation of cellular stress response**
- Restores cellular stress response, inhibiting viral replication
- Believed to be the only drug in development exploiting this MOA

## Product Profile

- **Broad-acting and potent antiviral in development for patients with COVID-19; potential application in other infectious diseases**
- 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 and emetic agent
- Potential benefit in other diseases including Zika, Ebola and other Coronaviruses

## The Opportunity

- **Ongoing discussions with FDA following pre-IND feedback; targeting Phase 2/3 trial initiation in Q3<sup>§</sup>**
- 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

<sup>§</sup>Subject additional capital

<sup>\*</sup>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 hepatitis<sup>1</sup> and varicella-zoster virus<sup>2</sup>
- 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)	<b>IC<sub>50</sub> = 0.47 µM**</b>	Bojkova et al. NatureResearch. 2020 Mar 11; in review <a href="https://doi.org/10.21203/rs.3.rs-17218/v1">https://doi.org/10.21203/rs.3.rs-17218/v1</a>
SARS-CoV-2 (Vero-E6)	<b>EC<sub>50</sub> = 0.46 µM***</b>	Choy et al. Antiviral Research. 2020 Apr 3; pre-proof <a href="https://doi.org/10.1016/j.antiviral.2020.104786">https://doi.org/10.1016/j.antiviral.2020.104786</a>
HCoV-OC43	<b>EC<sub>50</sub> = 0.30 / CC50 = 2.69</b>	Shen et al. J Virol. 2019 May 29;93(12). pii: e00023-19. doi: 10.1128/JVI.00023-19.
HCoV-NL63	<b>EC<sub>50</sub> = 1.43 / CC50 = 3.63</b>	
MERS-CoV	<b>EC<sub>50</sub> = 0.34 / CC50 = 3.08</b>	
MHV-A59	<b>EC<sub>50</sub> = 0.12 / CC50 = 3.51</b>	
MERS-CoV	<b>EC<sub>50</sub> = 0.014</b>	
SARS-CoV	<b>EC<sub>50</sub> = 0.051</b>	Dyall et al. Antimicrob Agents Chemother. 2014 Aug;58(8):4885-93. doi: 10.1128/AAC.03036-14.
ZIKV-MR766	<b>IC<sub>50</sub> = 9.15e-009</b>	Yang et al. Cell Discov. 2018 Jun 5;4:31. doi: 10.1038/s41421-018-0034-1.
ZIKV-FSS13025	<b>IC<sub>50</sub> = 1.072e-008</b>	
ZIKV-PRVABC59	<b>IC<sub>50</sub> = 9.591e-009</b>	
EBOV-Vero E6	<b>IC<sub>50</sub> = 16.9 nM</b>	
HSV-2	<b>EC<sub>50</sub> = 0.03 / CC<sub>50</sub> = 1.12</b>	Andersen et al. Viruses. 2019 Oct 18;11(10). pii: E964. doi: 10.3390/v11100964.
HMPV	<b>EC<sub>50</sub> = 0.14 / CC<sub>50</sub> = 1</b>	
HIV M184V	<b>EC<sub>50</sub> = 0.012 – 0.03</b>	Chaves Valadao et al. Molecules. 2015 Jun 22;20(6):11474-89. doi: 10.3390/molecules200611474.
HCMV	<b>EC<sub>50</sub> = 40 nM / CC<sub>50</sub> = 8 µM</b>	Mukhopadhyay et al. PLoS Pathog. 2016 Jun 23;12(6):e1005717. doi: 10.1371/journal.ppat.1005717.

\* EC<sub>50</sub> / CC<sub>50</sub> values = µM (unless otherwise noted)

\*\* For reference, the IC<sub>50</sub> of hydrochloroquine against SARS-CoV-2 is 4.51 µM at MOI 0.01

\*\*\* For reference, the EC<sub>50</sub> 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

- $IC_{50} = 0.47 \mu M^1$
- $EC_{50} = 0.46 \mu M^2$
- Synergy between remdesivir and emetine was observed – remdesivir at  $6.25 \mu M$  in combination with emetine at  $0.195 \mu M$  may achieve 64.9% inhibition in SARS-CoV-2 viral yield<sup>2</sup>

## High and long duration lung tissue concentrations<sup>3</sup>

- $EC_{50}$  concentrations of emetine  $\sim 1,872x$  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 treated<sup>4</sup>
- 90 patients with herpes zoster treated<sup>5</sup>

1 <https://www.researchsquare.com/article/rs-17218/v1>

2 <https://doi.org/10.1016/j.antiviral.2020.104786>

3 Asano et al. [European Journal of Drug Metabolism and Pharmacokinetics](#) volume 27, pages 17–27 (2002)

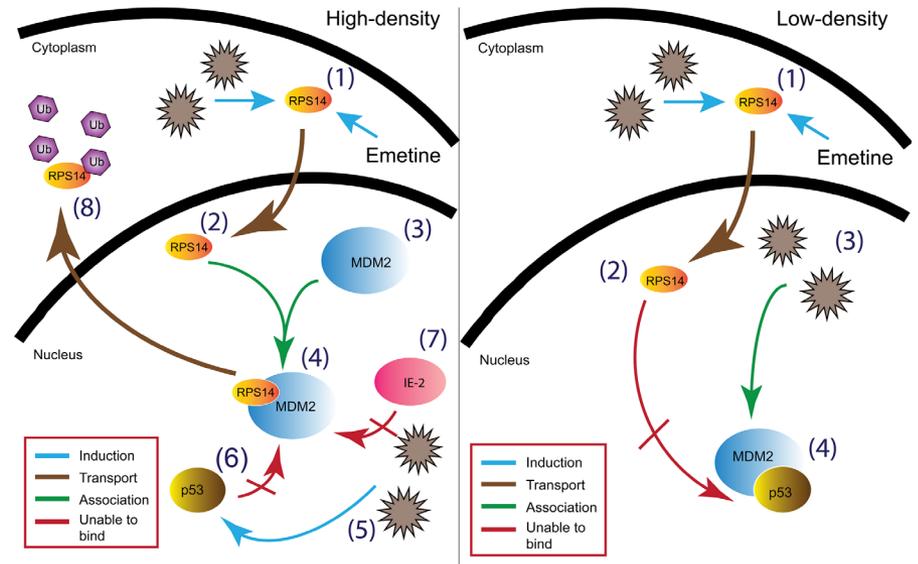
4 Del Puerto et al. *Pren. méd. argent.*, 55: 818, 1968

5 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 toxicity<sup>1</sup>
- Electrocardiographic abnormalities are seen, but not often associated with significant cardiac symptoms<sup>2,3,4</sup>
  - 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.  $\geq 650$  mg): hypotension, tachycardia, cardiomyopathy, myocarditis, precordial pain, gallop rhythm (on auscultation), dyspnea, cardiac dilatation, congestive failure, and death have been reported<sup>5</sup>
- Toxicity with emetine appears to be cumulative-dose related and independent of schedule<sup>1,6</sup>
- Complete reversibility of cardiac adverse effects<sup>6</sup>

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+ (mild to moderate)
  - High-risk, symptomatic adults
  - Not requiring hospitalization (outpatient)
    - Part A: 30-150 patients (adaptive)
    - Part B: 300 patients (projected)
- **Endpoints**
  - Clinical endpoints (rate of hospitalization, mortality)
  - Viral load/shedding assessments (quantitative) by saliva/mouthwash, rectal and/or nasopharyngeal swabs
  - Exploratory laboratory endpoints included
- **Doses**
  - Administer subcutaneously (SC) at low doses
    - Arm 1: Cumulative Dose 50 mg
    - Arm 2: Cumulative Dose 150 mg



# 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
- Assuming FDA supports moving forward, Acer aims to submit IND in June
- Targeting IND clearance by late June

# 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**
- $\beta_2$  and  $\beta_3$  adrenergic receptor agonist; selective  $\beta_1$  and  $\alpha_2$  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 observed<sup>1</sup>**
- Statistically-significant improvement in event-free survival (EFS) compared to control in vEDS patients (n=53)<sup>1</sup>

## 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 investigations<sup>2</sup>**

- 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 evidence<sup>2</sup>**

- 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 investigation<sup>1</sup>**

- 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 years<sup>1</sup>
- No approved therapeutic options for vEDS
  - Current treatment is focused on surgical intervention

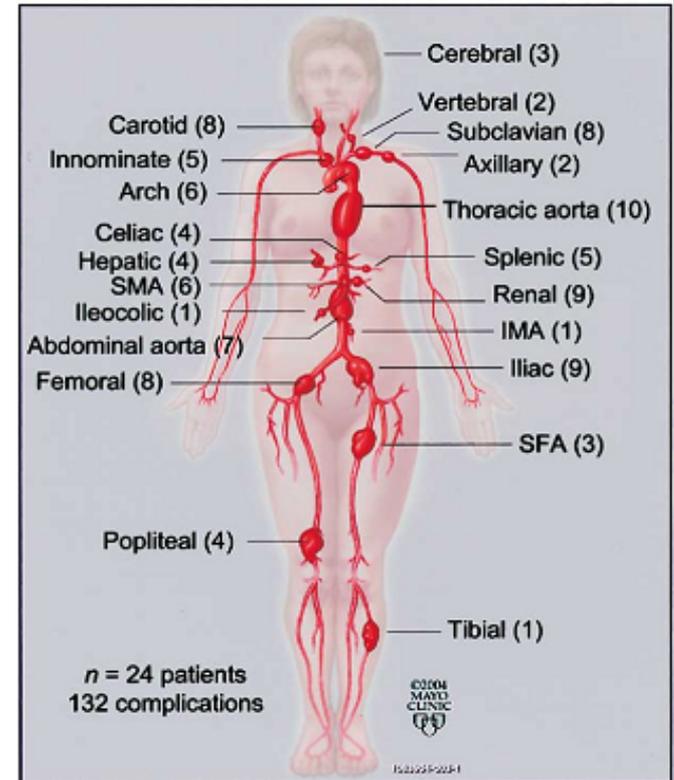
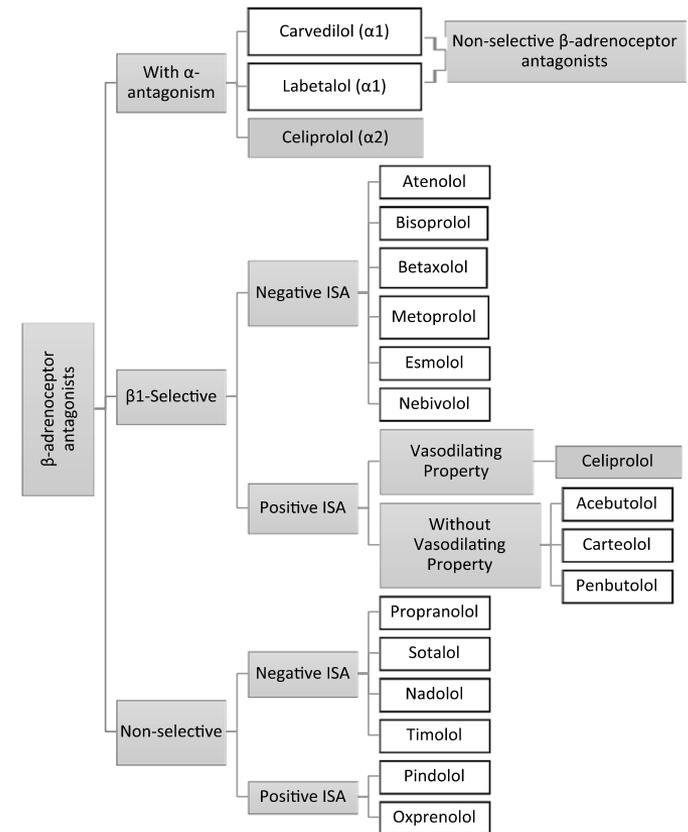


Fig. 3 Distribution of 132 vascular complications in 24 patients with a clinical diagnosis of EDS type IV. J Vasc Surg 2005;42:98-106.

# Unique Mechanism of Action

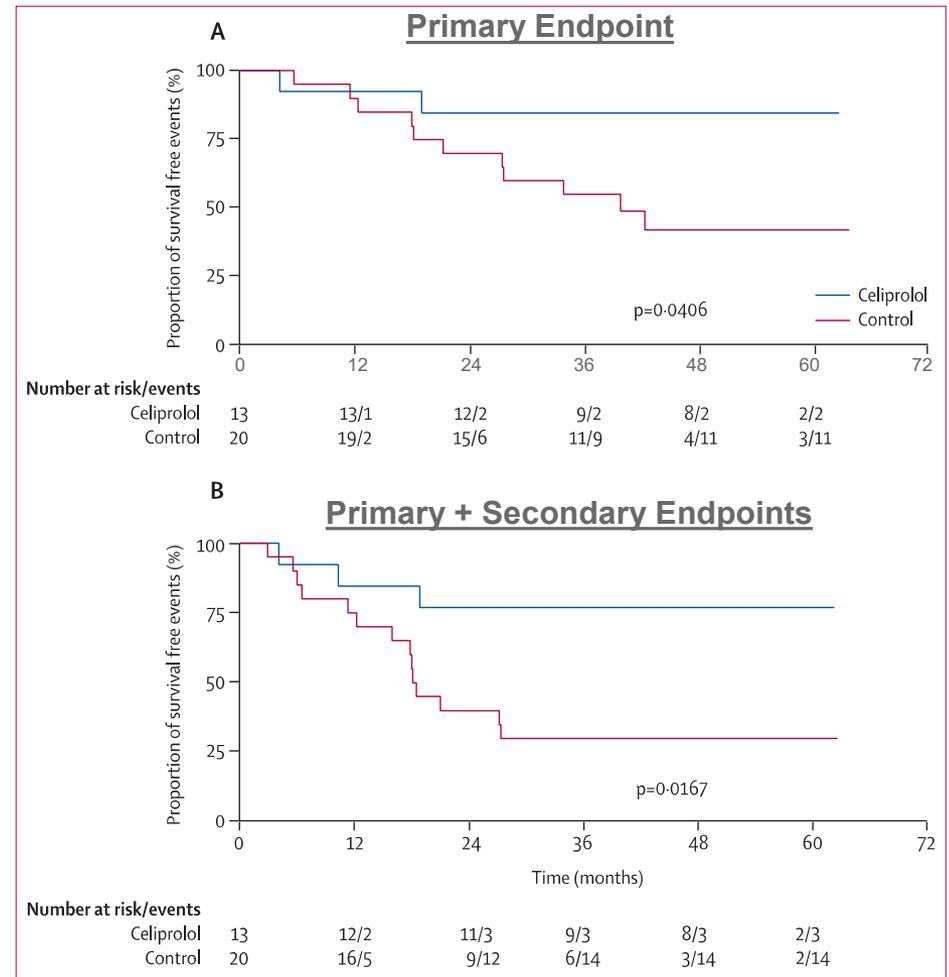
- EDSIVO™ has a unique pharmacological profile:
  - $\beta_2$  and  $\beta_3$  adrenergic receptor agonist
  - Selective  $\beta_1$  and  $\alpha_2$  adrenergic receptor antagonist
  - Intrinsic sympathomimetic activity (ISA+)
  - Lacks non-specific membrane effects
  - Activates endothelial Nitric Oxide 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 ( $\beta_1$  antagonism)
- EDSIVO's™ potential beneficial effects in vEDS patients are 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 NH<sub>4</sub><sup>+</sup> 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 NH<sub>4</sub><sup>+</sup>
- **UCDs:** Currently treated with RAVICTI<sup>®</sup>, BUPHENYL<sup>®</sup>, AMMONUL<sup>®</sup>, 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<sup>®</sup>
- **MSUD:** POC study<sup>1</sup> suggests ~60% of patients have 30% reduction in Leucine

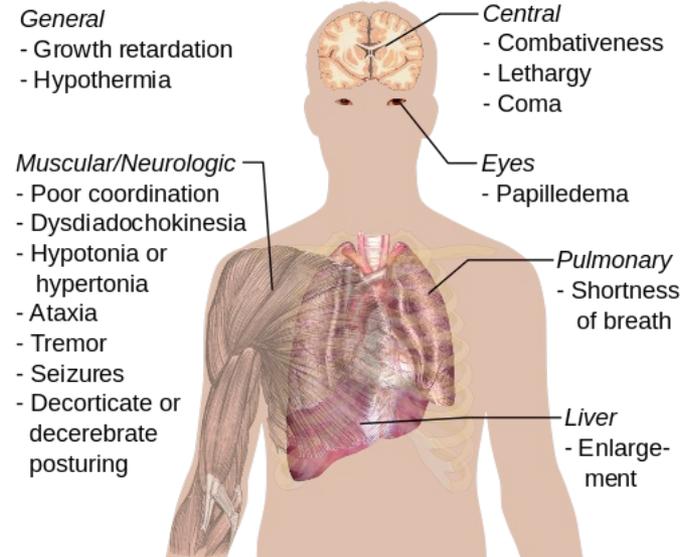
## The Opportunity

- **Anticipate NDA submission for UCD Q1 2021\*<sup>§</sup>**
- **UCDs:** >2,000 patients in the U.S.; ~600 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



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[http://upload.wikimedia.org/wikipedia/commons/7/76/Symptoms\\_of\\_hyperammonemia.svg](http://upload.wikimedia.org/wikipedia/commons/7/76/Symptoms_of_hyperammonemia.svg).

# 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\*\*\*

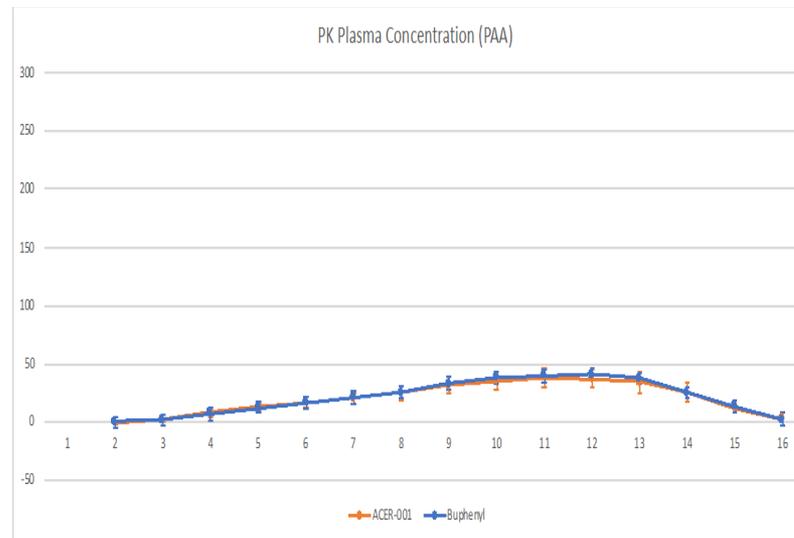
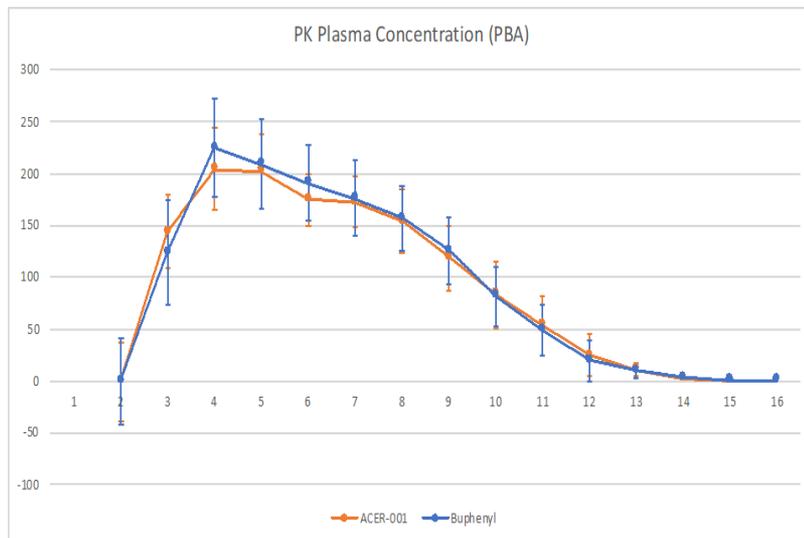
# ACER-001: Differentiation

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

# UCDs: Clinical & Regulatory Path

- Bioavailability and bioequivalence (BE) trials:
  - Part A: single-center, single-blind, randomized, single-dose crossover study designed to evaluate bioavailability of three different oral suspension formulations of ACER-001 compared to BUPHENYL® in 20 healthy adult subjects
    - ✓ Successfully completed and optimal formulation of ACER-001 identified
  - Part B: single-center, single-blind, randomized, single-dose crossover study to demonstrate bioequivalence of the optimal formulation of ACER-001 (chosen from Part A) compared to BUPHENYL® in 36 healthy adult subjects
    - ✓ Successfully completed in Q1 2020
- Taste Assessment trials:
  - Taste assessment of three different formulations of ACER-001 (multi-particulate powder) assessed relative to BUPHENYL® (powder) using certified taste-testers
    - ✓ Successfully completed and informed selection of optimal formulation of ACER-001
- NDA: Anticipate submission Q1 2021<sup>\$</sup> pending successful outcome of additional nonclinical work and 12-month long-term stability data

# UCDs: Bioequivalence Trial Results (Part A)



Lab Name	Parameter	Geometric Mean Difference	Lower 90% Confidence Limit	Upper 90% Confidence Limit
PBA	Cmax	98.01	93.85	102.36
	AUCt	98.87	96.33	101.47
	AUCinf	98.85	96.32	101.45
PAA	Cmax	97.51	92.82	102.44
	AUCt	95.94	90.35	101.87
	AUCinf	95.16	88.92	101.84

**PBA = phenylbutyrate; PAA = phenylacetate**

# UCDs: Market Opportunity

- Target existing Rx market share in UCDs
  - Currently 1,100 patients diagnosed with ~600 patients on Rx therapy\*
  - 2018 U.S. revenue for RAVICTI® & BUPHENYL® = \$248.4M
  - Goal: transition patients from RAVICTI® & BUPHENYL® to ACER-001 and capture a portion of new UCDs Rx
- “Transition” Value Story: A cost-effective, taste masked alternative for UCDs (assuming successful studies and FDA approval):
  - Bioequivalence to BUPHENYL®
  - Greater compliance/adherence compared to BUPHENYL® expected due to differentiated formulation providing taste masked alternative
  - Competitively priced vs. RAVICTI®
  - Payer engagement strategy to support switching

# ACER-001: Exclusivity / IP

- Filed formulation patent application (filed Oct. 2016)
- Issued patents (US/EP): “Methods of modulation of branched chain acids and uses thereof” [US PATENT NO. 10,092,532] in MSUD
  - Exclusive license rights from Baylor College of Medicine
- UCDs: 505(b)(2) application - 3 years potential market exclusivity from FDA approval
- 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

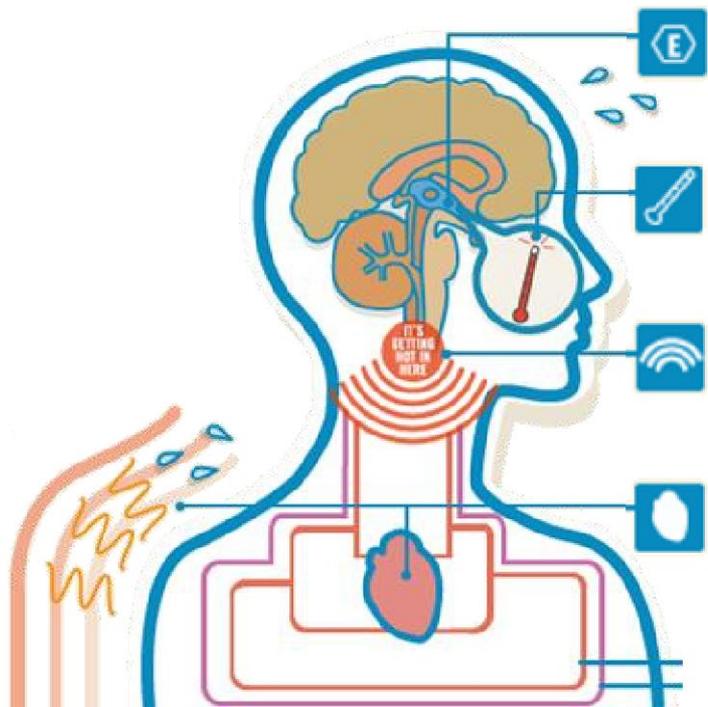
- **Acer licensed worldwide rights to osanetant from Sanofi in December 2018**
- Anticipate submitting IND in Q4 2020
- Multiple potential orphan opportunities
- Currently no other NK3R antagonists in development in iVMS space

# 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
- In March 2005, Sanofi-Aventis discontinued the development of osanetant 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 flashes<sup>5</sup>
- Up to 35% complain of “extremely bothersome” symptoms up to two years after their surgery<sup>6</sup>

## Men with HR+ Prostate Cancer (CaP) receiving Leuprolide

- 80% of men experience hot flashes<sup>3</sup>
- 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 flashes<sup>1</sup>
- 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 tamoxifen<sup>2</sup>

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

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

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

<sup>4</sup>Abildgaard, J, et al., JNCI Cancer Spectrum, 2018, Vol. 0, No. 0

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

<sup>6</sup>Griffiths, E, et al: The Obstetrician & Gynaecologist, 2005: 7:23-27

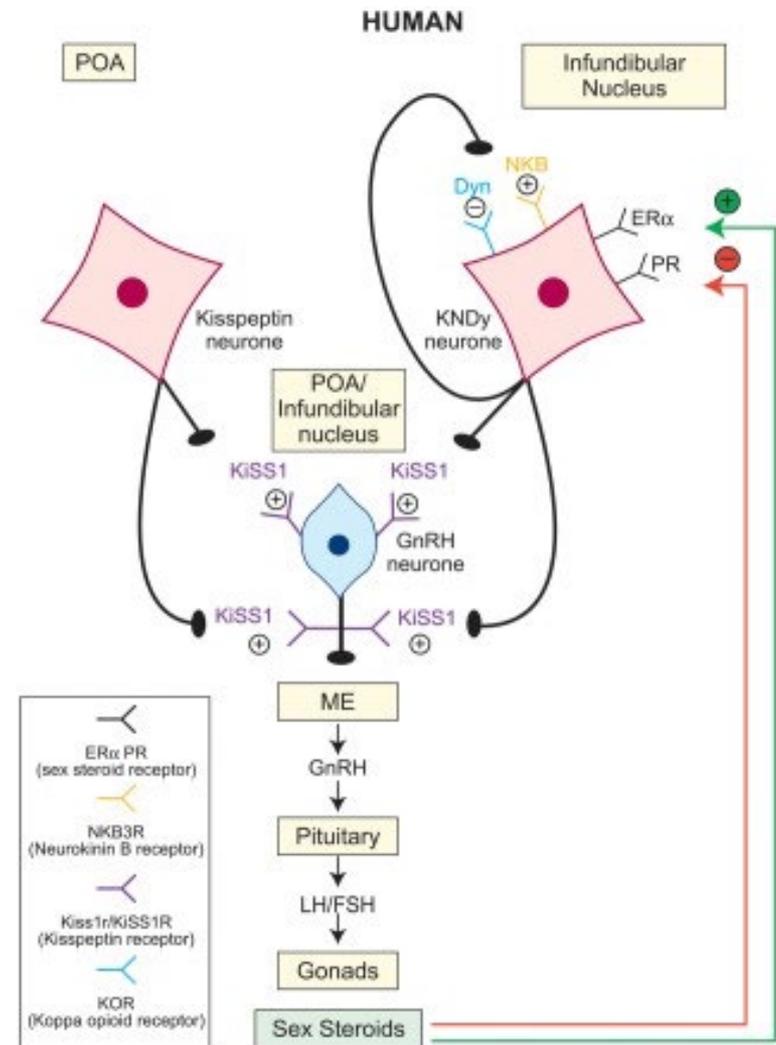
# iVMS: The Unmet Need

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- 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 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)

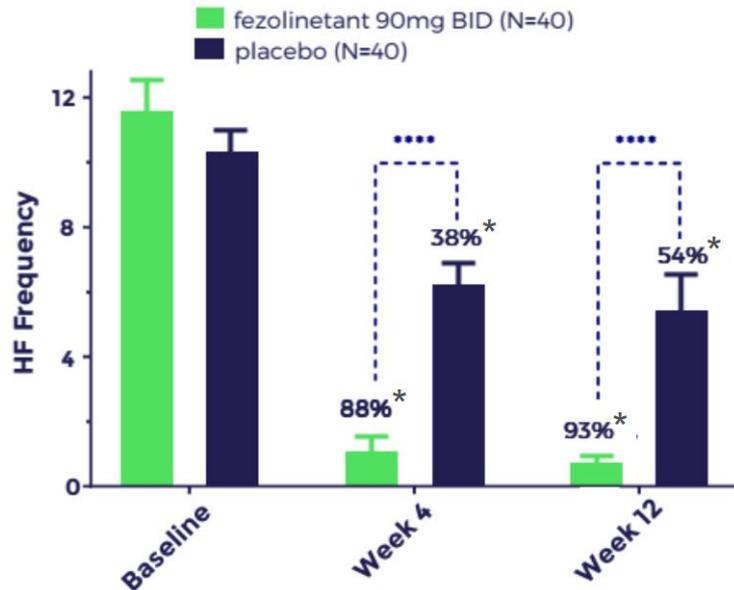
- Neurokinin B (NKB) belongs to a group of neuropeptides, called tachykinins or neurokinins, that includes substance-P (SP), neurokinin A (NKA), and two N-terminally extended forms of NKA, neuropeptide g and neuropeptide K
- The biological effects of tachykinins are mediated through specific receptors 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)



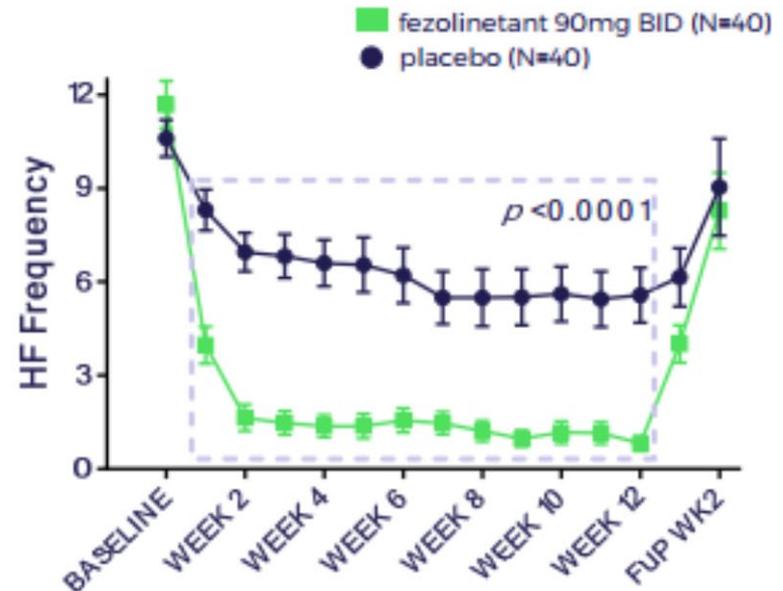
# NK3R Antagonist Clinical POC in VMS

- Fezolinetant is a NK3R antagonist being developed by Astellas

## Average Daily Hot Flash Frequency Reported as per FDA Guidance



\* : % decrease from the baseline

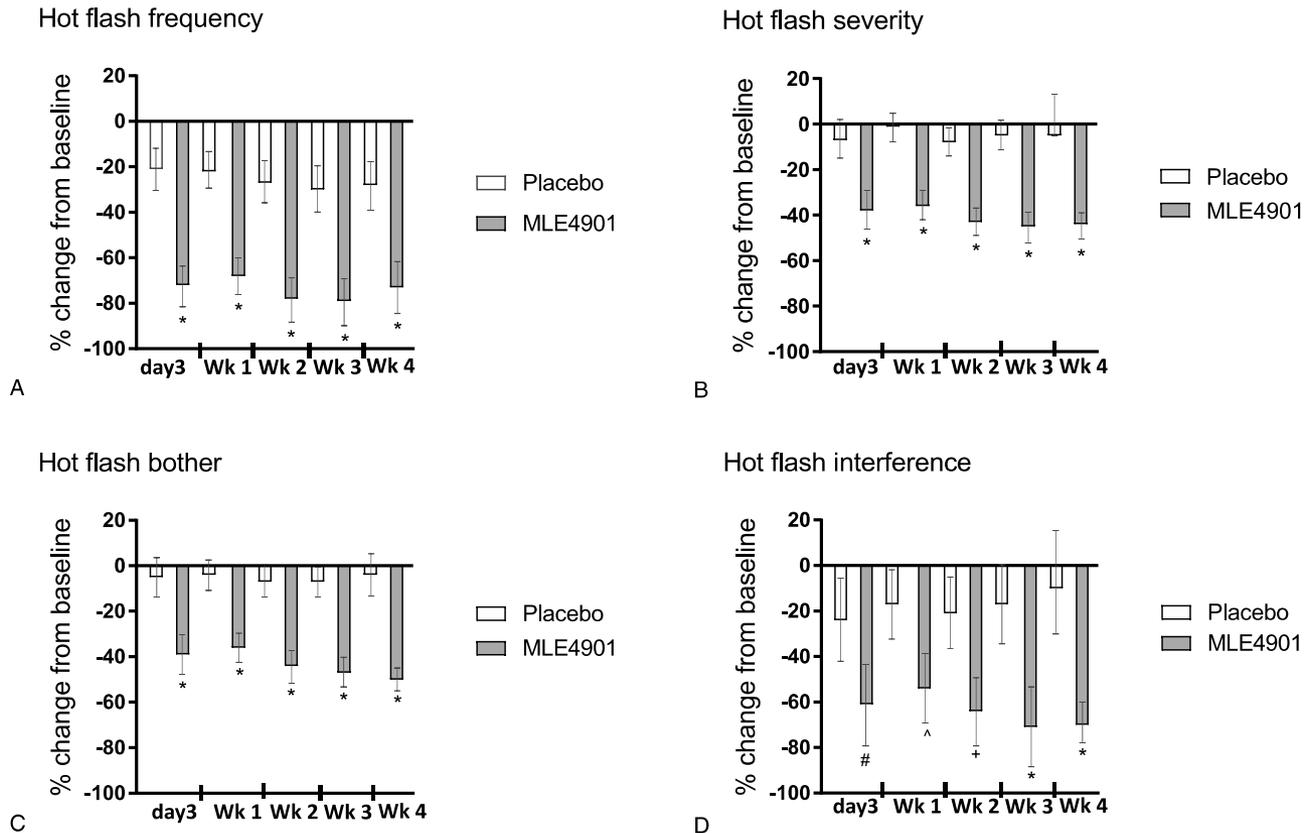


### At Week 4:

- 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



**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*, 2017<sup>18</sup>.

# Osanetant: Clinical Development Plan

- Acer is partnering with leading universities to design & conduct a clinical trial 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
- This initial Phase 1/2 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

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- 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 Q1 2021, subject to additional capital

# Financial Overview

- Cash
  - \$12.1M as of December 31, 2019
  - 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:	<b>Q2 2020</b>
• Emetine Phase 2/3 trial initiation* <sup>§</sup> :	<b>Q3 2020</b>
• Osanetant IND submission:	<b>Q4 2020</b>
• Osanetant initiate Phase 1/2 <sup>§</sup> :	<b>Q1 2021</b>
• ACER-001 (UCD) NDA submission** <sup>§</sup> :	<b>Q1 2021</b>
- Expected to have sufficient capital into Q4 2020, excluding support for the planned emetine trial and EDSIVO™ development and precommercial activities

\*Subject to successful IND submission and clearance

<sup>§</sup>Subject to additional capital

\*\*Assuming successful outcomes of additional nonclinical work and 12-month long-term stability data



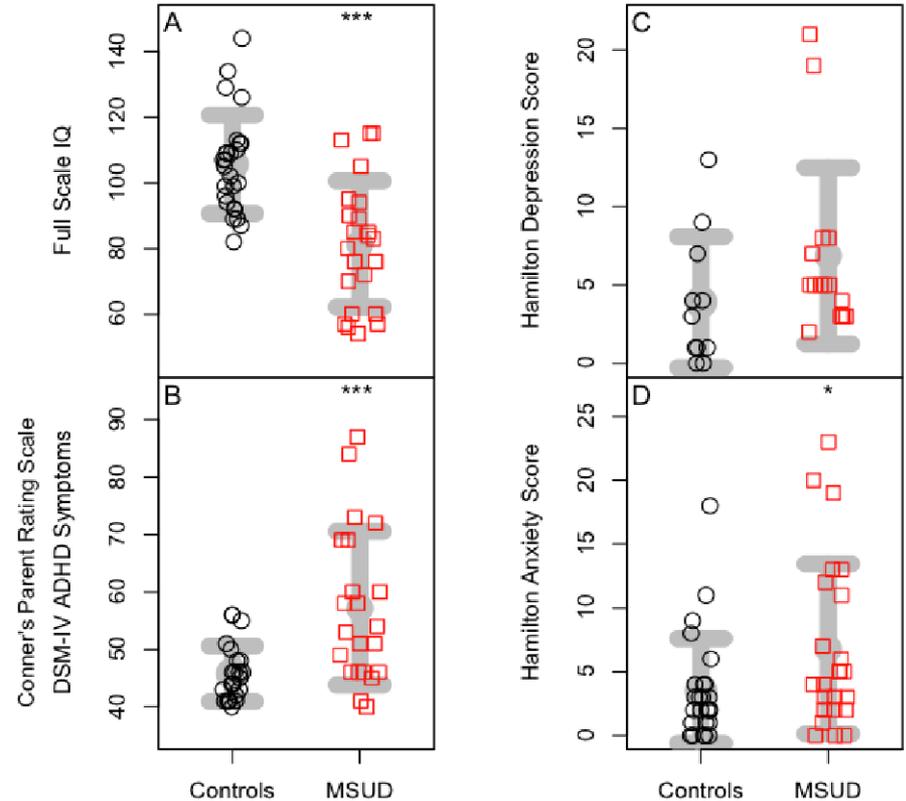
acertherapeutics

## Reference Slides



# Maple Syrup Urine Disease (MSUD)

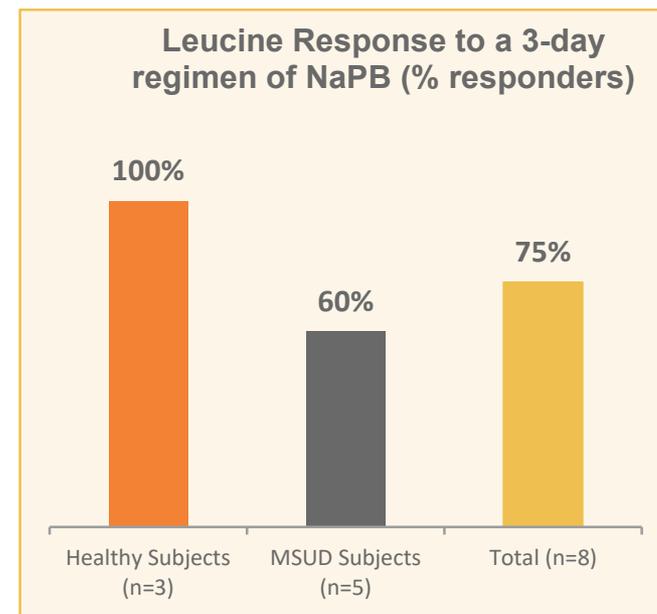
- MSUD is an inborn error of Branched-chain Amino Acid (BCAA) – leucine, isoleucine, valine – metabolism
  - Caused by deficiency of the mitochondrial Branched-chain Keto Acid Dehydrogenase complex (BCKDC)
  - ~800 patients in U.S., ~3,000 patients worldwide
  - MSUD Family Support Group has >500 patients
  - 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 study<sup>1</sup> at BCM – 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 demonstrated statistically significant leucine reduction 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

<sup>1</sup>Brunetti-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 by end of 2020§