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

Corporate Presentation

November 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 the potential for our product candidates 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; our ability to secure the additional capital necessary to fund our various product candidate development programs; the adequacy of our capital to support our future operations and our ability to successfully fund, initiate and complete clinical trials and regulatory submissions; 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 fund our various product candidate development programs and 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 and requirements 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: $6.2M as of September 30, 2020, combined with additional $1.0M of proceeds subsequently received from ATM stock sales and Lincoln Park stock purchase agreement
  - Expected to have sufficient capital to fund current operations into Q1 2021, excluding support for the planned emetine Phase 2/3 clinical trial, which is also subject to ongoing discussions with FDA

Leadership Team

Chris Schelling **CEO & Founder**	• 21 years; strategic commercial development & orphan	BIOMARIN
Harry Palmin **Chief Operating & Financial Officer**	• 25+ years; corporate & finance experience	Novelos
Matt Seibt **Chief Commercial Officer**	• 22 years; sales, market access & product launch	Biogen
John Klopp **Chief Technical Officer**	• 18 years; orphan manufacturing & commercialization	BIOMARIN
Don Joseph, JD **Chief Legal Officer & Secretary**	• 25+ years; general counsel & senior management	bvgh BIO Ventures for Global Health
Stacey Bain, Ph.D. **VP, Clinical Operations**	• 22 years; clinical operations & drug development	WuXi CLINICAL
Renee Carroll **VP, Regulatory Affairs**	• 25+ years; regulatory affairs, all phases of development	sunovion

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Investment Highlights

- Acer's pipeline includes four programs:
  - **Emetine** for the treatment of COVID-19
  - **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)
  - **EDSIVO™** (celiprolol) for the treatment of vascular Ehlers-Danlos syndrome (vEDS) in patients with a confirmed type III collagen (COL3A1) mutation
  - **Osanetant** for the treatment of induced Vasomotor Symptoms (iVMS)

- 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 milestones:
  - Emetine animal efficacy study results: **Q4 2020**
  - EDSIVO™ request FDA meeting to discuss confirmatory evidence plan: **Q4 2020**
  - Emetine IND submission and Phase 2/3 trial initiation*$: **H1 2021**
  - ACER-001 BE fed trial completion: **Q1 2021**
  - ACER-001 pre-NDA meeting with FDA: **mid-H1 2021**
  - ACER-001 (UCD) NDA submission**$: **Q2 2021**
  - Osanetant IND submission: **Q2 2021**
  - Osanetant Phase 1/2 trial initiation*$: **H2 2021**

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*Subject to successful IND submission and clearance
$Subject to additional capital
**Assuming successful outcomes of BE trial under fed conditions, additional nonclinical work and long-term stability data

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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	*			
ACER-001 (taste-masked, immediate-release form of sodium phenylbutyrate)					
Urea Cycle Disorders	Evaluating bioequivalence to BUPHENYL®				**
Maple Syrup Urine Disease	Inhibition of BCKD kinase to increase BCAA metabolism				
EDSIVO™ (celiprolol)					
vascular Ehlers-Danlos syndrome (COL3A1+)	Induces vascular dilatation and smooth muscle relaxation				***
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
**Requires bioequivalence (BE) trial under fed conditions
***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

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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 50 million cases and 1.25 million deaths worldwide (as of 11/9/2020)

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 IND submission and Phase 2/3 trial initiation in H1 2021[$*]**
- Proposed trial will evaluate emetine in high-risk, symptomatic adult patients with COVID-19 infection not requiring hospitalization
- Pursuing multiple non-dilutive financing options
- Acer to oversee supply and contract manufacture of emetine
- Anticipate in vivo efficacy results from ongoing animal studies evaluating emetine's anti-viral activity against COVID-19 by the end of Q4 2020

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[$]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 hepatitis[1] and varicella-zoster virus[2]
- 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)	**IC_{50} = 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)	**EC_{50} = 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)	**EC_{50} < 0.01 µM**	Ianevski et al. 2020 May. Antiviral options against SARS-CoV-2 infection. doi.org/10.1101/2020.05.12.091165
HCoV-OC43	**EC_{50} = 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	**EC_{50} = 1.43 / CC50 = 3.63**	
MERS-CoV	**EC_{50} = 0.34 / CC50 = 3.08**	
MHV-A59	**EC_{50} = 0.12 / CC50 = 3.51**	
MERS-CoV	**EC_{50} = 0.014**	Dyall et al. Antimicrob Agents Chemother. 2014 Aug;58(8):4885-93. doi: 10.1128/AAC.03036-14.
SARS-CoV	**EC_{50} = 0.051**	
ZIKV-MR766	**IC_{50} = 9.15e-009**	Yang et al. Cell Discov. 2018 Jun 5;4:31. doi: 10.1038/s41421-018-0034-1.
ZIKV-FSS13025	**IC_{50} = 1.072e-008**	
ZIKV-PRVABC59	**IC_{50} = 9.591e-009**	
EBOV-Vero E6	**IC_{50} = 16.9 nM**	
HSV-2	**EC_{50} = 0.03 / CC_{50} = 1.12**	Andersen et al. Viruses. 2019 Oct 18;11(10). pii: E964. doi: 10.3390/v11100964.
HMPV	**EC_{50} = 0.14 / CC_{50} = 1**	
HIV M184V	**EC_{50} = 0.012 – 0.03**	Chaves Valadao et al. Molecules. 2015 Jun 22;20(6):11474-89. doi: 10.3390/molecules200611474.
HCMV	**EC_{50} = 40 nM / CC_{50} = 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

*EC_{50} / CC_{50} values = µM (unless otherwise noted)

**For reference, the EC50 of remdesivir is 23.15 µM at MOI 0.02; paper demonstrates that emetine is synergistic with remdesivir

1. Del Puerto et al. Pren. méd. argent., 55: 818, 1968.
2. Annamalai et al. Emetine Hydrochloride in the Treatment of Herpes Zoster. 1968.

Emetine: Uniquely Suited for COVID-19

Nanomolar potency in SARS-CoV-2 in vitro models

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

High and long duration lung tissue concentrations[4]

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

Clinical experience with parenteral emetine

- 600+ patients with viral hepatitis treated[5]
- 90 patients with herpes zoster treated[6]

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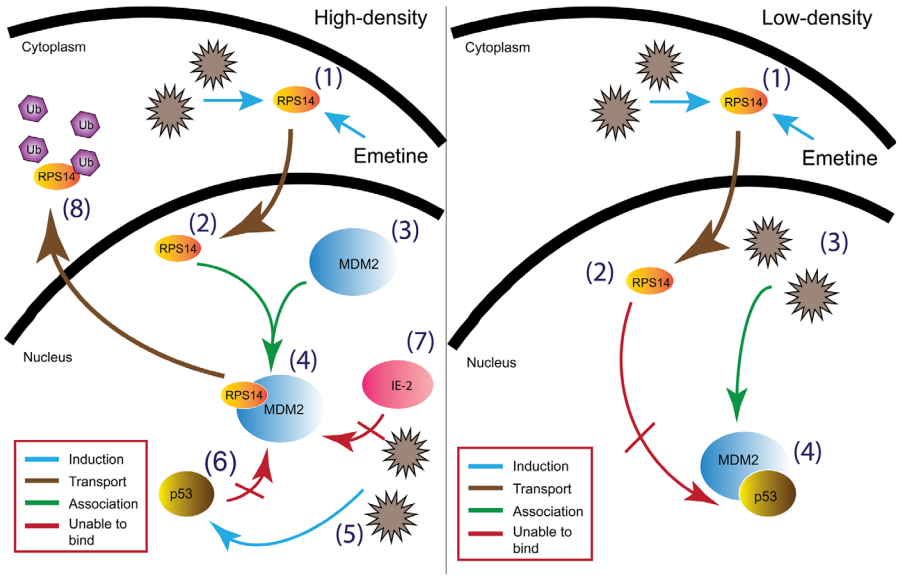
1 Bojkova, D. et al. Proteomics of SARS-CoV-2-infected host cells reveals therapy targets. Nature https://doi.org/10.1038/s41586-020-2332-7 (2020).
2 Ianevski et al. 2020 May. Antiviral options against SARS-CoV-2 infection. doi.org/10.1101/2020.05.12.091165.
3 Choy et al. Antiviral Res. 2020 Jun; 178: 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).

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PLoS Pathogens 12(6):e1005717, June 2016.

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[1]

- Electrocardiographic abnormalities were observed, 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 reported[5]

- Toxicity with emetine appears to be cumulative-dose related and independent of schedule[1,6]

- Complete reversibility of cardiac adverse effects[6]

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 and saliva/mouthwash
  - 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

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*Subject to successful IND submission and clearance, and additional capital

Emetine: Regulatory Path

- Multiple pre-IND briefing packages submitted to the Division of Antivirals (DAV) in April, June and September 2020
- Discussions ongoing regarding requirements needed to submit IND
- Assuming FDA supports moving forward, Acer aims to submit IND followed by potential clinical trial initiation in H1 2021*

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ACER-001: Overview

Mechanism of Action

- **Small molecule with unique MOAs in various disorders**
- **UCDs**: NaPB is a prodrug of phenylacetate, a NH_4^+ 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_4^+
- **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 under fasted conditions
- ACER-001 under fasted conditions achieved >2x C_{max} of PBA vs. under fed conditions
- **MSUD**: POC study[1] suggests ~60% of patients have 30% reduction in Leucine

The Opportunity

- **Anticipate NDA submission for UCD Q2 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

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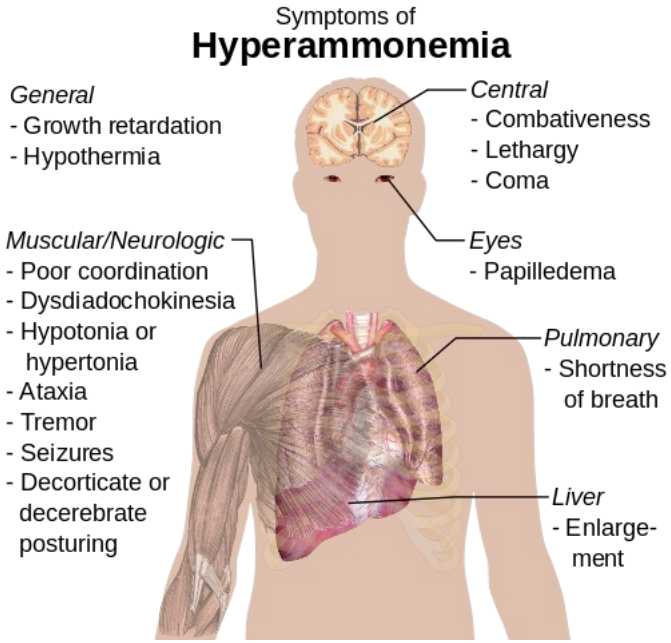
[1]Brunetti-Pierri et al., Hum Mol Genet. 2011 February 15; 20(4): 631–640.
*Assuming successful outcomes of BE trial under fed conditions, additional nonclinical work and long-term stability data
$Subject to additional capital

UCDs: Clinical Manifestations

- Newborns with severe urea cycle disorders become significantly 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 an ornithine transcarbamylase (OTC) deficiency, typical neuropsychological complications include developmental delay, learning disabilities, intellectual disability, attention deficit hyperactivity disorder (ADHD), and executive function deficits



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

Ah Mew N, et al.. Urea cycle disorders overview. Gene Reviews. Seattle, Washington: University of Washington, Seattle; 1993.
Lichter-Knoecki U., et al. Ornithine Transcarbamylase Deficiency, Gene Reviews. Seattle, Washington: University of Washington, Seattle; 1993-2019.

UCDs: Medical Management

- Chronic treatment options for UCDs include:
  - Restricted Diet
  - Liver Transplantation
  - Carbaglu (for treatment of NAGS only)
  - Sodium Benzoate (does not have an FDA or EMA approval)
  - **Phenylbutyrate (BUPHENYL®, RAVICTI®)**

	BUPHENYL® (sodium phenylbutyrate) *	RAVICTI® (glycerol phenylbutyrate) Oral Liquid *
Differentiation	Sodium phenylbutyrate Foul odor and bitter taste; Considered unpalatable[1,2] Powder / Tablets	Glycerol phenylbutyrate Tasteless, odorless Liquid (oil)

* BUPHENYL® and RAVICTI® are registered trademarks of Horizon Pharma, Inc.

[1] 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

[2] Koren et al. Averting the foul taste of pediatric medicines improves adherence and can be lifesaving – Pheburane® (sodium phenylbutyrate) Patient Preferences and Adherence 2016:10 2141-2144

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

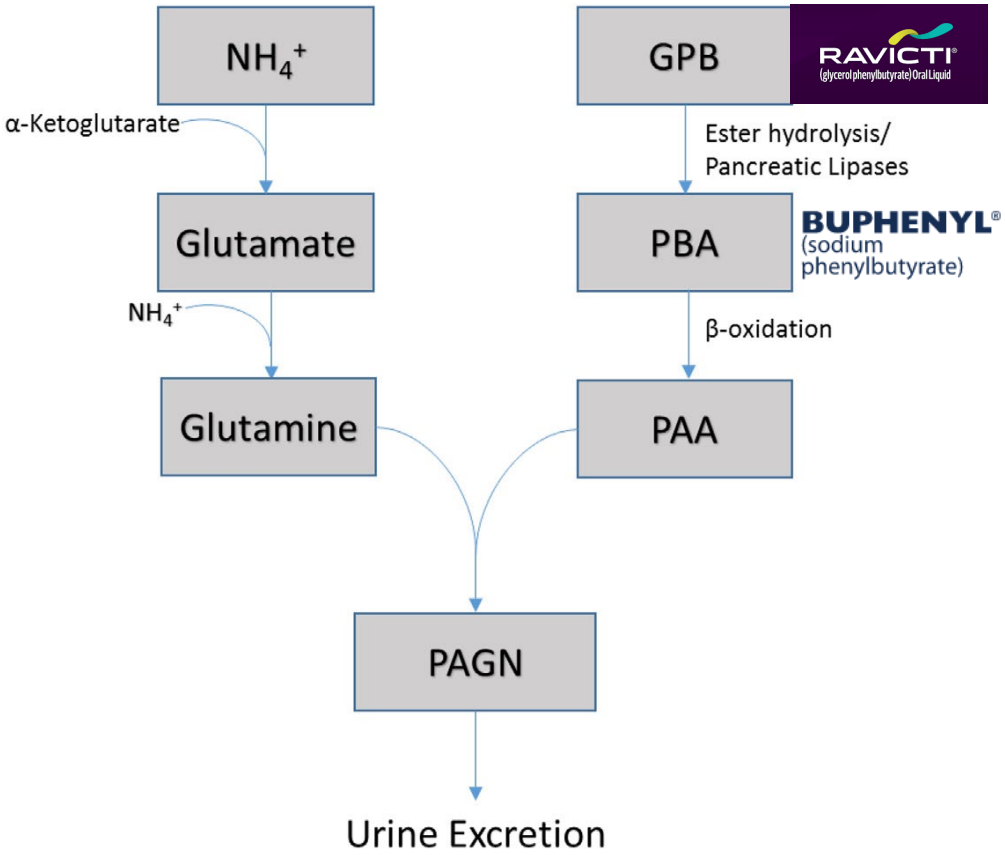


Fig. 1. Metabolizing pathway and mechanism of action of GPB.
GPB (glycerol phenylbutyrate); PAA (phenylacetic acid); PBA (phenylbutyric acid); PAGN (phenylacetylglutamine).

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Berry S, et al. Pharmacokinetics of glycerol phenylbutyrate in pediatric patients 2 months to 2 years of age with urea cycle disorders. Molecular Genetics and Metabolism 125 (2018) 251–257.

Unmet Need in Nitrogen Scavengers

- **BUPHENYL®**: Foul odor and foul/bitter taste; considered unpalatable[1]
  - 64% of patients reported it is difficult to take because of taste
  - Physicians reported that 25-33% of patients took 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[1]

- **RAVICTI®**: Tasteless/Odorless
  - 75% of the BUPHENYL® patients switched to RAVICTI®[3]
  - Pricing has risen to levels considered challenging[3]
  - Reports of difficult access, unaffordability, and forced switches back to sodium phenylbutyrate
    - Example: BUPHENYL® and RAVICTI® blocked on JPMorgan Chase plan Rx formulary[2]
  - Some patients are not meeting the treatment goal of <0.5 ULN (~17.5 umol/L)[4]
  - Patients and physicians desire a taste-masked, effective, and affordable treatment option[3]

- **Sodium Benzoate**:
  - Does not have an FDA approval for UCD
  - 36% non-compliance rate due to tolerability[1]
  - Less effective in nitrogen excretion than NaPB or GPB[3]

[1]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.

[2]https://www.caremark.com/portal/asset/Formulary_Drug_Removals_JPMC.pdf

[3]Acer Market Research

[4]Nicola Longo & Robert J. Holt (2017) Glycerol phenylbutyrate for the maintenance treatment of patients with deficiencies in enzymes of the urea cycle, Expert Opinion on Orphan Drugs, 5:12, 999-1010

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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 INFORMATION [2]
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.

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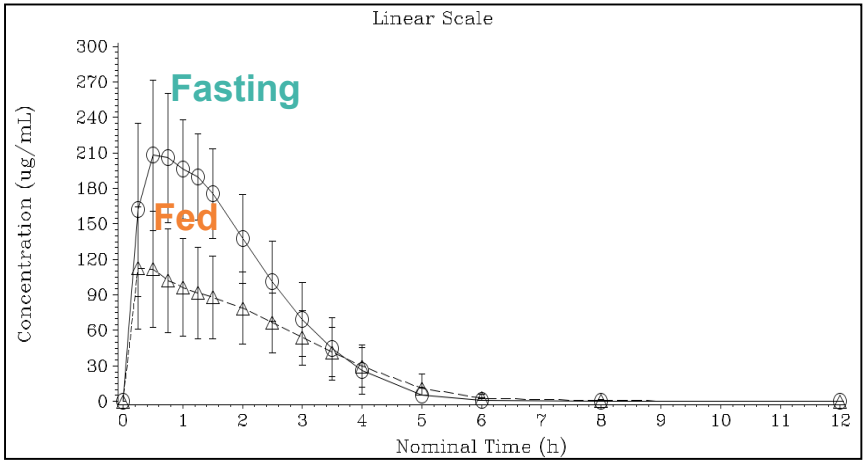
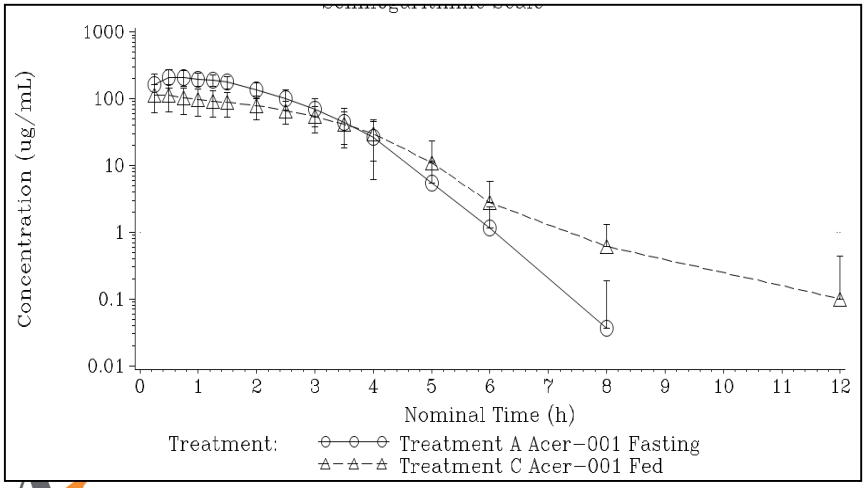
1 https://www.hzndocs.com/BUPHENYL-Prescribing-Information.pdf
2 https://www.hzndocs.com/RAVICTI-Prescribing-Information.PDF

NaPB: Food Effect

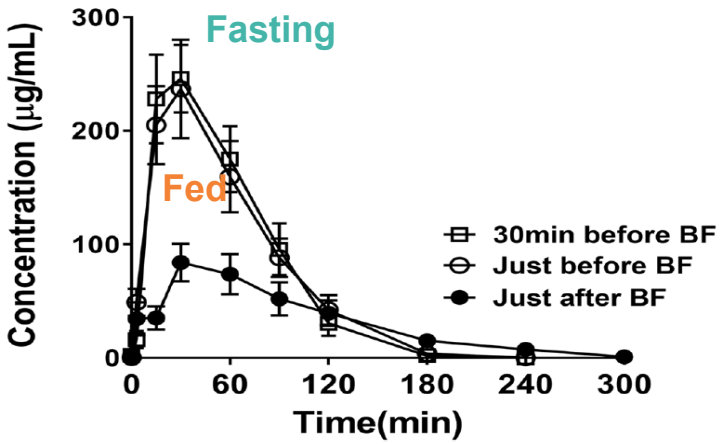
- Maximum concentration (C_{max}) ~2x higher under fasted/pre-meal conditions
- Comparable PK between ACER-001 and NaPB under fed conditions*

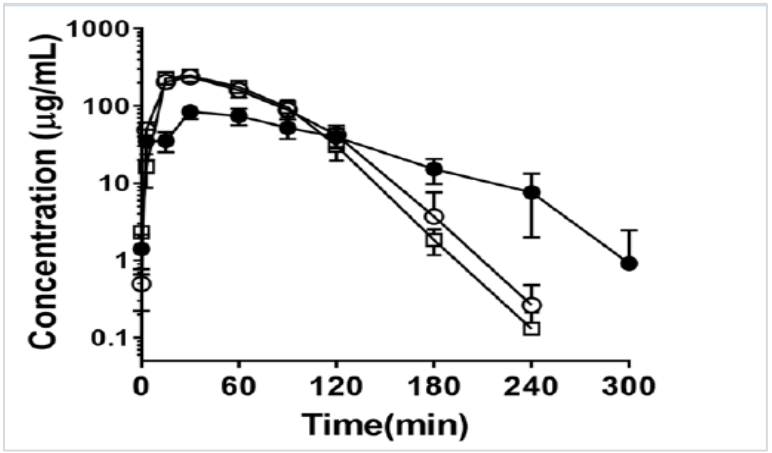
ACER-001[1]





NaPB[2]





*Based on data comparison of ACER-001 under fed conditions vs. published data of NaPB under fed conditions

1 ACER-001 Pivotal BE/BA Study (Part B) in healthy volunteers

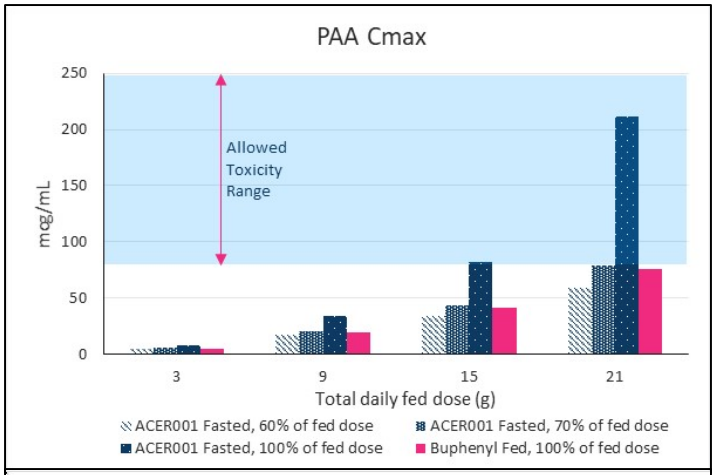
2 Sci Rep 9, 17075 (2019). https://doi.org/10.1038/s41598-019-53628-x

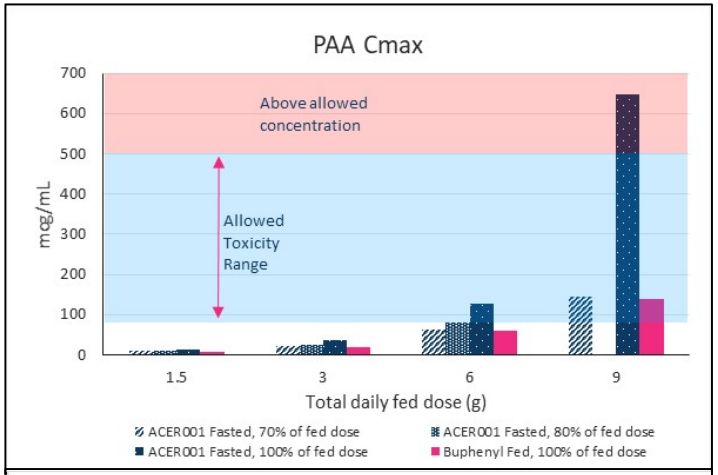
PK: Rosa & Co. In Silico Model

Adult Virtual Patient

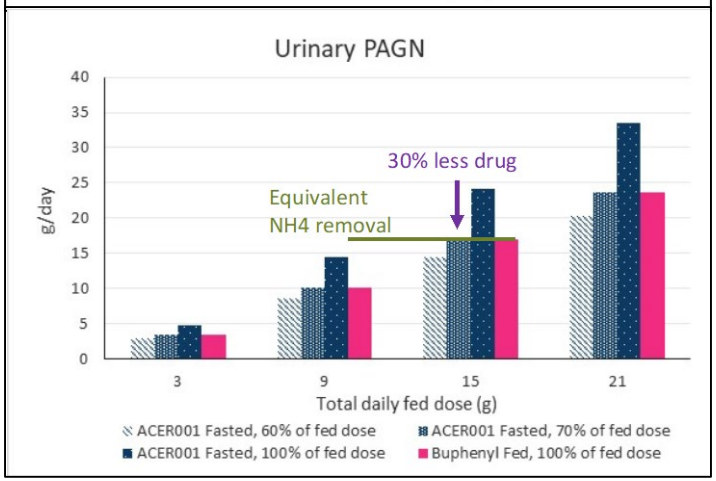
Child Virtual Patient

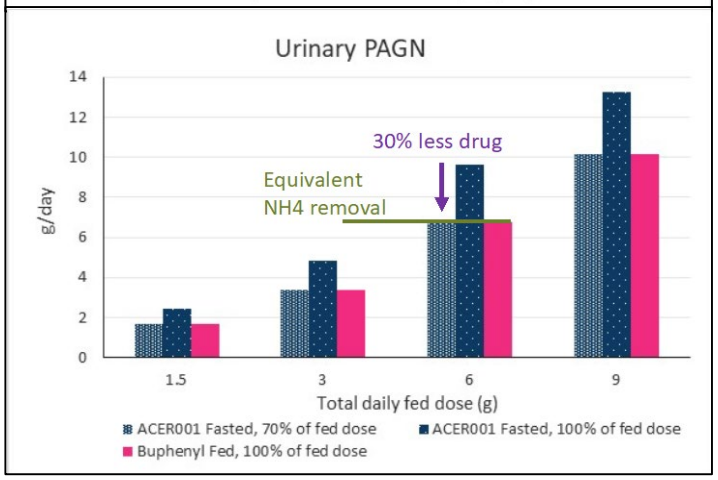
PAA (Safety[1,2,3])





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)

1 Mol Genet Metab. 2013 Dec; 110(4): 446-453.
2 Pediatr Res. 1986 Nov; 20(11):1117-21.
3 Cancer. 1995 Jun 15; 75(12):2932-8.

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Food Effect: 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 states[1]
- Dosing in a pre-meal setting 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 PFIC[2]
- ACER-001's taste-masked formulation should improve palatability / tolerability of the drug when administered under fed or pre-meal conditions

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1 United States Patent number US8642012B2
2 Sci Rep 9, 17075 (2019). https://doi.org/10.1038/s41598-019-53628-x

UCDs: Clinical & Regulatory Paths

- ✓ BE trial under fasted conditions successfully completed in Q1 2020
- ✓ Received FDA Type C meeting feedback in August 2020
- BE trial under fed conditions:
  - Plan to complete in Q1 2021
- Anticipate pre-NDA meeting with FDA in mid-H1 2021
- 505(b)(2) NDA: anticipate submission Q2 2021[$] pending successful outcome of BE trial under fed conditions, additional nonclinical work and long-term stability data
- Evaluate in parallel[$] or after initial potential FDA approval under fed conditions:
  - Pre-meal administration of ACER-001 with dose reduction which would include additional clinical studies[$] to demonstrate efficacy and safety in UCDs
  - MSUD
  - Other potential indications

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[$]Subject to additional capital

ACER-001: Differentiation

Phenylbutyrate Formulations			
	ACER-001[1] (Investigational)	RAVICTI®	BUPHENYL®
Efficacy / Safety in UCDs	✓	✓	✓
Palatability / Compliance	✓	✓	✗[2]
Pricing (Per Patient Per Year)	TBD, likely near BUPHENYL®	$200k-$1.2M[3] (avrg ~$900K)	$200k-$400k[4]
Formulation	Multi-Particulate (Sachet)	Oil (Tablespoons)	Powder/Tablets (up to 40 tablets/day)

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1 Subject to FDA approval
2 Molecular Genetics & Metabolism Reports 8 (2016) 43-47.
3 RAVICTI® and BUPHENYL® pppy is based on patient weight and WAC price

UCDs: Market Opportunity

- Concentrated treater community
  - ~100 metabolic disease centers manage vast majority of patients
- Target existing Rx market share in UCDs
  - Currently about 1,100 patients diagnosed with ~600 patients on Rx therapy*
  - 2019 U.S. Revenue for RAVICTI® & BUPHENYL® = $239M
  - Goal: switch patients from RAVICTI® & BUPHENYL® to ACER-001 and capture a portion of new UCD Rx
- "Switch" Value Story: A cost-effective, taste masked alternative for UCDs (assuming successful studies and FDA approval):
  - Bioequivalence to BUPHENYL®
  - Taste-masked formulation designed to improve tolerability
  - Competitively priced vs RAVICTI®
  - Payer engagement strategy to support switching

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*https://www.sec.gov/Archives/edgar/data/1386858/000119312515110284/d899054dex992.htm
Horizon IR Presentation

ACER-001: IP / Exclusivities

- IP:
  - Filed formulation composition of matter patent application (priority date Oct. 2016)
  - Issued patents (US/EP): “Methods of modulation of branched chain acids and uses thereof” [US PATENT NO. 10,092,532], licensed from Baylor College of Medicine relating to MSUD
  - In addition, we continue to pursue new patents and exclusivity possibilities, based on our development plans and product attributes

- Regulatory Exclusivities:
  - MSUD: Granted U.S. Orphan Drug Designation: 7 years market exclusivity from FDA approval
  - Pediatric exclusivity: +6 months added (if pediatric indication study approved)

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**
- β2 and β3 adrenergic receptor agonist; selective β1 and α2 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[1]**
- 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 path forward**
- Expect to request a meeting with the FDA by the end of Q4 2020 on Acer's proposed plan to provide confirmatory evidence that may support potential NDA resubmission
- Neither resubmission nor the prospect of approval of EDSIVO™ NDA is assured

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[1]Ong Lancet 2010; 376: 1476-84.

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
- Pursuing next steps
  - Expect to submit meeting request with FDA by the end of Q4 2020 regarding Acer's proposed plan to provide sufficient confirmatory evidence that may support potential NDA resubmission*
- Updates to be provided as appropriate and the company may discontinue the process at any point where risk/benefit no longer justifies continued resources

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*Neither EDSIVO™ NDA resubmission nor approval is assured

FDA: Substantial Evidence of Effectiveness

THE QUANTITY OF CLINICAL EVIDENCE TO ESTABLISH EFFECTIVENESS

Two adequate and well-controlled clinical investigations[2]

- 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[2]

- 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[1]

- 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

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1 FDA Guidance Document (1998) 'Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products'.
2 FDA Guidance Document (2019) 'Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products'.

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[1]
- No approved therapeutic options for vEDS
  - Current treatment is focused on surgical intervention

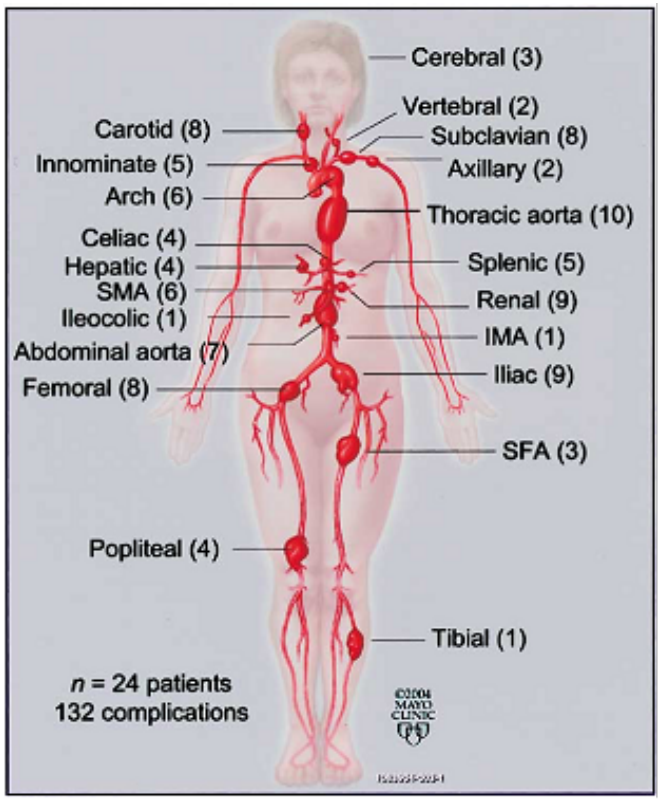

Fig. 3 Distribution of 132 vascular complications in 24 patients with a clinical diagnosis of EDS type IV. J Vasc Surg 2005;42:98-106.

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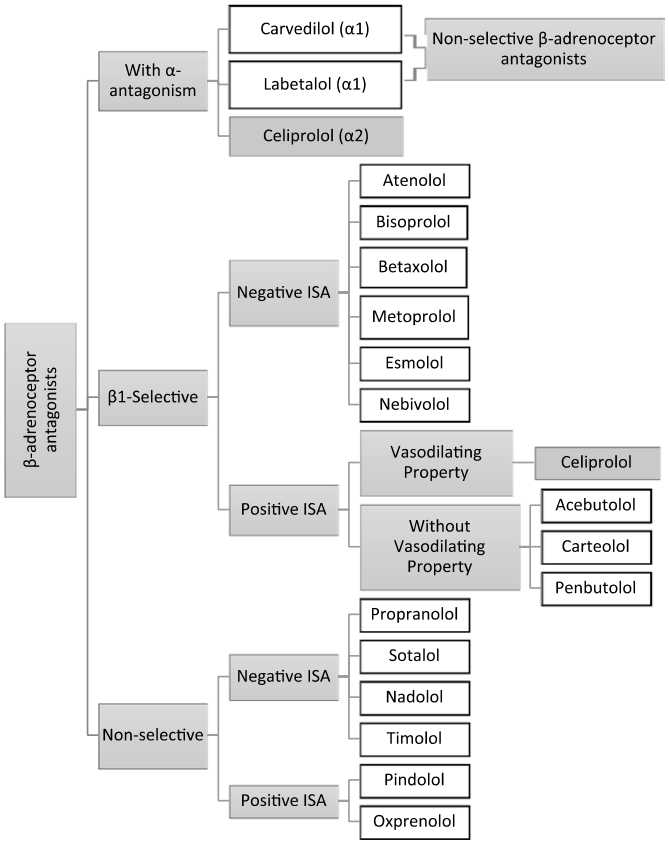
[1]Pepin Genet Med. 2014 Dec;16(12):881-8.

Unique Mechanism of Action

- EDSIVO™ has a unique pharmacological profile:
  - β2 and β3 adrenergic receptor agonist
  - Selective β1 and α2 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 (β1 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



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Cardiology in Review 2017;25: 247–253.
*Hypertension 2003 Nov;42(5):1004-13.

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

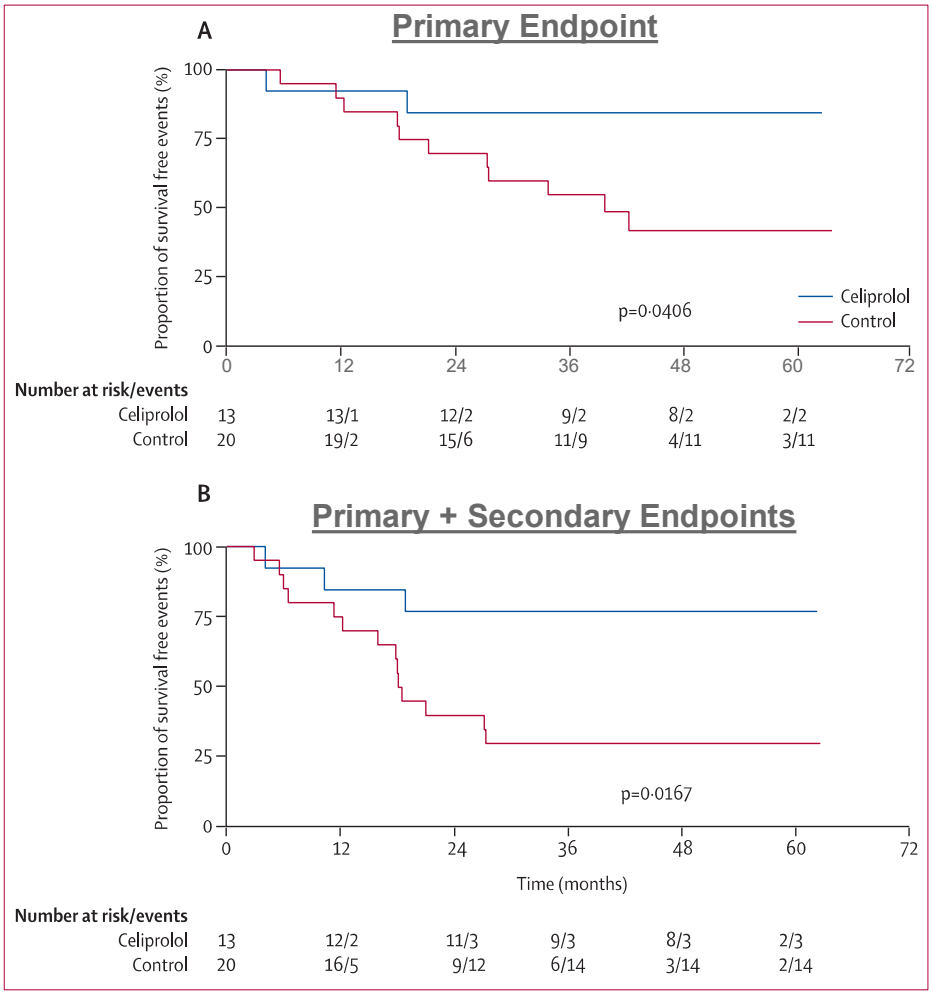

Figure 3: **Kaplan-Meier curves of event-free survival in 33 patients with positive *COL3A1* mutation**
Primary endpoint (A). Primary and secondary endpoints (B).

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Ong Lancet 2010; 376: 1476-84.

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 and KNDy neurons
- NK3R antagonism is an alternative to hormone replacement therapy for the treatment VMS by mimicking the negative feedback of estrogen on KNDy neurons

Disease Overview

- **Induced Vasomotor Symptoms (iVMS)**
  - iVMS are well documented with the use of cancer therapies and certain surgical procedures
  - Symptoms such as hot flashes can appear immediately and be severe after reduction in estrogen production or estrogen blockade
  - KNDy neurons are important for thermoregulation and become hypertrophied in the absence of estrogen

Product Profile

- **Clinical and laboratory safety results are available from 21 completed Phase 1 and 2 studies (409 healthy subjects and 822 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**
- Targeting IND submission in Q2 2021
- Plan to initiate Phase 1/2 trial in H2 2021**
- Currently no other NK3R antagonists in development in iVMS space

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*Am J Psychiatry. 2004 Jun;161(6):975-84.

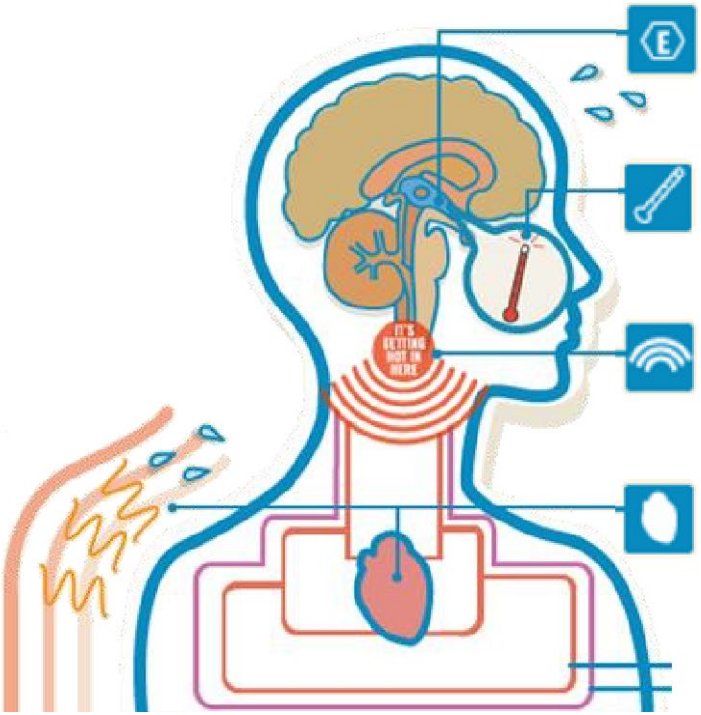
**Subject to successful IND submission and clearance, and additional capital

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 409 healthy subjects and 822 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

The Oncologist, Oct 2003, vol.8 no.5 474-487.
http://www.everydayhealth.com/menopause/science-behind-the-hot-flash.aspx

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[5]
- Up to 35% complain of "extremely bothersome" symptoms up to two years after their surgery[6]

Men with HR+ Prostate Cancer (CaP) receiving Leuprolide

- 80% of men experience hot flashes[3]
- 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[1]
- 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[2]

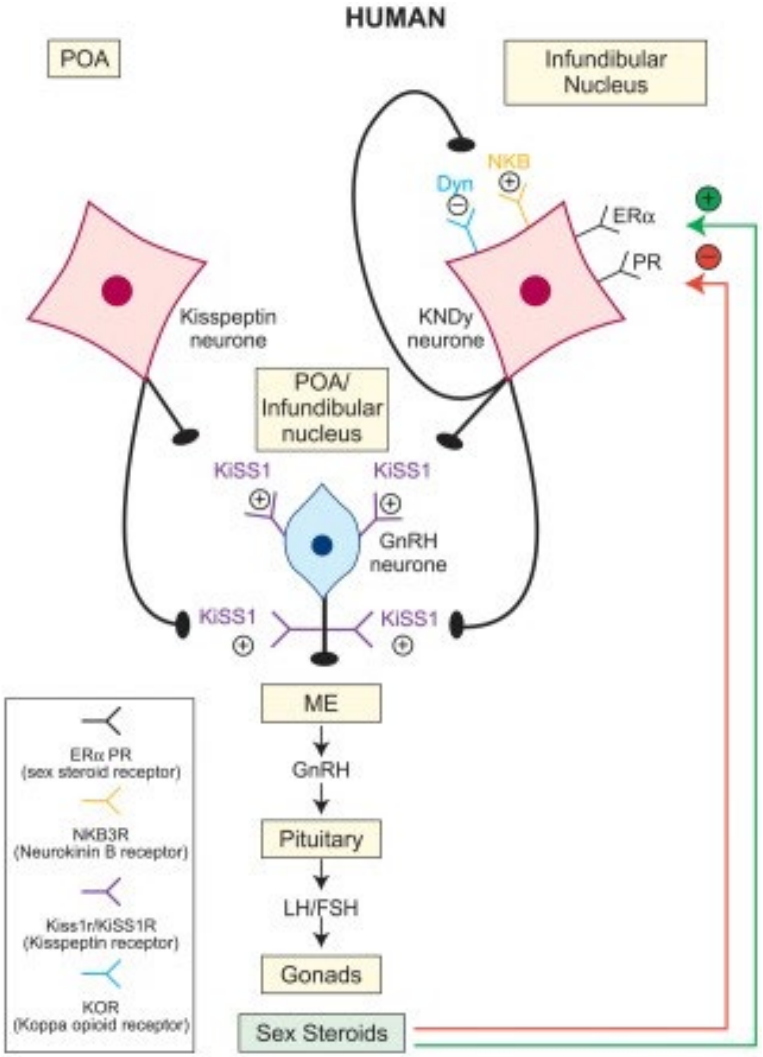
[1]Moon, Z. et al., JOURNAL OF PSYCHOSOMATIC OBSTETRICS & GYNECOLOGY, 2017 VOL. 38, NO. 3, 226–235.
[2]Nichols, H, et al., JNCI J Natl Cancer Inst, 2015, 1–8.
[3]Challapalli, A, et al., Clinical and Translational Radiation Oncology 10 (2018) 29–35.
[4]Abildgaard, J, et al., JNCI Cancer Spectrum, 2018, Vol. 0, No. 0.
[5]L. Johnson, et al. American Society for Reproductive Medicine, 2014 Vol 102 No. 3, Supplement, e249.
[6]Griffiths, E, et al: The Obstetrician & Gynaecologist, 2005: 7:23-27.

iVMS: The Unmet Need

- iVMS are well documented with the use of cancer therapies and certain surgical procedures
- Symptoms such as hot flashes can appear immediately and be severe
- 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 cancer therapy and BRCA2 post-PBSO can obtain help with significantly impactful and limiting iVMS

NK3 Receptor (Neurokinin B)

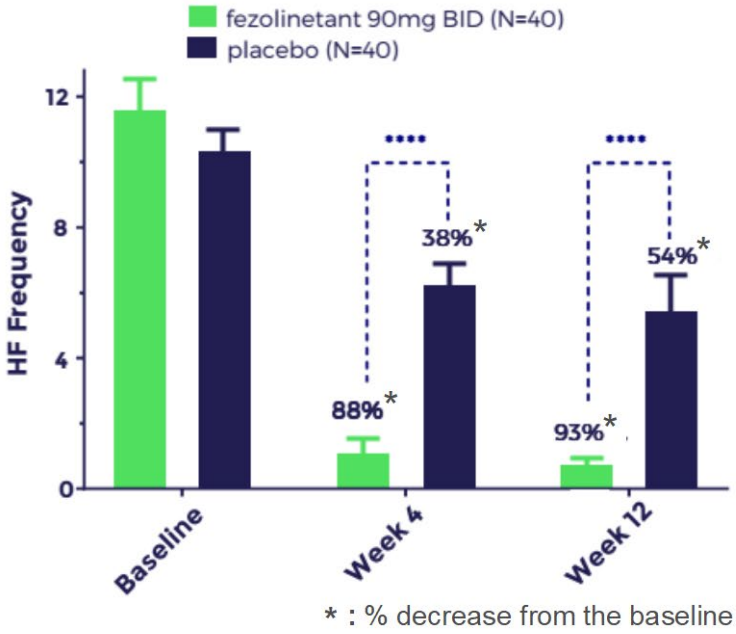
- Neurokinin B (NKB) belongs to a group of neuropeptides, called tachykinins or neurokinins, that includes substance-P (SP), neurokinin A (NKA), and two N-terminally extended forms of NKA, neuropeptide g and neuropeptide K
- The biological effects of tachykinins are mediated through specific receptors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



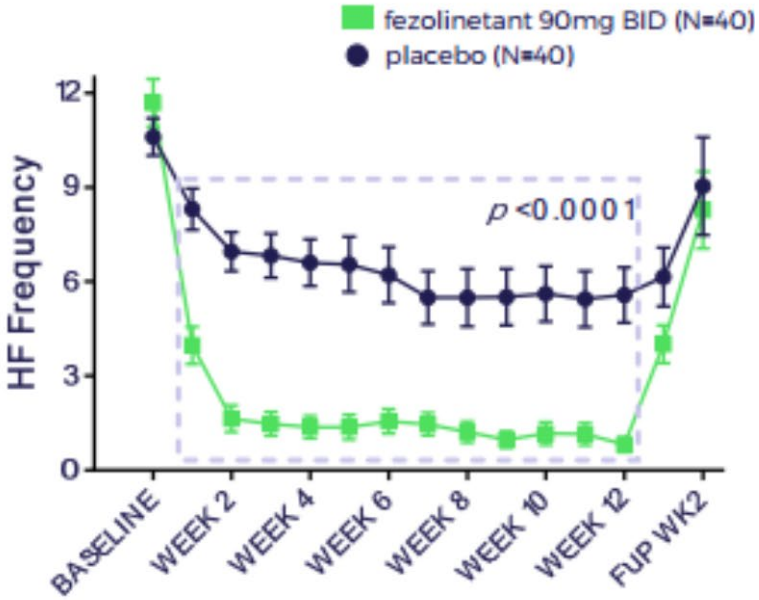
NK3R Antagonist Clinical POC in VMS

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

Average Daily Hot Flash Frequency Reported as per FDA Guidance



* : % 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*

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Herman Depypere et al., ENDO2017.

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 flushes

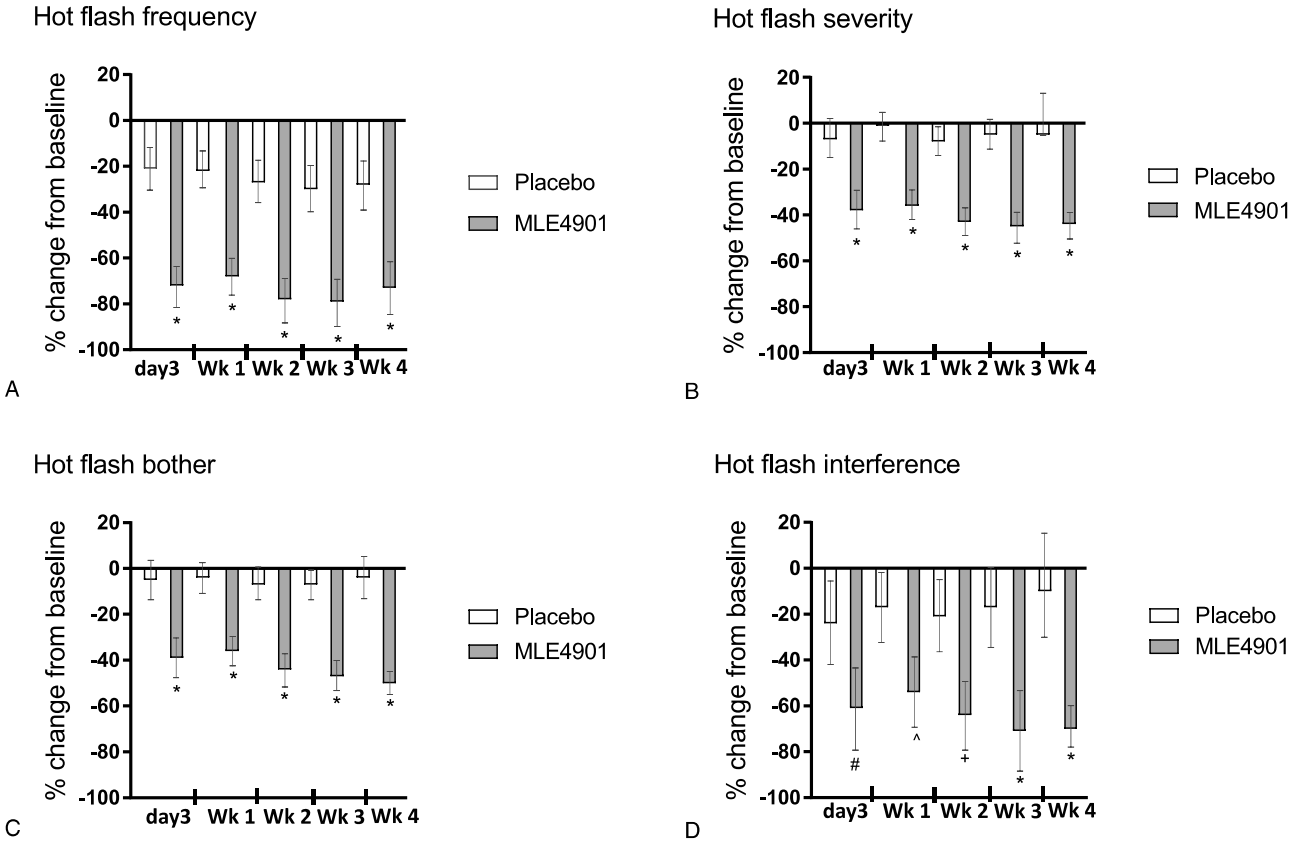

FIG. 2. Hot flash frequency (A), severity (B), bother (C), and interference (D) outcomes: results are presented as percentage change with 95% CIs from baseline at each time point during the treatment period (ie, on day 3 of treatment, and then weekly mean total for each week (wk) of the 4-week treatment period for both placebo (white) and MLE4901 (gray). Minimum $n = 33$; maximum $n = 37$. $^{*}P < 0.0001$, $^{\#}P = 0.0006$, $^{\wedge}P = 0.0011$, $^{+}P = 0.0001$. Week 4 data adapted from Prague et al, *Lancet*, 2017[18].

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Prague J., et al. Menopause. 2018 Aug;25(8):862-869.

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

- Initial Phase 1/2 BRCA+ trial:
  - 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: Timelines / Exclusivity

- Targeting IND submission in Q2 2021
- Plan to initiate Phase 1/2 trial in H2 2021, subject to successful IND submission and clearance, and additional capital
- 5-year NCE exclusivity
- Have rights to pending patent applications for methods of treating iVMS

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Financial Overview

- Cash
  - $6.2M as of September 30, 2020, combined with additional $1.0M of proceeds subsequently received from ATM stock sales and Lincoln Park stock purchase agreement
  - Expected to have sufficient capital to fund current operations into Q1 2021, excluding support for the planned emetine Phase 2/3 clinical trial, which is also subject to ongoing discussions with FDA

- Capitalization as of October 26, 2020
  - 12.3M shares of common stock outstanding
  - 13.6M shares of common stock fully diluted

- $95M invested through October 26, 2020

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Summary

- Acer's pipeline includes four programs:
  - **Emetine** for the treatment of COVID-19
  - **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)
  - **EDSIVO™** (celiprolol) for the treatment of vascular Ehlers-Danlos syndrome (vEDS) in patients with a confirmed type III collagen (COL3A1) mutation
  - **Osanetant** for the treatment of induced Vasomotor Symptoms (iVMS)

- 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 milestones:
  - Emetine animal efficacy study results: **Q4 2020**
  - EDSIVO™ request FDA meeting to discuss confirmatory evidence plan: **Q4 2020**
  - Emetine IND submission and Phase 2/3 trial initiation*$: **H1 2021**
  - ACER-001 BE fed trial completion: **Q1 2021**
  - ACER-001 pre-NDA meeting with FDA: **mid-H1 2021**
  - ACER-001 (UCD) NDA submission**$: **Q2 2021**
  - Osanetant IND submission: **Q2 2021**
  - Osanetant Phase 1/2 trial initiation*$: **H2 2021**

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*Subject to successful IND submission and clearance
$Subject to additional capital
**Assuming successful outcomes of BE trial under fed conditions, additional nonclinical work and long-term stability data

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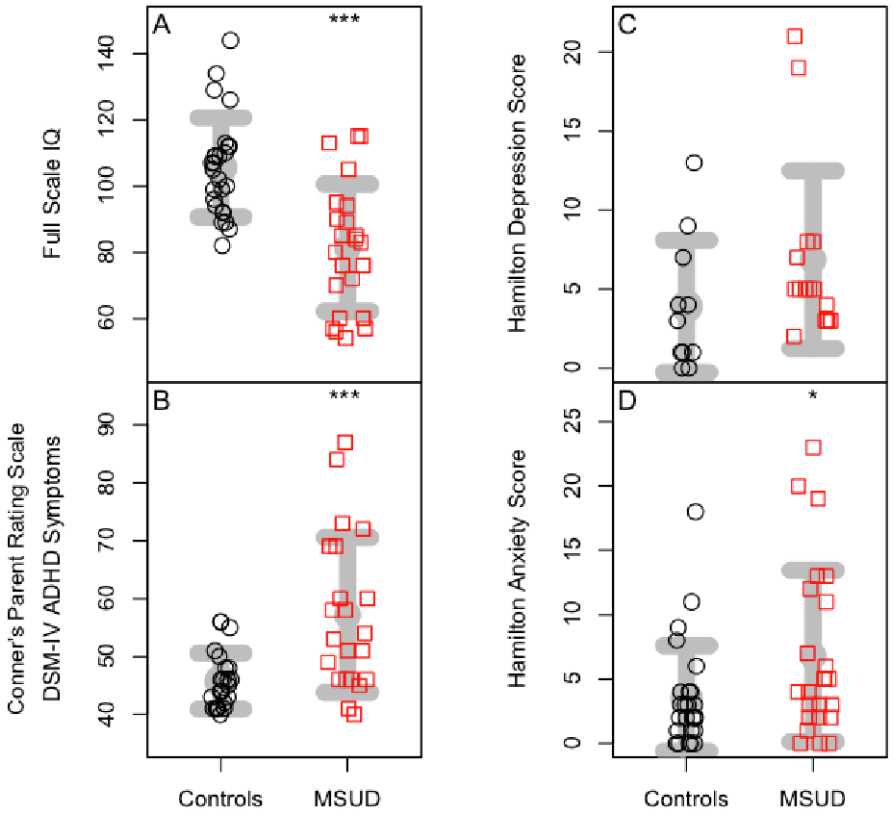
Reference Slides

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*

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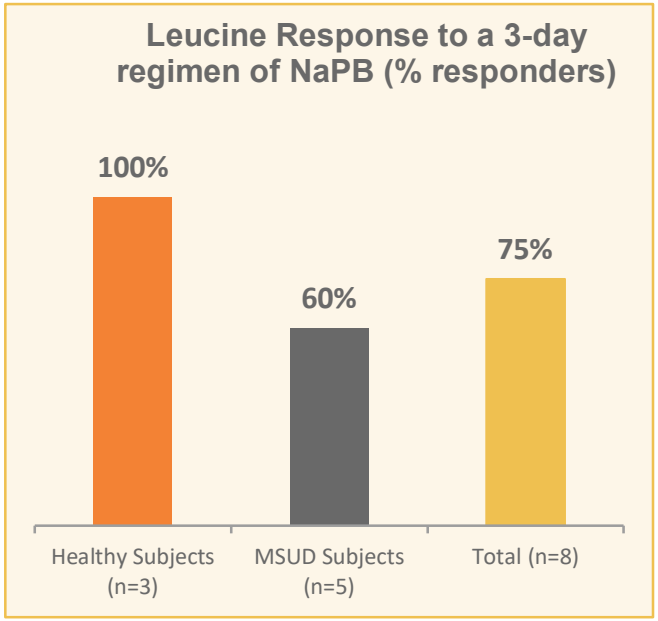
*Muelly 2011 Neuropsychiatric and Neurochemical Sequelae of MSUD.

MSUD: Clinical POC Study

- Design: Open label pilot study[1] 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

[1]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

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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$

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*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