



acertherapeutics

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



Corporate Presentation

November 19, 2021

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 for clinical study enrollment or regulatory actions, or otherwise, 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 for ACER-801, EDSIVO™ or our other products; 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, 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

- Offices: **Newton, MA** and **Bend, OR**
- Headcount: **33**
- Founded: **December 2013**
- Public: **September 2017**
- Cash as of September 30, 2021: **\$14.2M**
 - Plus \$10.0M Second Development Payment in two tranches following FDA acceptance for filing and review of an NDA for ACER-001 in a UCD per Collaboration Agreement with Relief
 - Expected to have sufficient capital to fund current operations into mid-2022^{\$}

Leadership Team

Chris Schelling CEO & Founder	<ul style="list-style-type: none"> 22 years; strategic commercial dev. & orphan 	
Harry Palmin COO & CFO	<ul style="list-style-type: none"> 25+ years; corporate & finance experience 	
Matt Seibt Chief Commercial Officer	<ul style="list-style-type: none"> 22 years; sales, market access & product launch 	
Jeff Davis Chief Business Officer	<ul style="list-style-type: none"> 25+ years; business & corporate development 	
John Klopp Chief Technical Officer	<ul style="list-style-type: none"> 19 years; orphan manufacturing & commercialization 	
Don Joseph, JD Chief Legal Officer	<ul style="list-style-type: none"> 25+ years; general counsel & senior management 	

Terrie Kellmeyer, Ph.D. Group VP, Clinical Development		William DeVincenzi VP, Quality	
Stacey Bain, Ph.D. VP, Clinical Operations		Jeffrey Edwards, Ph.D. VP, Clinical Sciences	
Renee Carroll VP, Regulatory Affairs		Tanya Hayden VP, Program/Alliance Mgt	
Alka Chawla, M.D. VP, Medical Director		John Hilton VP, Marketing/Strategic Insights	

Investment Highlights

- Acer's pipeline includes four programs:
 - **ACER-001** (sodium phenylbutyrate) for the treatment of various inborn errors of metabolism, including urea cycle disorders (UCDs) and Maple Syrup Urine Disease (MSUD)
 - **ACER-801** (osanetant) for the treatment of induced vasomotor symptoms (iVMS)
 - **EDSIVO™** (celiprolol) for the treatment of vascular Ehlers-Danlos syndrome (vEDS) in patients with a confirmed type III collagen (COL3A1) mutation
 - **ACER-2820** (emetine) a host-directed therapy against a variety of infectious diseases
- 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:

✓ ACER-801 IND submitted:	Q4 2021
• EDSIVO™ IND submission, work toward SPA, request BTD	Q4 2021
• ACER-801 Phase 2a clinical trial initiation*§:	Q1 2022
• EDSIVO™ DiSCOVER clinical trial initiation**§:	Q1 2022
• ACER-001 (UCDs) PDUFA target action date:	June 5, 2022

* Subject to IND clearance

** Subject to successful IND submission and clearance, and agreement on SPA

§ Subject to additional capital

Clinical Pipeline

Program / Indication	Novel MOA / Unique Characteristics	Preclinical	Phase 1	Phase 2	Phase 3	NDA
ACER-001 (sodium phenylbutyrate)						
Urea Cycle Disorders	Nitrogen-binding agent	PDUFA: June 5, 2022				
Maple Syrup Urine Disease	Inhibition of BCKD kinase to increase BCAA metabolism					
ACER-801 (osanetant)						
Induced vasomotor symptoms (iVMS)	Neurokinin 3 receptor antagonist	\$				
EDSIVO™ (celiprolol)						
Vascular Ehlers-Danlos syndrome (COL3A1+)	Induces vascular dilatation and smooth muscle relaxation			\$		
ACER-2820 (emetine)						
Broad-spectrum antiviral	Host-directed therapy	\$				

Overview

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

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

Product Profile

- **Nitrogen-binding agent for use as adjunctive therapy in the chronic management of patients with UCDs**
- **UCDs**: Bioequivalence trials showed ACER-001 has similar relative bioavailability to BUPHENYL® in healthy volunteers under both fasted and fed conditions
- ACER-001 under fasted conditions achieved $>2\times C_{\text{max}}$ of PBA vs. fed conditions
- **MSUD**: POC study¹ suggests ~60% of patients have 30% reduction in Leucine

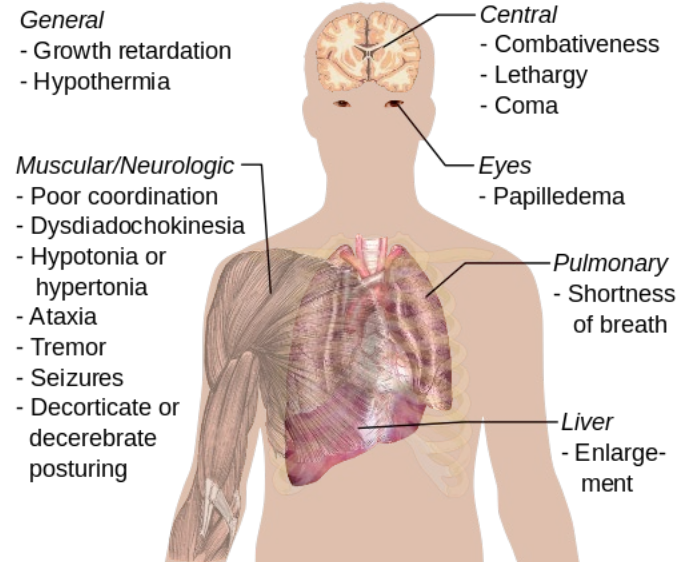
The Opportunity

- **NDA filing accepted for FDA review; PDUFA target action date June 5, 2022**
- **UCDs**: ~700 patients treated with sodium / glycerol phenylbutyrate.
- **MSUD**: ~800 treatment-eligible patients in the U.S.; 3,000 patients worldwide
- Advantageous orphan pricing likely with robust program to support patient access and reimbursement
- Collaboration and License Agreement with Relief Therapeutics for development and commercialization of ACER-001

Urea Cycle Disorders

- 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

Symptoms of Hyperammonemia



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

Mechanism of Action

Ammonia-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

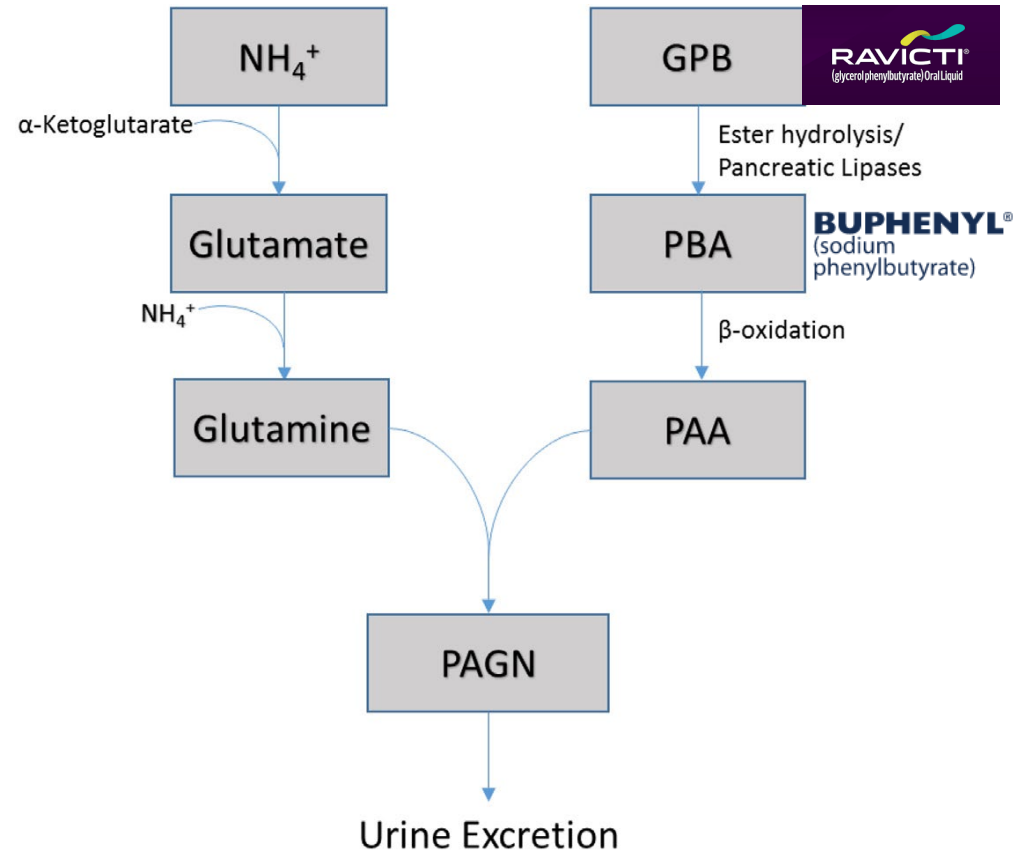


Fig. 1. Metabolizing pathway and mechanism of action of GPB. GPB (glycerol phenylbutyrate); PAA (phenylacetic acid); PBA (phenylbutyric acid); PAGN (phenylacetylglutamine).

Unmet Need

- **BUPHENYL®:** Foul odor and foul/bitter taste; considered unpalatable¹
 - 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 discontinuation¹
- **RAVICTI®:** Tasteless/Odorless
 - 75% of BUPHENYL® patients switched to RAVICTI®²
 - Pricing has risen to levels considered challenging²
 - Reports of difficult access, unaffordability, and forced switches back to sodium phenylbutyrate
 - Example: BUPHENYL® and RAVICTI® blocked on JPMorgan Chase plan Rx formulary³
 - 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 option²

1 Shchelochkov et al., Molecular Genetics and Metabolism Reports 8 (2016) 43-47.

2 Acer Market Research

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

4 Nicola Longo & Robert J. Holt (2017) Expert Opinion on Orphan Drugs, 5:12, 999-1010.

Product Differentiation

Phenylbutyrate Formulations			
	ACER-001*	RAVICTI®	BUPHENYL®
Efficacy / Safety in UCDs	✓	✓	✓
Palatability / Compliance	✓	✓	X**
Pricing (Per Patient Per Year)	TBD, likely near BUPHENYL®	\$174K-\$1.3M*** (avg \$950K)	\$204K-\$402K*** (avg \$300K)
Formulation	Multi-Particulate (Sachet)	Oil (Tablespoons)	Powder/Tablets (up to 40 tablets/day)

Clinical & Regulatory Paths

NDA for UCDs: PDUFA target action date June 5, 2022

- ✓ BE trial under fasted conditions completed in Q1 2020
- ✓ BE trial under fed conditions completed in Q1 2021
- ✓ Type B (pre-NDA) meeting with FDA conducted in Q2 2021
- ✓ Reached agreement with FDA on initial Pediatric Study Plan (iPSP) in Q3 2021
- ✓ 505(b)(2) NDA for UCDs: NDA filing accepted for review by FDA in Oct. 2021

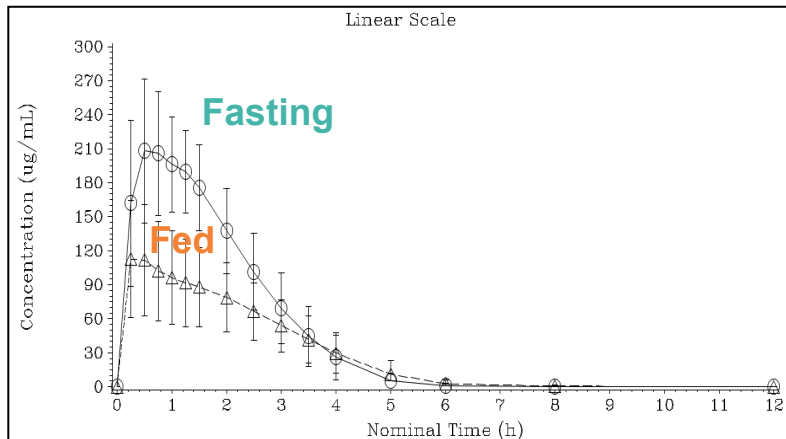
Lifecycle Opportunities

- Evaluate after initial potential FDA approval for UCDs (under fed conditions)^{\$}:
 - Pre-meal administration of ACER-001, which would require additional nonclinical and clinical studies^{\$} to demonstrate efficacy and safety in UCDs
 - MSUD
 - Other potential indications

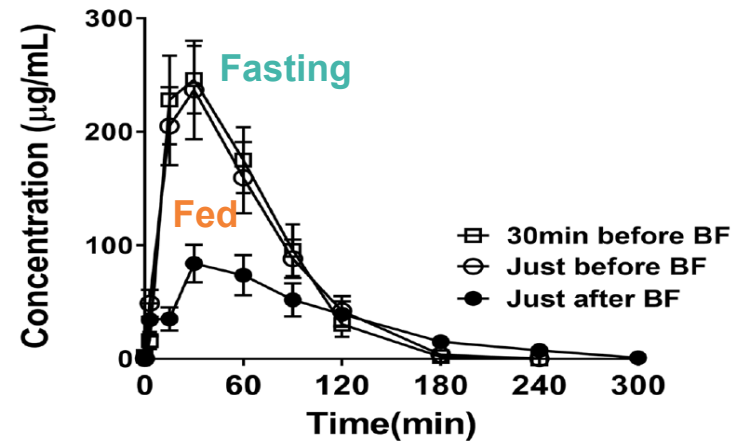
Food Effect

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

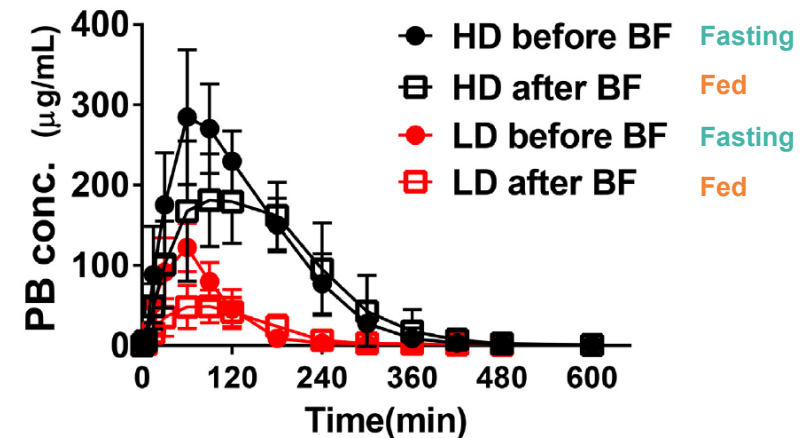
ACER-001¹



NaPB (Nakano)²



NaPB (Osaka)³



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

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

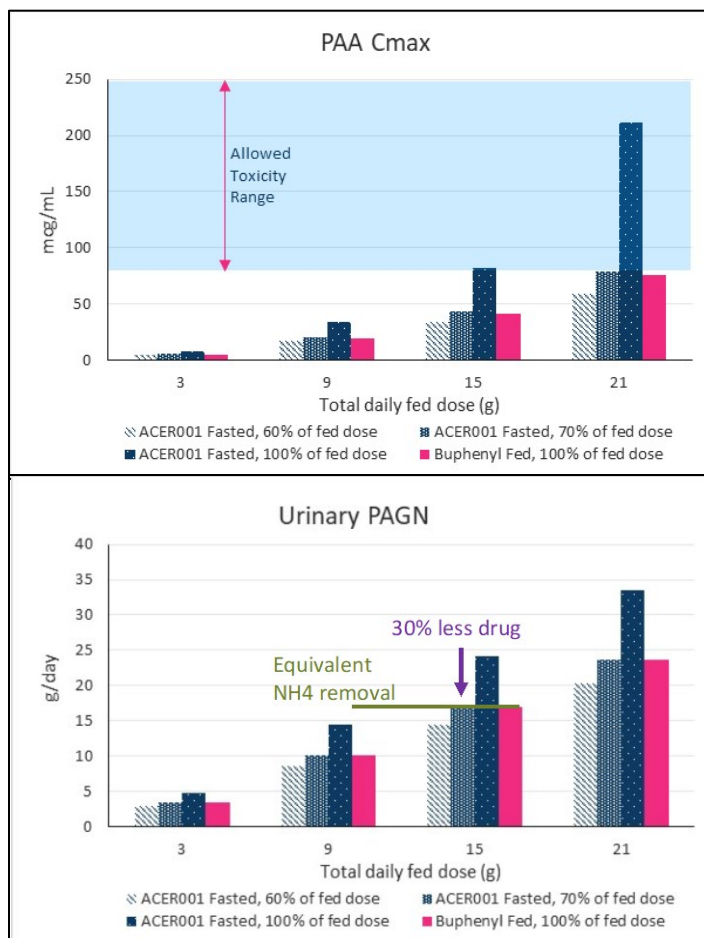
² Nakano S, et al. Sci Rep 9, 17075 (2019). <https://doi.org/10.1038/s41598-019-53628-x>

³ Osaka S, et al. Molecular Genetics and Metabolism (2021). <https://www.sciencedirect.com/science/article/abs/pii/S1096719221000366>

Food Effect: In Silico Model

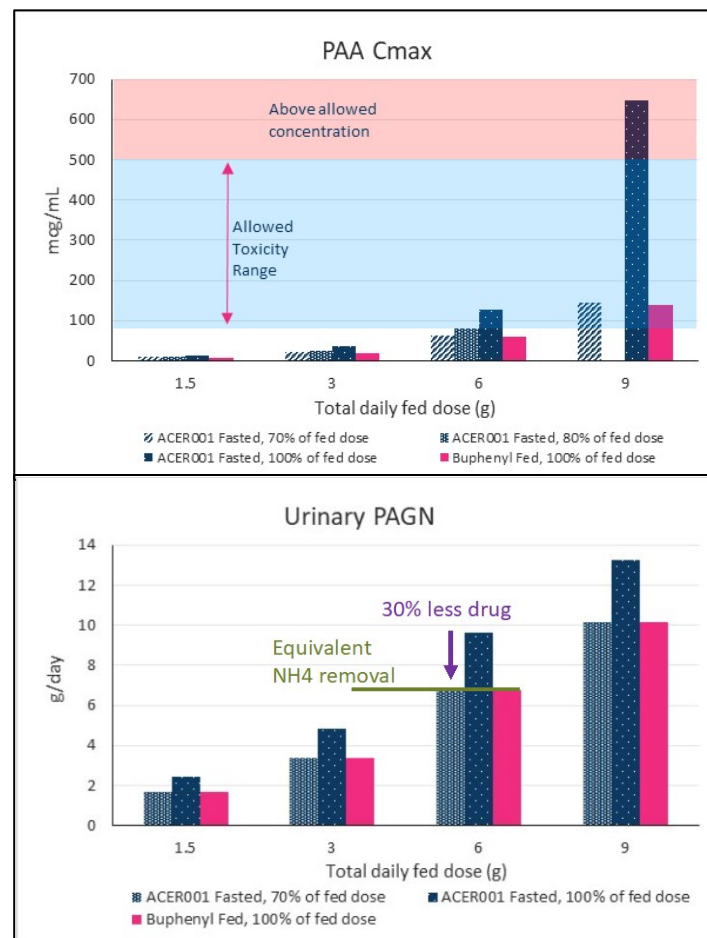
Adult Virtual Patient

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



Child Virtual Patient

uPAGN
(Efficacy)



- Model predicted 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 (inverse correlation with blood ammonia AUC)

Food Effect: Summary

- Dosing and Administration for BUPHENYL[®], RAVICTI[®] and Pheburane[®] are all instructed to be given with food¹
 - There is a significant food effect with NaPB
 - The pharmacokinetic (PK) and pharmacodynamic (PD) properties of RAVICTI[®] are indistinguishable in the fed or fasted states²
- Dosing in a pre-meal setting should increase exposure, and theoretically improve ammonia control / outcomes in UCDs patients
 - Pre-meal administration of ACER-001 in UCDs will require additional nonclinical and clinical studies to demonstrate efficacy and safety and are subject to additional capital
- 2x the C_{max} of PBA may also improve efficacy in other disorders (where PBA is the active moiety), such as MSUD and PFIC³
- ACER-001's formulation may improve tolerability of the drug when administered under fasted (pre-meal) conditions

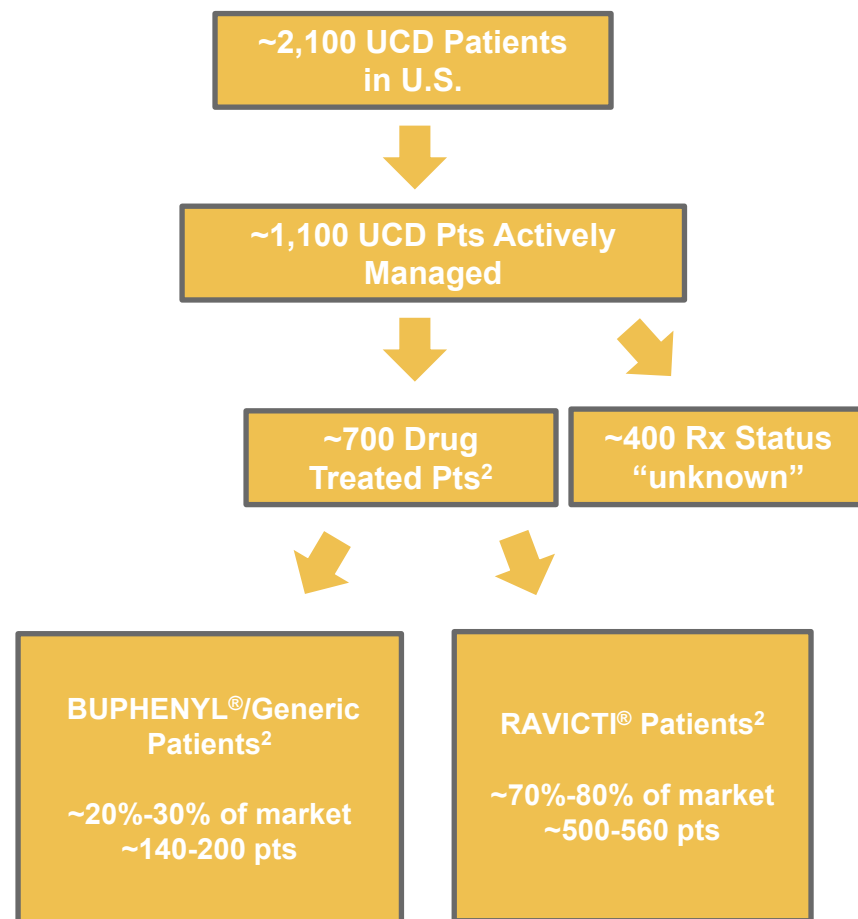
1 Initial ACER-001 proposed UCD instructions to include administration with food

2 United States Patent number US8642012B2

3 Nakano S, et al. Sci Rep 9, 17075 (2019). <https://doi.org/10.1038/s41598-019-53628-x>

ACER-001 Value Proposition

- Taste-masked formulation designed to improve palatability of NaPB
- Bioequivalence trials showed ACER-001 has similar relative bioavailability to BUPHENYL[®] under both fasted and fed conditions
- Fasted (pre-meal) dosing data suggests ability to subsequently optimize Rx dosing approach¹
- Pricing projected to be significantly lower than current RAVICTI[®] price
- Robust patient support services program to remove barriers to care
- Payer engagement strategy to alleviate insurance paperwork and support switching
- Acer's commitment to support the UCD community and on-going IEM research



IP / Exclusivities

- IP:
 - Issued patents (US/EP):
 - “Palatable compositions including sodium phenylbutyrate and uses thereof” (US PATENT NO. 11,154,521), including pharmaceutical composition claims covering ACER-001’s taste-masked, multi-particulate dosage formulation for oral administration
 - Proprietary position in U.S. until 2036
 - “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
 - MSUD: Pediatric exclusivity: +6 months added (if pediatric indication study approved)

Agreement with Relief Therapeutics

- ✓ Signed Collaboration and License Agreement March 19, 2021
- ✓ Acer received \$30.0M to date (\$1.0M Option Fee + \$14.0M Reimbursement Payment + \$10.0M First Development Payment + \$5.0M 1st tranche of Second Development Payment)
- Relief to pay Acer additional \$5.0M 2nd tranche of Second Development Payment upon the earlier of January 14, 2022 or 15 business days following Acer written notice
- ✓ Acer retained development and commercialization rights in the U.S., Canada, Brazil, Turkey and Japan
 - Split net profits from Acer's territories 60%:40% in favor of Relief
- ✓ Relief licensed rights for the rest of the world
 - Acer will receive 15% royalty on all Net Sales in Relief's territories
 - Acer could also receive up to \$6.0M for UCD and MSUD approvals in EU

Overview

Disease Overview

- **Induced vasomotor symptoms (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

Mechanism of Action

- **ACER-801 (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

Product Profile

- **Believed to have largest body of clinical safety data for any NK3R antagonist**
- Clinical and laboratory safety results are available from 23 completed Phase 1 and 2 studies (387 healthy subjects and 822 patients were treated with osanetant)*
- Oral bioavailability, readily crosses the blood-brain barrier

The Opportunity

- **Acer licensed worldwide rights to ACER-801 from Sanofi in Dec. 2018**
- IND submitted in Q4 2021
- Plan to initiate Phase 2a clinical trial in Q1 2022**\$
- Currently no other NK3R antagonists in development in iVMS space

* Meltzer H, et al. Am J Psychiatry. 2004 Jun;161(6):975-84

** Subject to IND clearance

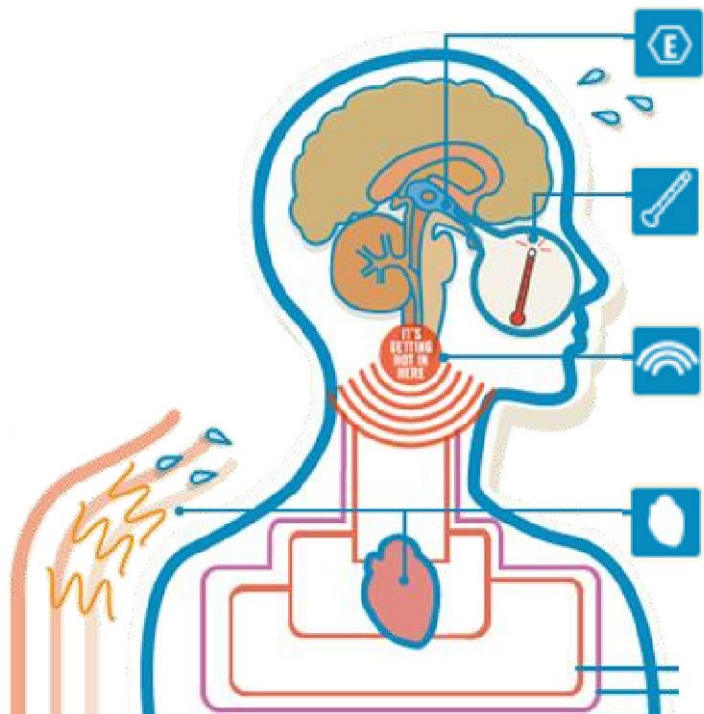
\$ Subject to additional capital

History

- Acer acquired worldwide rights to osanetant from Sanofi in December 2018
- Osanetant 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 23 completed Phase 1 and 2 studies in which 387 healthy subjects and 822 patients (schizophrenia, depression, others) 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)

- 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

Induced Vasomotor Symptoms (iVMS)

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

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

Men with HR+ Prostate Cancer (CaP) receiving Leuprolide

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

Women with HR+ Breast Cancer (CaB) receiving Tamoxifen

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

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

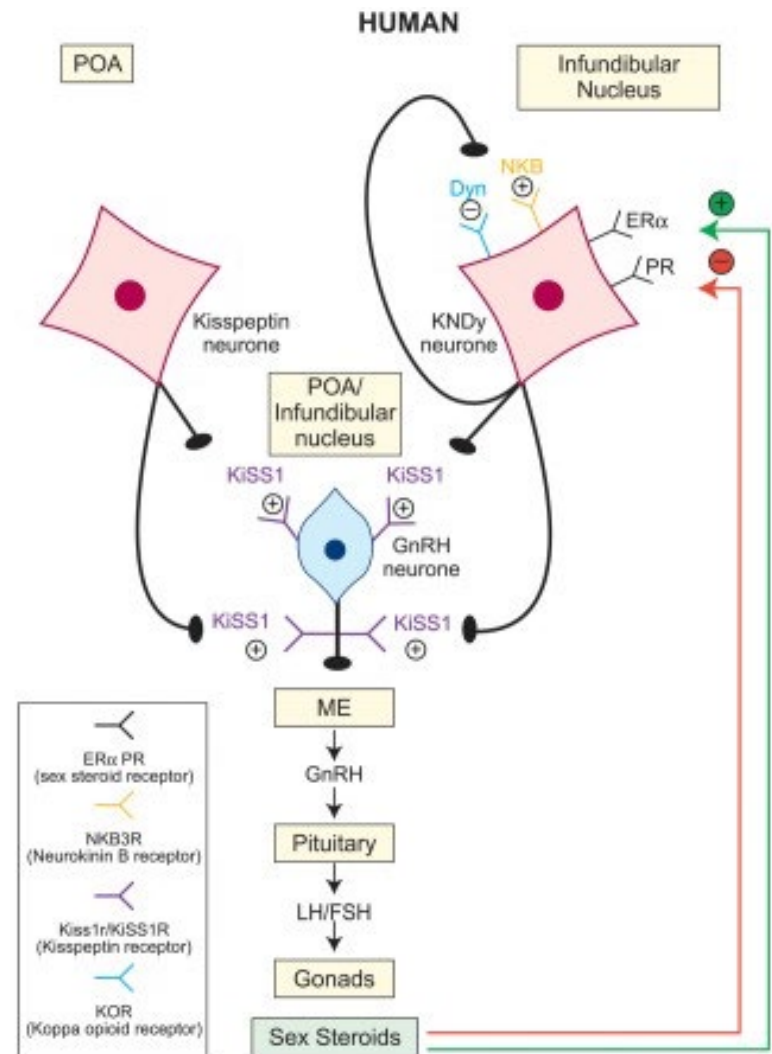
⁴ Abildgaard J. et al., JNCI Cancer Spectrum, 2018, Vol. 0, No. 0

⁵ Johnson L. 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

Mechanism of Action

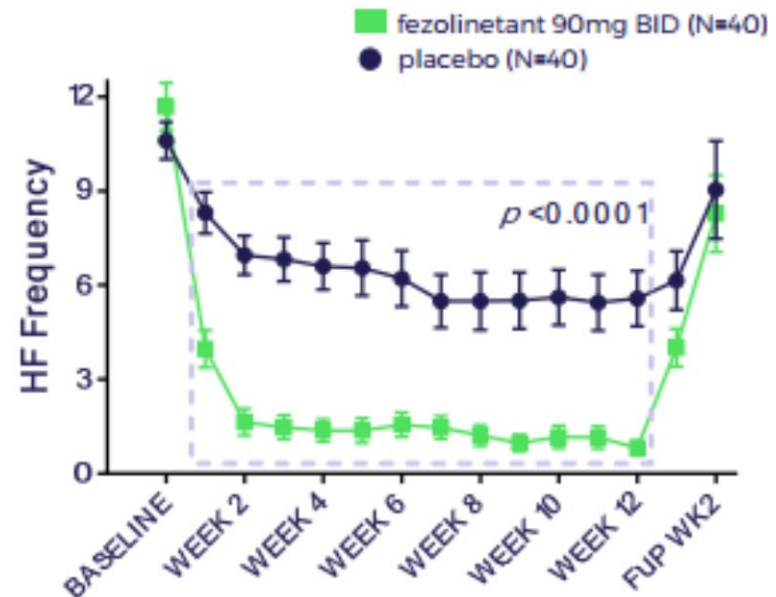
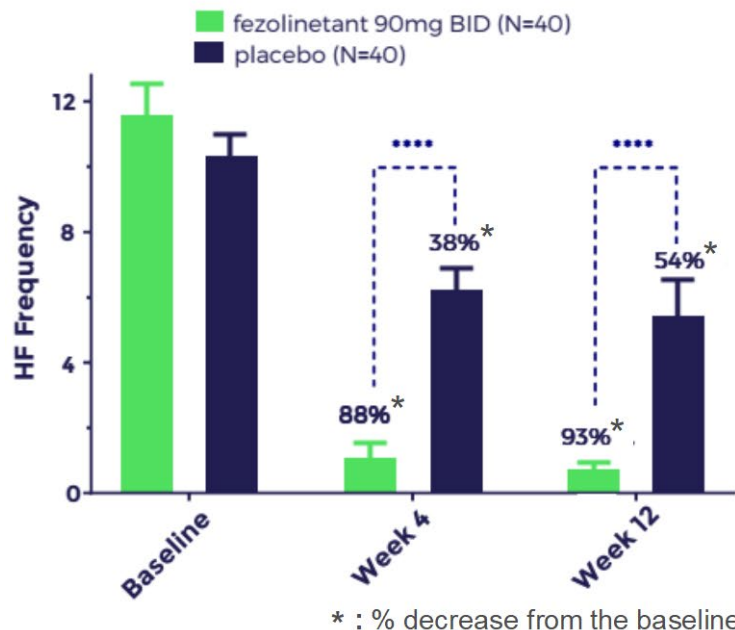
- Neurokinin B (NKB) belongs to a group of neuropeptides, called tachykinins or neurokinins, that includes substance-P (SP), neurokinin A (NKA), and two N-terminally extended forms of NKA, neuropeptide g and neuropeptide K
- The biological effects of tachykinins are mediated through specific receptors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



Clinical POC in VMS: NK3R Antagonist

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

Average Daily Hot Flash Frequency Reported as per FDA Guidance



At Week 4:

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

Clinical POC in VMS: NK3R Antagonist

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

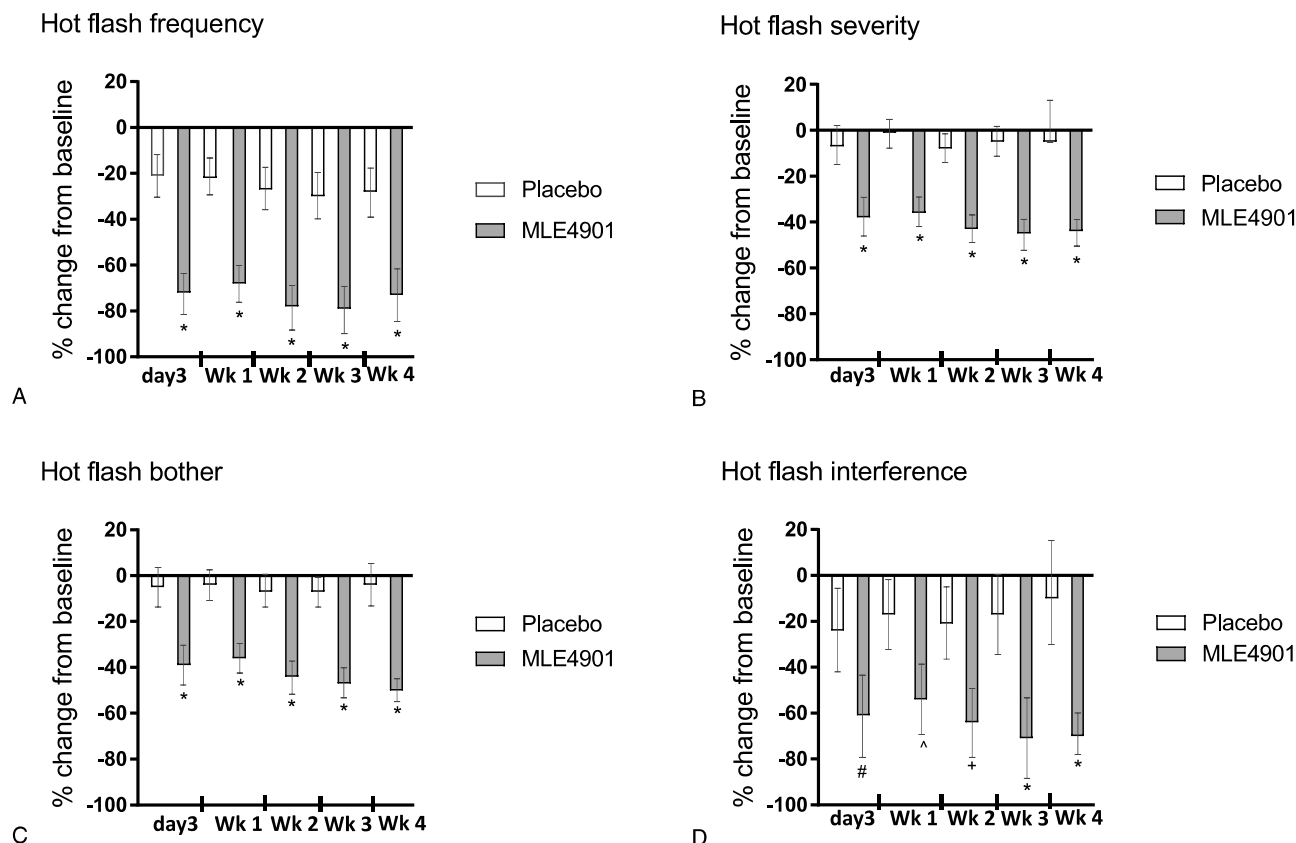


FIG. 2. Hot flash frequency (A), severity (B), bother (C), and interference (D) outcomes: results are presented as percentage change with 95% CIs from baseline at each time point during the treatment period (ie, on day 3 of treatment, and then weekly mean total for each week (wk) of the 4-week treatment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

Development Plan

- Acer is partnering with leading institutions to design and conduct clinical trials to evaluate ACER-801 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
- Planning to initiate Phase 2a clinical trial in Q1 2022[§]:
 - Evaluate PK, efficacy and safety in postmenopausal women with VMS
 - Identify the optimal dosing strategy to advance into subsequent efficacy studies in cancer patients with iVMS

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: 76% reduction in risk of arterial events observed in COL3A1+ subpopulation¹**
- Statistically-significant improvement in event-free survival (EFS) compared to control in vEDS patients (n=53)¹

The Opportunity

- **Planning pivotal clinical trial following FDA Type B meeting feedback***
- Proposed DiSCOVER Phase 3 decentralized (virtual) clinical trial[§] expected to take ~3.5 years to complete once enrolled
- FDA indicated agreement w/Acer plan to submit proposed protocol under a Special Protocol Assessment (SPA) w/possible breakthrough therapy designation (BTD)

¹ Ong K, et al. Lancet 2010; 376: 1476-84.

* There can be no assurance that the clinical trial will be successful, or that any resubmission of the original NDA will be approved

[§] Subject to additional capital to conduct and complete the trial

Vascular Ehlers-Danlos Syndrome (vEDS)

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

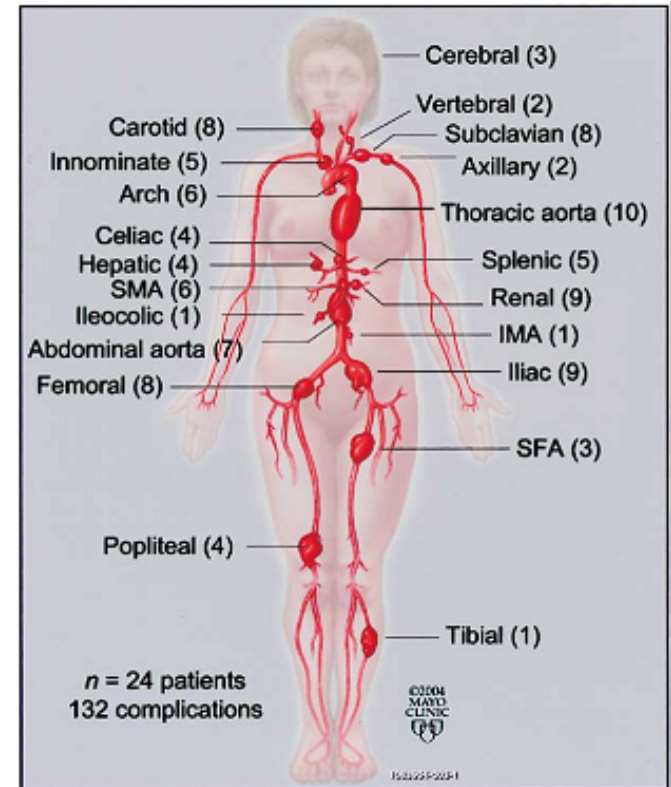
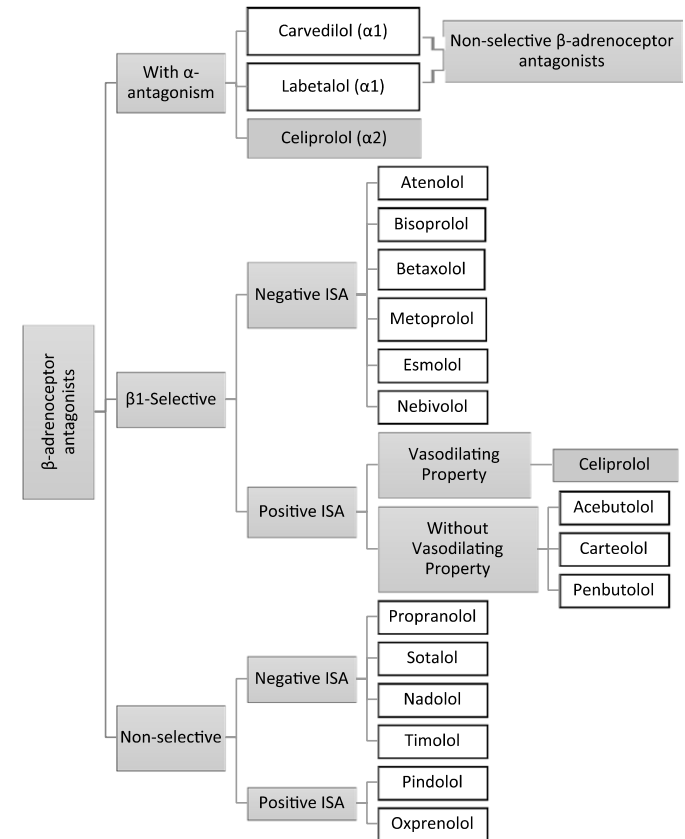


Fig. 3 Distribution of 132 vascular complications in 24 patients with a clinical diagnosis of EDS type IV. J Vasc Surg 2005;42:98-106.

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



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

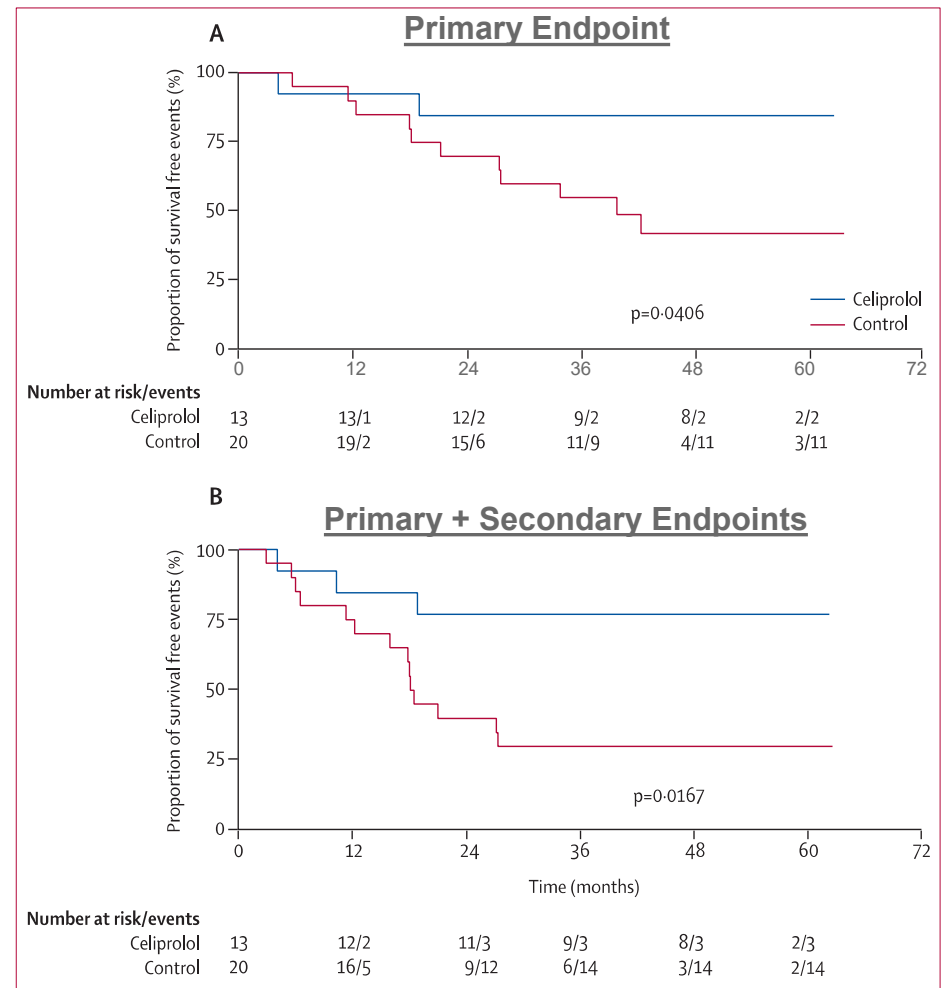


Figure 3: Kaplan-Meier curves of event-free survival in 33 patients with positive COL3A1 mutation
Primary endpoint (A). Primary and secondary endpoints (B).

EDSIVO™ Planned Clinical Trial

- Proposed **DiSCOVER** trial design* following Type B FDA meeting feedback:
 - **DiSCOVER: D**ecentralized **S**tudy of **C**eliprolol **o**n **v**EDS-related **E**vent **R**eduction
 - A Phase 3, U.S.-based prospective, randomized, double-blind, placebo-controlled decentralized (virtual) clinical trial
 - Approximately 3.5 years to complete once fully enrolled*
 - Acer to coordinate with FDA to reach agreement on Special Protocol Assessment (SPA)
 - Primary endpoint: vEDS-related clinical events in patients treated with celiprolol vs. placebo
 - Statistical plan that considers the rare disease classification of vEDS
 - Enrollment: approximately 200 COL3A1+ U.S. vEDS patients
 - Modest safety data collection required based on celiprolol's known safety profile ^{1,2,3,4}

* Subject to successful IND submission and clearance, agreement on SPA, and additional capital to conduct and complete the trial

1 Ong K, et al. Lancet 2010; 376: 1476-84.

2 Nawarskas J, et al. Cardiology in Review 2017;25: 247–253

3 Frank M, et al. Vascular Ehlers-Danlos Syndrome: Long-Term Observational Study. J Am Coll Cardiol. 2019 Apr, 73 (15) 1948–1957

4 Baderkhan, H, et al. Celiprolol Treatment in Patients with Vascular Ehlers-Danlos Syndrome. European Journal of Vascular and Endovascular Surgery. November 20, 2020

Next Steps

- Q4 2021:
 - Submit IND and SPA request to FDA for **DiSCOVER** clinical trial
 - Identify ~200 COL3A1+ patients in the U.S. for trial participation
 - ~1,000 U.S. patients potentially available following evaluation of vEDS diagnosis code (ICD10: 79.6)
 - Launched www.discoverceliprolol.com as an outreach tool for interested parties
- Obtain up to ~\$15.0M to conduct and complete pivotal trial – from potential current and future funding sources, including but not limited to:
 - Current cash
 - Strategic partnership
 - Other non-dilutive sources
 - Potential ACER-001 revenue
- Request breakthrough therapy designation (BTD)
- Planning to initiate pivotal **DiSCOVER** trial in Q1 2022*

* Subject to successful IND submission and clearance, agreement on SPA, and additional capital to conduct and complete the trial

Disease Overview

➤ **Broad-spectrum Antiviral**

- In vitro +/- in vivo data across multiple virus families, including coronavirus, filovirus, flavivirus, herpesvirus, togavirus, arenavirus, HIV, influenza

Mechanism of Action

➤ **Host-directed Therapy**

- Restores cellular stress response by interrupting the viral-induced MDM2-P53 loop, by shepherding RPS14 from cytosol into the nucleus, thus inhibiting viral replication
- Few drugs in development that are host-directed; believed to be only drug exploiting this particular MOA

Product Profile

➤ **Small molecule (SQ) used previously in tens of thousands of humans as an antiprotozoal, emetic, and antiviral agent**

- Toxicity is related to cumulative dose; reasonable safety profile administered as subcutaneous injection in humans up to 10 mg/kg cumulative dose

The Opportunity

➤ **Pursuing multiple non-dilutive funding options for emetine development in a variety of infectious diseases, including COVID-19**

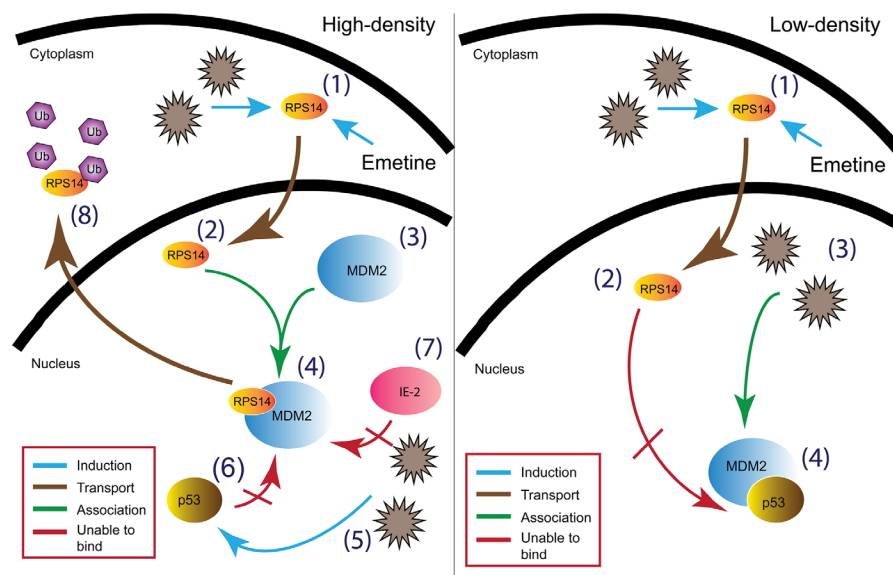
- Evaluating development pathways against viruses utilizing animal rule / Medical Countermeasure (MCM) pathway
 - Applied for MCDC funding for Ebola; received positive feedback and placed in “basket” if additional funding becomes available
 - Application for BARDA funding for COVID-19 remains active

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
- 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
- Clinically, emetine has been used to treat approximately 700 patients (including pediatrics) with viral hepatitis¹ and varicella-zoster virus²

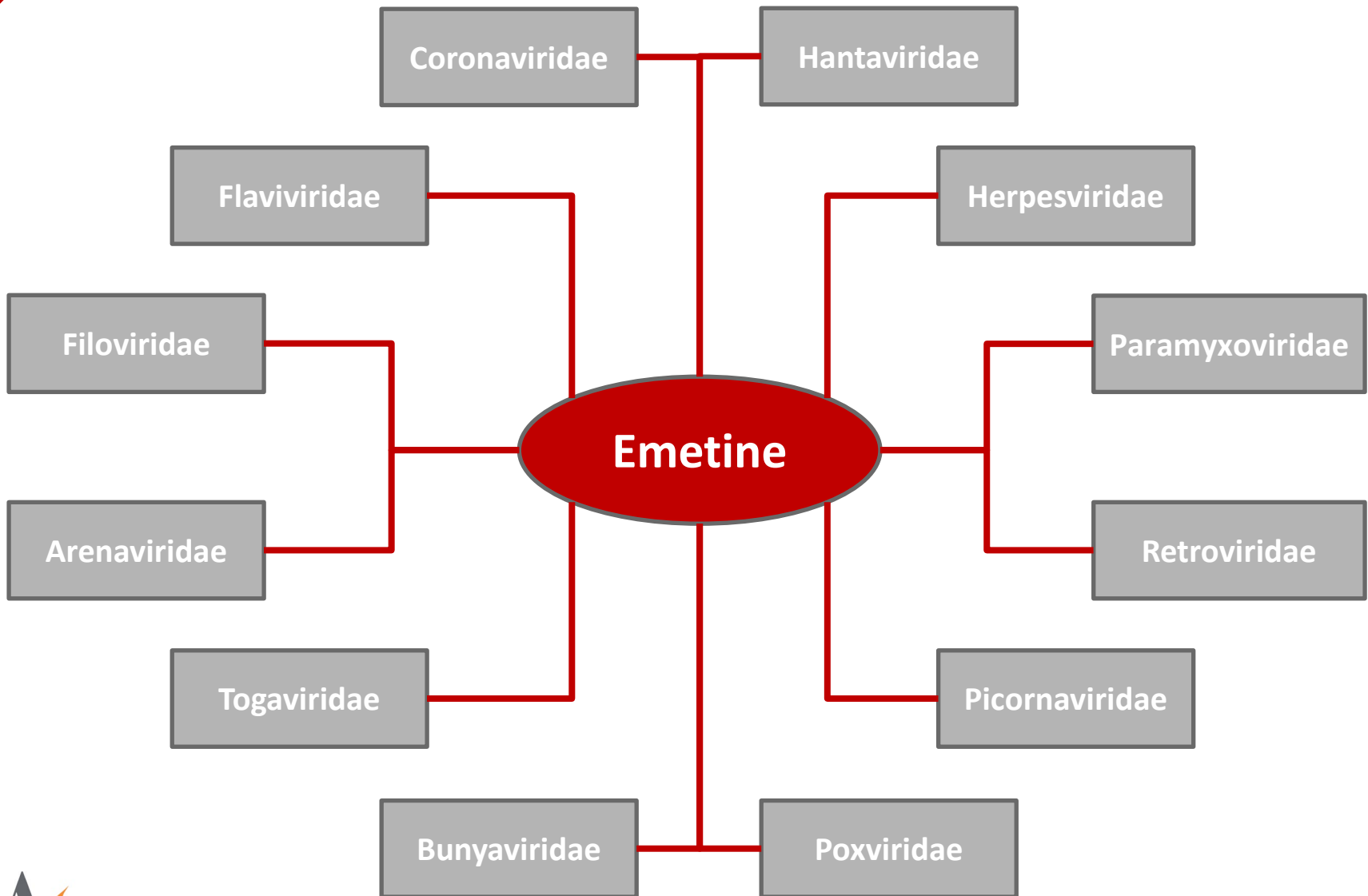
Mechanism of Action

- Viral infections have developed evolutionary mechanisms for inhibiting the cellular stress response and promote ribosome biogenesis to facilitate viral replication
- **Host-directed Therapy:** 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).

Broad-spectrum, Antiviral Activity



Nanomolar Potency In Vitro

	Virus Type	Antiviral Activity*	Reference
Coronaviridae	SARS-CoV-2 (Vero-E6)	EC ₅₀ = 0.007	Wang et al. Molecular Biomedicine 1:14 https://doi.org/10.1186/s43556-020-00018-9 (2020).
	SARS-CoV-2 (Caco-2)	IC ₅₀ = 0.47	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	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	Ianevski et al. 2020 May. Antiviral options against SARS-CoV-2 infection. https://doi.org/10.1101/2020.05.12.091165
	SARS-CoV	EC ₅₀ = 0.051	Dyall et al. Antimicrob Agents Chemother. 2014 Aug;58(8):4885-93. doi: 10.1128/AAC.03036-14.
	MERS-CoV	EC ₅₀ = 0.014	
	MERS-CoV	EC ₅₀ = 0.34 / CC ₅₀ = 3.08	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 / CC ₅₀ = 3.63	
	HCoV-OC43	EC ₅₀ = 0.30 / CC ₅₀ = 2.69	
	MHV-A59	EC ₅₀ = 0.12 / CC ₅₀ = 3.51	
Flaviviridae	WNV	IC ₅₀ = 0.148	Unpublished Data on File (USAMRIID)
	DENV	IC ₅₀ = 0.023	Unpublished Data on File (USAMRIID)
	DENV1, 3 & 4 (Huh-7)	IC ₅₀ < 0.5	Low et al. J Antivir Antiretrovir 1: 062-071.
	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	
Filoviridae	EBOV-Vero E6	IC ₅₀ = 0.0169	Yang et al. Cell Discov. 2018 Jun 5;4:31. doi: 10.1038/s41421-018-0034-1.
	EBOV	IC ₅₀ = 0.222	Unpublished Data on File (USAMRIID)
Arenaviridae	LASV	IC ₅₀ = 0.055	Unpublished Data on File (USAMRIID)
Togaviridae	VEEV	IC ₅₀ = 0.133	Unpublished Data on File (USAMRIID)
	CHIKV	IC ₅₀ = 0.029	Unpublished Data on File (USAMRIID)
Bunyaviridae	RVFV	IC ₅₀ = 0.093	Unpublished Data on File (USAMRIID)
Hantaviridae	HTNV-G	ED ₅₀ = 9.9*10 ⁻⁶	Mayor et al. <i>Viruses</i> 2021, 13, 685.
Herpesviridae	HCMV	EC ₅₀ = 0.040 / CC ₅₀ = 8	Mukhopadhyay et al. PLoS Pathog. 2016 Jun 23;12(6):e1005717. doi: 10.1371/journal.ppat.1005717.
	HSV-2	EC ₅₀ = 0.03 / CC ₅₀ = 1.12	Andersen et al. <i>Viruses</i> . 2019 Oct 18;11(10). pii: E964. doi: 10.3390/v11100964.
Paramyxoviridae	HMPV	EC ₅₀ = 0.14 / CC ₅₀ = 1	Andersen et al. <i>Viruses</i> . 2019 Oct 18;11(10). pii: E964. doi: 10.3390/v11100964.
	NDV	EID ₅₀ = 0.053 HA unit	Khandelwal et al. Antiviral Research 144 (2017) 196-204.
Retroviridae	HIV M184V	EC ₅₀ = 0.012 – 0.03	Chaves Valadao et al. <i>Molecules</i> . 2015 Jun 22;20(6):11474-89. doi: 10.3390/molecules200611474.
Picornaviridae	EV-A71 (Vero)	EC ₅₀ = 0.049 / CC ₅₀ = 10	Tang et al. Antiviral Research 173 (2020) 104650. https://doi.org/10.1016/j.antiviral.2019.104650 .
	EV-D68	EC ₅₀ = 0.019	
	Echov-6	EC ₅₀ = 0.045	
	CV-A16	EC ₅₀ = 0.083	
	CV-B1	EC ₅₀ = 0.051	
Poxviridae	NP-S-EGFP (BSC40)	IC _{99S} = 0.100	Deng et al. Journal of Virology, Dec. 2007, p. 13392-13402.

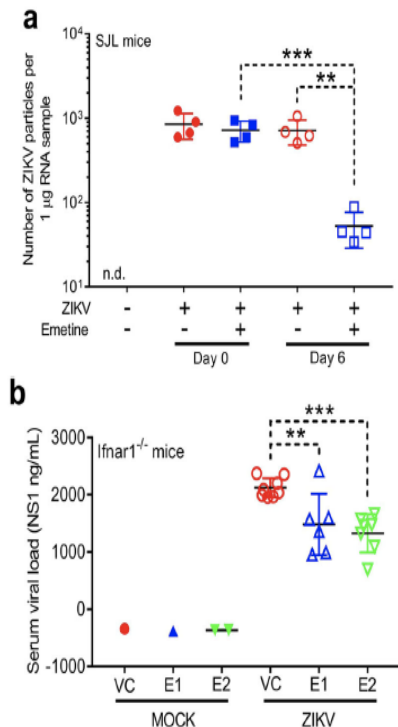
EC₅₀ = concentration of a drug that gives half-maximal response. IC₅₀ = concentration of an inhibitor where the response is reduced by half
 CC₅₀ = 50% cytotoxic concentration

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

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

In Vivo Efficacy Data

Zika virus¹

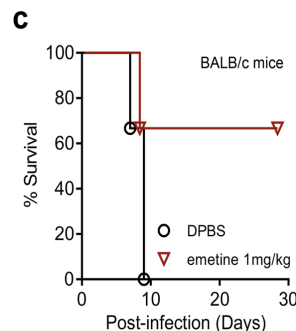


Emetine suppresses ZIKV virus load in vivo.

a Three-month-old SJL male mice were infected retro-orbitally with ZIKVBR followed by IP administration of emetine (1 mg/kg/day) for the next 6 days (N = 4 mice per group). Two groups of SJL mice (N = 4) received the same volume of vehicle buffers. Statistical analysis by two tailed t-test. **p = 0.0014, ***p = 0.0005.

b Ifnar1^{-/-} mice were dosed with emetine 1 mg/kg (E1, N = 6), 2 mg/kg (E2, N = 7), and PBS (VC, N = 8), respectively.

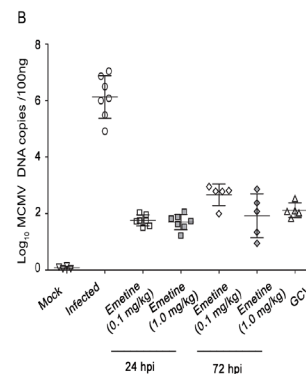
Ebola virus¹



Emetine inhibits EBOV infection in vivo

c The survival curve of MA-EBOV infected mouse treated with 1 mg/kg emetine every day. Six to eight week-old female BALB/c mice were randomly assigned into groups (N=6 animals). All the mice were challenged with a lethal dose of 1000 times the LD50 mouse adapted EBOV via IP treatments with either emetine (1 mg/kg/day) or PBS (same volume for the control group) were initiated at 3 h before the challenge and continued for up to 6 days post infection. Survival was monitored for 28 days post infection.

Cytomegalovirus²



Emetine achieves high tissue concentrations and is efficacious against MCMV replication.

B Quantitative real-time PCR of viral gB was performed on DNA extracted from blood at day 14 post infection. Emetine was administered orally starting 24 hpi or 72 hpi at 0.1 or 1.0 mg/kg every 3 days. GCV dose was 10 mg/kg/dose administered intraperitoneally twice daily.

Enterovirus³

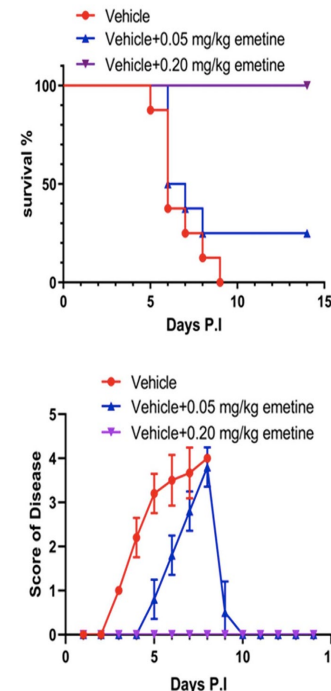


Diagram of the mice infection model (A), survival rates (B) and clinical scores (C) of two-week KM mice infected with EV-A71 GZ-CII strain and treated with emetine. The treated mice were monitored for two weeks after infection. Disease score definition as followings: Healthy, 0 point; Lethargy and inactivity, limb weakness, 1 point; Less exercise, limb paralysis, 2 points; Quadriplegic, moribund, 3 points; Death, 4 points.

¹ Yang S, et al. Cell Discovery (2018) 4:31

² Mukhopadhyay R, et al. PLoS Pathog 12(6):e1005717, 2016

³ Tang Q, et al. Antiviral Research 173 (2020) 104650.

PK & Tox Data

- Non-clinical pharmacokinetic studies show that emetine rapidly concentrates in the tissues, reaching levels that are 1,000- to 3,000-fold greater than in the plasma
- Emetine has been detected in a variety of tissues, including the heart, liver, lungs, intestines, kidney, spleen, stomach, adrenals, and brain, with a long (days/weeks) tissue half-life
- However, the key target organs of toxicity identified in the literature are muscle and cardiac tissue. All identified studies (animals, in vitro, and humans) focused on muscle and cardiac effects
- Acute toxicity with emetine appears to be related to cumulative dose exposure, but also appears completely reversible ~3 weeks after cessation of therapy:

Species	Fatal Cumulative Dose	ROA
Mice	50-100 mg/kg	IP
Rats	10-25 mg/kg	IP
Rabbits	10-30 mg/kg	PO
Cats	10-25 mg/kg	PO
Dogs	6 mg/kg	IP
Humans	15-20 mg/kg	SQ

Clinical Safety

- Patients with solid tumors treated with 1 mg/kg/day emetine daily via SC injection for 10 days (cumulative dose 650 mg) did not experience any notable toxicity¹
- Electrocardiographic abnormalities 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 reported⁵
- Toxicity with emetine appears to be cumulative-dose related and independent of schedule^{1,6}
- Complete reversibility of cardiac adverse effects⁶

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

2 Banerjee J, et al J Assoc Physicians India 14:349-364

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

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

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

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

Financial Overview

- Cash as of September 30, 2021: **\$14.2M**
 - Plus \$10.0M Second Development Payment in two tranches following FDA acceptance for filing and review of an NDA for ACER-001 in a UCD per Collaboration Agreement with Relief
 - Expected to have sufficient capital to fund current operations into mid-2022^{\$}
- Capitalization as of November 19, 2021:
 - 14.3M shares of common stock outstanding
 - 16.3M shares of common stock fully diluted
- \$100.0M invested through November 19, 2021, excluding Relief collaboration
- No debt, no warrants

Summary

- Acer's pipeline includes four programs:
 - **ACER-001** (sodium phenylbutyrate) for the treatment of various inborn errors of metabolism, including urea cycle disorders (UCDs) and Maple Syrup Urine Disease (MSUD)
 - **ACER-801** (osanetant) for the treatment of induced vasomotor symptoms (iVMS)
 - **EDSIVO™** (celiprolol) for the treatment of vascular Ehlers-Danlos syndrome (vEDS) in patients with a confirmed type III collagen (COL3A1) mutation
 - **ACER-2820** (emetine) a host-directed therapy against a variety of infectious diseases
- 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:

✓ ACER-801 IND submitted:	Q4 2021
• EDSIVO™ IND submission, work toward SPA, request BTD:	Q4 2021
• ACER-801 Phase 2a clinical trial initiation*\$:	Q1 2022
• EDSIVO™ DiSCOVER clinical trial initiation**\$:	Q1 2022
• ACER-001 (UCDs) PDUFA target action date:	June 5, 2022

* Subject to IND clearance

** Subject to successful IND submission and clearance, and agreement on SPA

\$ Subject to additional capital



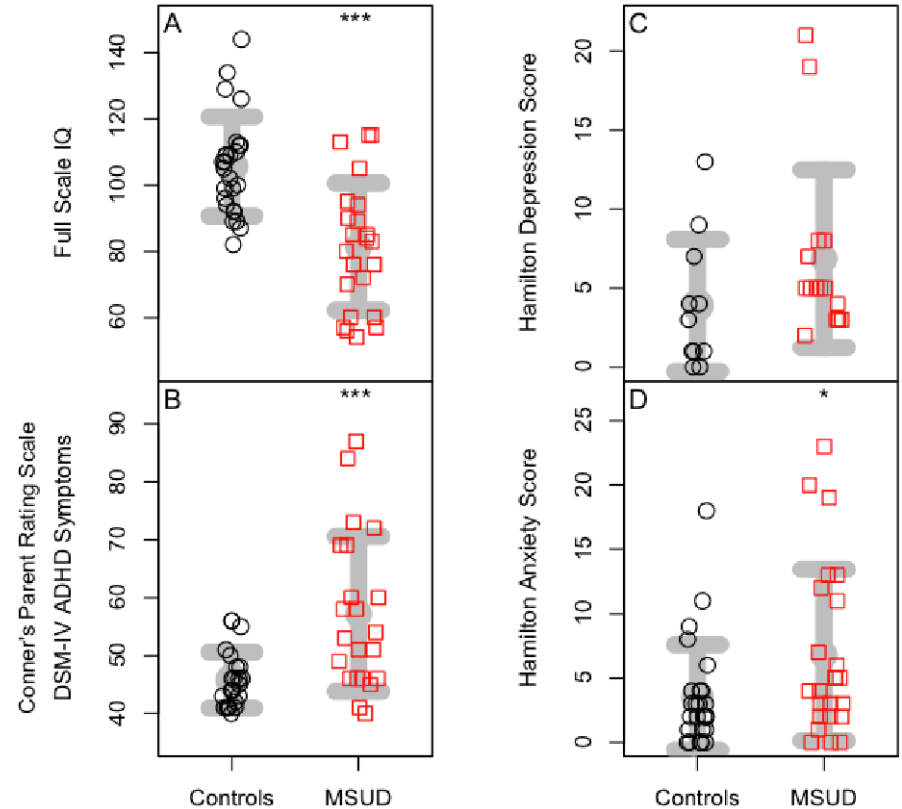
acertherapeutics

Reference Slides



Maple Syrup Urine Disease (MSUD)

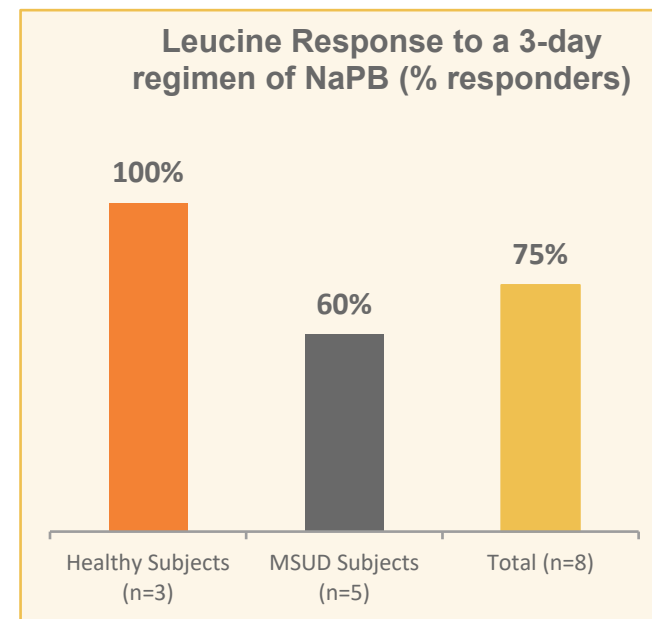
- MSUD is an inborn error of Branched-chain Amino Acid (BCAA) – leucine, isoleucine, valine – metabolism
 - Caused by deficiency of the mitochondrial Branched-chain Keto Acid Dehydrogenase complex (BCKDC)
 - ~800 patients in U.S., ~3,000 patients worldwide
 - MSUD Family Support Group has >500 patients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



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

MSUD: Clinical POC Study

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



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

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

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***
- Anticipate initiation of clinical studies in MSUD in 2022

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

** Afzal R, et al. Molecular Genetics and Metabolism Reports 15 (2018)

*** Acer Therapeutics: US Market Research – 2014