acertherapeutics

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

Corporate Presentation

August 23, 2022

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 are forward-looking statements. Examples of such statements include, but are not limited to, the Company’s expectations with respect to the clinical trials and anticipated milestones for ACER-001 (sodium phenylbutyrate), ACER-801 (osanetant) and EDSIVO™ (celiprolol), including timing, conditions, results, enrollment, duration and capital needs related thereto, and the Company’s expectations with respect to the sufficiency of its cash and cash equivalents and the duration thereof. Our pipeline products are under investigation and their safety and efficacy have not been established and there is no guarantee that any of our investigational products in development will receive health authority approval or become commercially available for the uses being investigated. 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 related to the drug development and the regulatory approval process, including the timing and requirements of regulatory actions. 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 Annual Report on Form 10-K and Quarterly Reports on Form 10-Q. 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: **41**
- Founded: **December 2013**
- Public: **September 2017**
- Cash as of June 30, 2022: **$14.5M**
  - Subsequent gross proceeds of $0.6M from ATM and equity line
  - Expected to have sufficient capital to fund current operations into Q4 2022
  - If ACER-001 receives U.S. FDA approval[1] by December 31, 2022, $42.5M could be funded through loan from Marathon, extending available capital for planned operations into H2 2023*

acertherapeutics

1 ACER-001 PDUFA date: January 15, 2023

* https://www.sec.gov/ix?doc=/Archives/edgar/data/0001069308/000119312522066842/d279077d8k.htm

Investment Highlights

- Acer's pipeline includes three clinical development 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) and other potential indications
  - **EDSIVO™** (celiprolol) for the treatment of vascular Ehlers-Danlos syndrome (vEDS) in patients with a confirmed type III collagen (COL3A1) mutation

- 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 in 2022/2023:
  - ACER-801 Phase 2a topline data[$]: **Q4, 2022**
  - ACER-001 (UCDs) PDUFA target action date[$,1]: **January 15, 2023**
  - ACER-001 (MSUD) Phase 2a trial initiation[$]: **Q1, 2023**
  - EDSIVO™ DiSCOVER trial full enrollment[$]: **Mid-2023**

acertherapeutics

[$] Subject to additional capital
1 PDUFA target action date does not guarantee timing of decision by FDA

Clinical Pipeline

Program / Indication	MOA / Type of Therapy	Preclinical	Phase 1	Phase 2	Phase 3	NDA
ACER-001 (sodium phenylbutyrate)						
Urea Cycle Disorders	Nitrogen scavenger therapy			PDUFA Date: Jan. 15, 2023 $,1		
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				$	

acertherapeutics

$ Additional capital required to support ACER-001 development (UCDs), and planned ACER-001 (MSUD), ACER-801 and EDSIVO™ clinical trials beyond Q4 2022

1 PDUFA target action date does not guarantee timing of decision by FDA

Overview

Disease Overview

- Urea cycle disorders (UCDs): a group of metabolic genetic diseases that lead to toxic build-up of ammonia (NH_4+)

Current Treatment Options

- ~800 UCDs US patients currently receiving a nitrogen binding agent
- BUPHENYL® + RAVICTI® US net sales (2021): ~$300M[2]

ACER-001 Profile

- Nitrogen-binding agent for use as adjunctive therapy in patients with UCDs involving deficiencies of CPS, OTC, or AS[3]
- Novel formulation designed for palatability while dissolving quickly
- To be supplied in a kit w/individual dosage envelopes; administered w/suspension agent and water
- Acer intends to provide significant stakeholder support

The Opportunity

- PDUFA date: January 15, 2023[$]
- Issued formulation composition of matter and use patents
- Other future development opportunities: MSUD[4], other potential indications

acertherapeutics

1 Payer claims data on file
2 https://ir.horizontherapeutics.com/static-files/47f395cb-4d8e-47a7-ba20-2f3c6f433e62
3 Abbreviations: CPS (carbamyl phosphate synthetase), OTC (ornithine transcarbamylase), AS (argininosuccinic acid synthetase)
$ Subject to additional capital; PDUFA target action date does not guarantee timing of decision by FDA
4 See MSUD slides in “Reference” section at end of this presentation

Resubmitted NDA Accepted for FDA Review

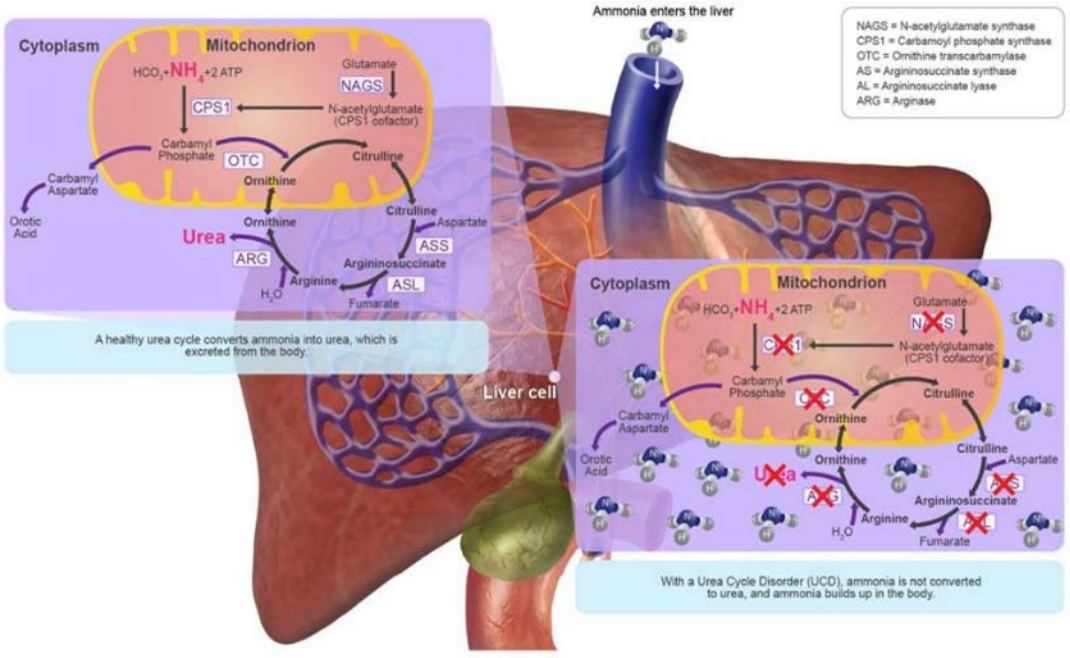
- Acer received a Complete Response Letter (CRL) to its NDA in late Q2 2022
- The CRL indicates that the FDA cannot approve the NDA in its current form
- The CRL states: "*[The FDA's] field investigator could not complete inspection of [Acer's third-party contract packaging manufacturer], because the facility was not ready for inspection. Satisfactory inspection is required before [the NDA] may be approved. Please notify us in writing when this facility is ready for inspection.*"
- The FDA did not cite any other approvability issues in the CRL pertaining to the NDA, nor request any additional clinical or pharmacokinetic studies be conducted prior to FDA approval. The FDA did provide one comment in the CRL (identified as "not an approvability issue") requesting additional existing nonclinical information to be provided in the resubmission of the NDA
- NDA resubmitted and accepted July 2022 as Class 2 resubmission
- PDUFA target action date: January 15, 2023$

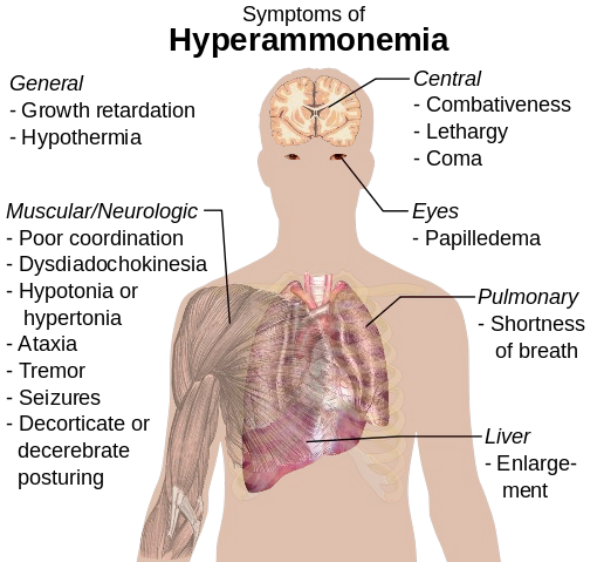
acertherapeutics

$ Subject to additional capital; PDUFA target action date does not guarantee timing of decision by FDA

Urea Cycle Disorders (UCDs)

- Urea Cycle Disorders (UCDs) are a group of rare, genetic disorders caused by mutations that result in a deficiency of one of the six enzymes or two transporters of the urea cycle
- These enzymes and transporters are responsible for removing ammonia from the bloodstream





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.

Mechanism of Action

Nitrogen Binding Agents

Alternative pathway treatment diverts nitrogen from the urea cycle to alternate routes of excretion

Nitrogen binding agents, containing phenylbutyrate, are all metabolized to phenylacetate (PAA)

PAA is the active moiety – it combines with glutamine, producing phenylacetylglutamine

Phenylacetylglutamine (PAGN) is then excreted by the kidneys in the urine

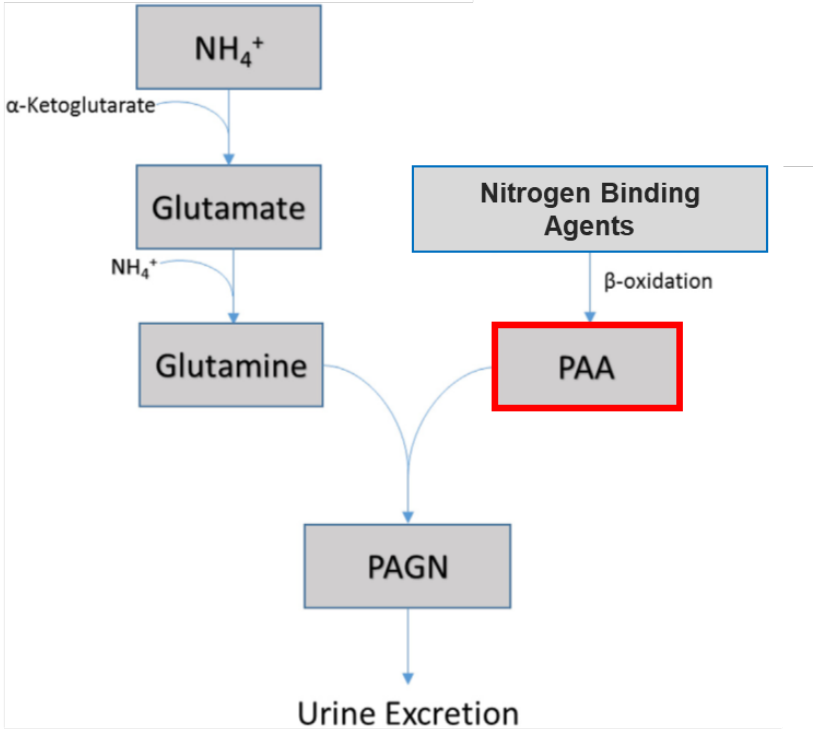


Fig. 1. Metabolizing pathway and mechanism of action of GPB.
GPB (glycerol phenylbutyrate); PAA (phenylacetic acid); PBA (phenylbutyric acid); PAGN (phenylacetylglutamine).

acertherapeutics

Berry S, et al. Molecular Genetics and Metabolism 125 (2018) 251–257.

Currently Marketed Treatment Options (US)[1]

- **Sodium Phenylbutyrate (BUPHENYL®, generics)**:
  - Aversive taste and odor[2]; considered unpalatable by some patients[3]
  - 64% of patients reported it is difficult to take because of taste[3]
  - Physicians reported that 25-33% of patients took less than target dose due to tolerability[3]
  - Only 25% of patients indicated that they never miss a dose[3]
  - 46% of patients reported taste as the reason for discontinuation[3]

- **RAVICTI®**: Consistently listed as one of the "10 Most Expensive Drugs in the World"[4]
  - Pricing has risen to levels considered challenging[5]
  - Reports of difficult access, unaffordability, and forced switches back to sodium phenylbutyrate[5]
  - Some patients are not meeting the treatment goal of <0.5 ULN (~17.5 umol/L)[6]

- Patients and physicians desire an effective and affordable treatment option[5]

1 PHEBURANE is approved by FDA for UCDs but not currently marketed in the US (based on available information)

2 Peña-Quintana L, et al. Profile of sodium phenylbutyrate granules for the treatment of urea-cycle disorders: patient perspectives. Patient Prefer Adherence. 2017 Sep 6;11:1489-1496.

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

4 https://pharmaoffer.com/blog/10-most-expensive-drugs-in-the-world/

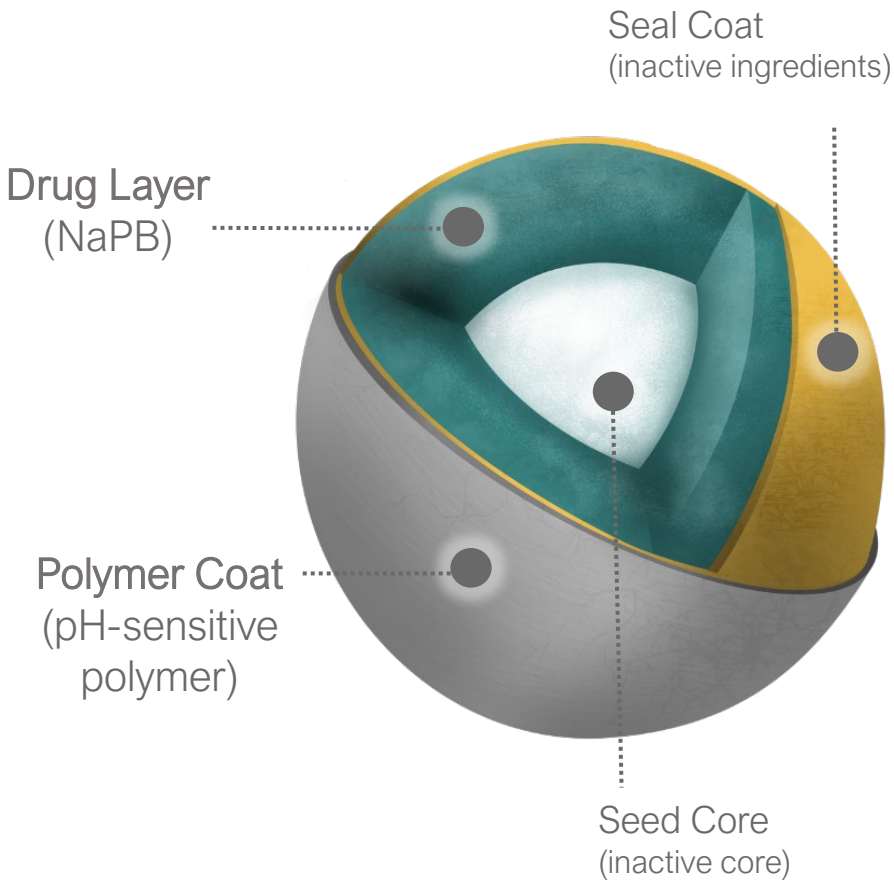
5 Acer Market Research

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

acertherapeutics

Product Differentiation

ACER-001 is a proprietary and **novel formulation of NaPB powder** that has shown bioequivalence to existing NaPB but with a pH-sensitive polymer coating that is **designed to minimize dissolution over 5 minutes after preparation**[1]



Drug Layer
(NaPB powder)

- Delivers the **proven ammonia control** of NaPB powder[1]

Polymer Coat
(pH-sensitive polymer)

- Designed to **minimize dissolution over 5 minutes after preparation**

acertherapeutics

1 Acer Therapeutics. Data on File. 2021.

Product Differentiation

Phenylbutyrate Formulations			
	In Development	*Marketed Products[1]*	
	ACER-001*	RAVICTI®	BUPHENYL®
Efficacy / Safety in UCDs	✓	✓	✓
Palatability / Compliance	✓	✓	✗**
Pricing (Per Patient Per Year)	TBD	$174K-$1.3M*** (avg $950K)	$204K-$402K*** (avg $300K)
Formulation	Polymer-coated (Packets)	Oil (Tablespoons)	Powder/Tablets (up to 40 tablets/day)
Packaging	Portable, premeasured packets	Bottle and syringe (bulk container)	Bottle (bulk container)

acertherapeutics

1 PHEBURANE is approved by FDA for UCDs but not currently marketed in the US (based on available information)
* Subject to FDA approval
** Shchelochkov et al., Molecular Genetics and Metabolism Reports 8 (2016) 43-47
*** RAVICTI® and BUPHENYL® pppy is based on patient weight and WAC price

ACER-001 Value Proposition

- Novel polymer-coated formulation for oral administration
- Designed for palatability[1]
- Convenient portable, premeasured packaging + additional dosing options
- 505(b)(2) NDA submission: trials showed ACER-001 has similar relative bioavailability to sodium phenylbutyrate powder
- Pricing projected to be significantly lower than current RAVICTI® price
- Robust patient support services program to address barriers to care
- Payer engagement strategy to support adoption
- Commitment to support the UCD community and on-going IEM research

Projected Prevalence[2]	~ 2,100
Diagnosed Patients[3]	~ 1,100
Patients Treated with Phenylbutyrate[3] (Ravicti®, Buphenyl®, generics)	~ 800
Market share for nitrogen binding agents[3]	75-80% Ravicti® 20-25% Buphenyl® or generic NaPB
2021 Net Revenue[4] (Ravicti®, Buphenyl®)	~$300M

acertherapeutics

1 Peña-Quintana L, et al. Profile of sodium phenylbutyrate granules for the treatment of urea-cycle disorders: patient perspectives. Patient Prefer Adherence. 2017 Sep 6;11:1489-1496.
2 https://www.drugs.com/slideshow/top-10-most-expensive-drugs-1274
3 Claims data analysis on file
4 https://ir.horizontherapeutics.com/static-files/47f395cb-4d8e-47a7-ba20-2f3c6f433e62; Represent North American sales

ACER-001: MSUD

Disease Overview

- Maple Syrup Urine Disease (MSUD): a rare, life-threatening metabolic disorder caused by a deficiency in an enzyme complex that metabolizes branched chain ketoacids, the breakdown products of the three branched-chain amino acids (BCAAs), leucine, valine, and isoleucine

Current Treatment Options

- Only treatment option is a life-long, protein-restricted diet
- Incidence: estimated at 1 in 185,000 people worldwide and 1 in 220,000 people in the U.S.[1]

ACER-001 Profile

- Multicenter study: 553 UCD patients treated with sodium phenylbutyrate showed decrease in plasma BCAA[2]
- Baylor College of Medicine study in MSUD patients: statistically significant reduction of leucine in 3/3 healthy subjects and 3/5 MSUD patients[3]
- Istanbul study in pediatric MSUD patients: significant reduction in leucine levels in MSUD patients experiencing an acute attack[4]

The Opportunity

- IND application submitted to FDA in July 2022
- Orphan designation in US and EU
- Q1 2023: Anticipated initiation of Phase 2a trial evaluating efficacy and safety of ACER-001 for potential treatment of MSUD patients, subject to IND clearance and available capital

1 Chapman, K, et al. (2018). Incidence of maple syrup urine disease, propionic acidemia, and methylmalonic aciduria from newborn screening data. Molecular Genetics and Metabolism Reports. 15. 106-109.

2 L.C. Burrage, et al., Sodium phenylbutyrate decreases plasma branched-chain amino acids in patients with urea cycle disorders, Mol. Genet. Metab. (2014)

3 Brunetti-Pierri et al. Phenylbutyrate therapy for maple syrup urine disease. Hum Mol Genet. 2011 February 15; 20(4): 631–640.

4 Zubarioglu T, et al. Impact of sodium phenylbutyrate treatment in acute management of maple syrup urine disease attacks: a single-center experience. J Pediatr Endocrinol Metab. 2020 Nov 11;34(1):121-126.

IP / Exclusivities

- Intellectual Property:
  - Issued patents:
    - US Patent 11,154,521 covering claims re: formulation compositions of matter (expires in 2036)
    - US Patent 11,202,767 covering claims re: certain methods of use (expires in 2036)
    - US Patent 10,092,532 covering claims re: methods of modulation of branched chain acids
      - Licensed from Baylor College of Medicine relating to MSUD
  - Continuing to pursue new patents and exclusivity possibilities, based on 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)
    - Granted EU Orphan Drug Designation: 10 years market exclusivity from EMA approval

Agreement with Relief Therapeutics

- ✓ Signed Collaboration and License Agreement Q1 2021
- ✓ To date, Acer has received $35.0M of funding
- ✓ Acer retained development and commercialization rights in the U.S., Canada, Brazil, Turkey and Japan
  - Split net profits from Acer's territories (60% to Relief; 40% to Acer)
- ✓ 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

- Vasomotor symptoms (VMS) are caused by a decrease in estrogen signaling in the brain, resulting in menopausal-like symptoms (hot flashes, night sweats, etc.)

Mechanism of Action

- 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

ACER-801 Profile

- ACER-801 (osanetant) is a non-hormonal, oral, selective neurokinin 3 receptor (NK3R) antagonist
- Clinical and laboratory safety results are available from 23 completed Phase 1 and 2 studies (387 healthy subjects and 821 patients)[2] in various patient populations

The Opportunity

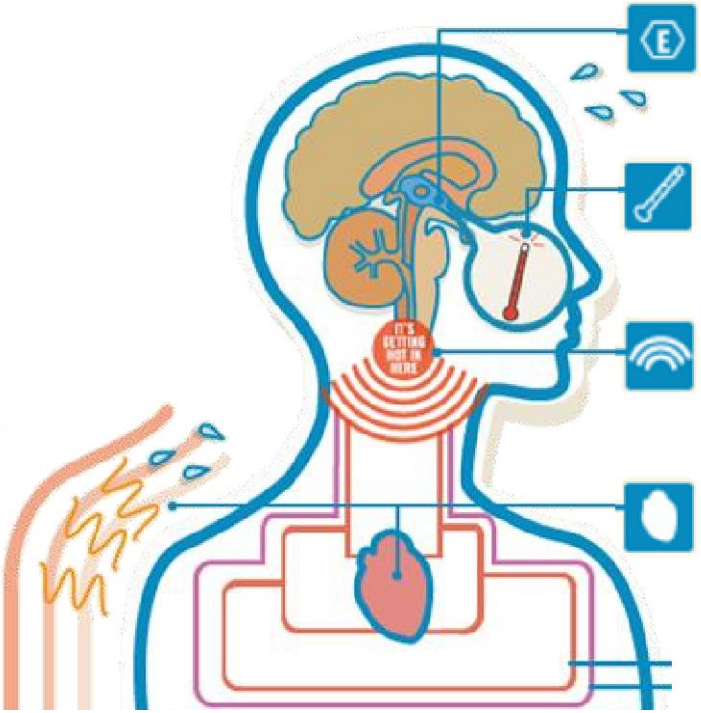
- Phase 2a proof of concept trial topline data anticipated in Q4 2022[$]
- Currently no other NK3R antagonists in development for iVMS
- Estimated size of iVMS opportunity in US ~250,000 patients[3]
- Acer maintains worldwide rights to ACER-801
- Composition of matter and methods of use patents filed

acertherapeutics

1 Rada G., et al. Cochrane Database Syst Rev. 2010 Sep 8;(9):CD004923.
2 Meltzer H, et al. Am J Psychiatry. 2004 Jun;161(6):975-84
$ Subject to additional capital
3 Trinity Partners 2020

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

Roth A, et al. The Oncologist, Oct 2003, vol.8 no.5 474-487.
Levine B. 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

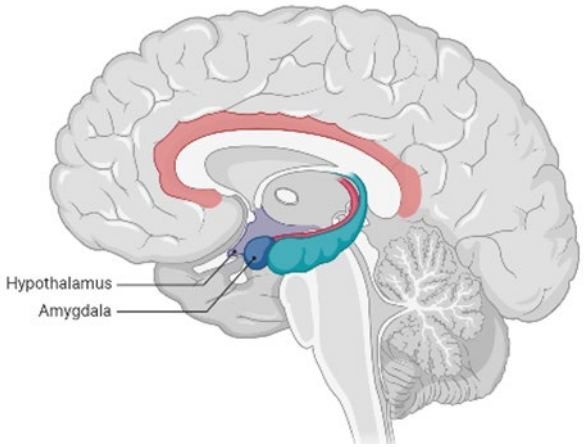
Women with HR+ Breast Cancer (CaB) receiving Tamoxifen

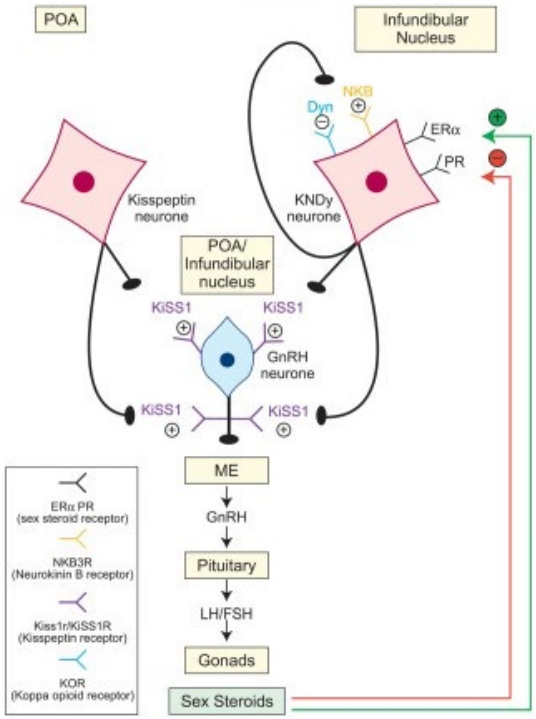
- 84% of women experienced hot flashes[1]
- 80% experienced night sweats
- 60% experienced severe symptoms
- Symptoms persisted throughout 5 years of treatment and were mainly attributed to tamoxifen
- After 4.5 years, 46% of women had discontinued tamoxifen[2]

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 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;TAC2 gene) is a stimulatory molecule that activates the neurokinin 3 receptor (NK3R) found in the arcuate nucleus (ARC) of the hypothalamus and the central amygdala regions of the brain
- The hypothalamus controls body homeostasis and the kisspeptin/ neurokinin B/dynorphin (KNDy) neurons in the ARC are responsible for thermoregulation
- The central amygdala is critical for the perception of emotions, including fear memory consolidation
- Thermoregulation (hot flashes) is mediated by a balance between estrogen (inhibitory/protective) and neurokinin B (stimulatory) signaling in KNDy neurons

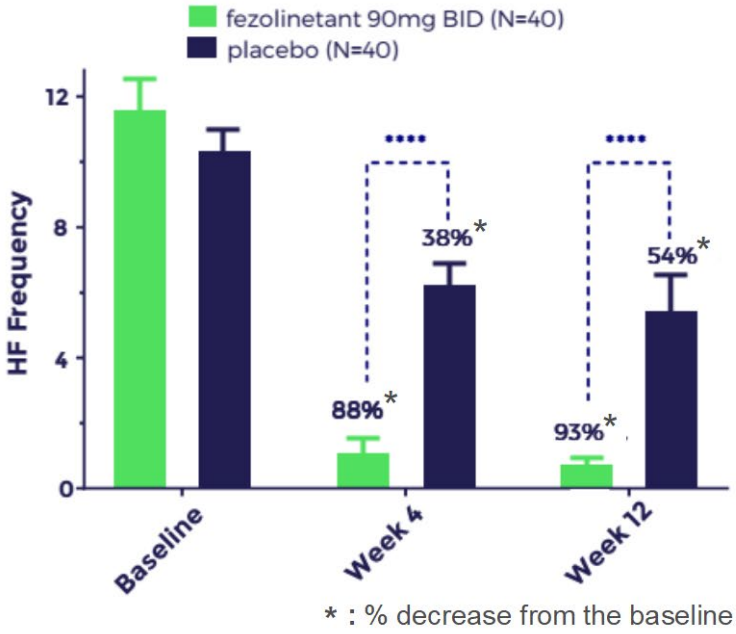




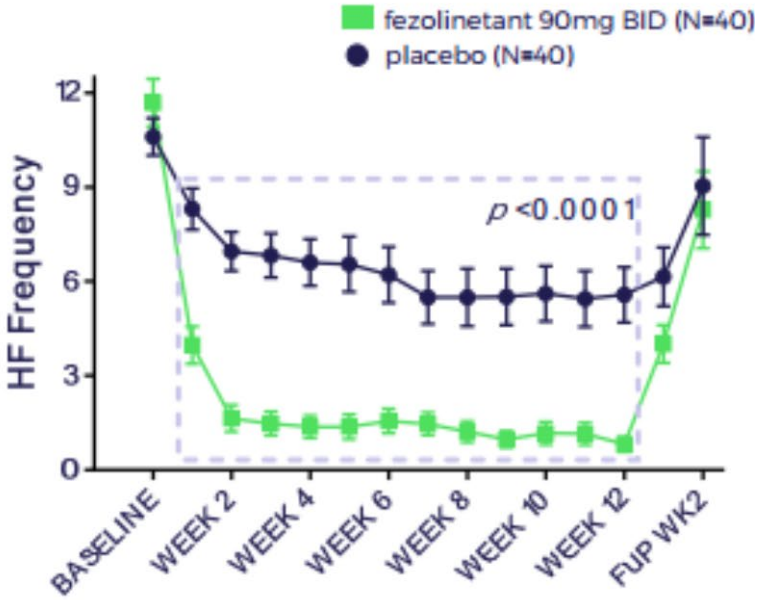
Clinical POC in VMS: NK3R Antagonist

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

Average Daily Hot Flash Frequency Reported as per FDA Guidance



* : % decrease from the baseline



Depypere H, et al. ENDO2017

Clinical POC in VMS: NK1,3R Antagonist

- Elinzanetant (NT-814) is a dual NK1,3R antagonist for the treatment of vasomotor symptoms in postmenopausal women

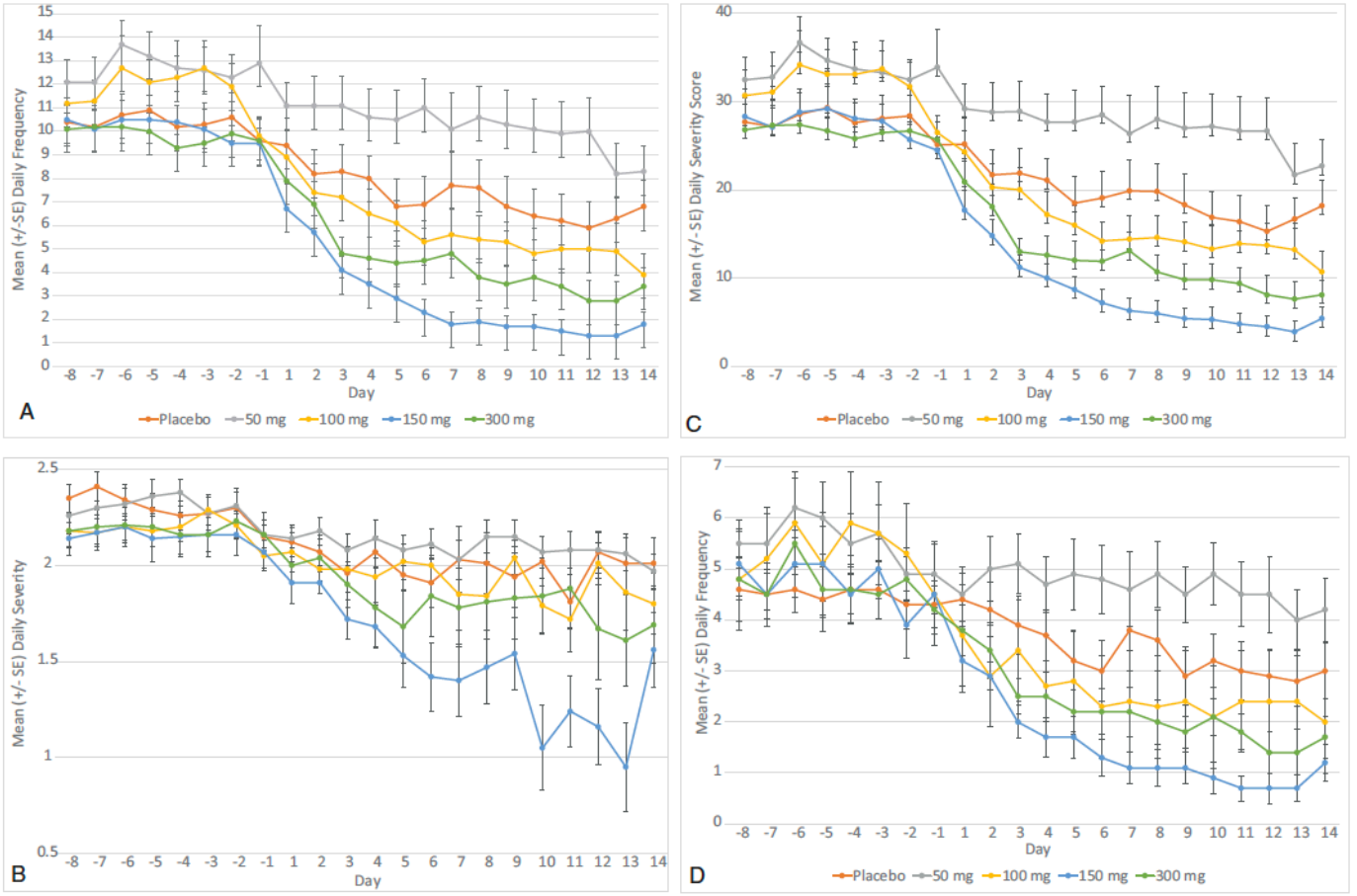


FIG. 2. Daily frequency of: moderate and severe hot flashes **(A)**, Severity of hot flashes **(B)**, daily hot flash severity score[a] **(C)**, and waking at night due to night sweats **(D)**, by day. Data shown are mean ± standard error ([a]severity score = [number of mild hot flashes × 1] + [number of moderate hot flashes × 2] + [number of severe hot flashes × 3]).

Trower M, et al. Menopause. 2020 May; 27(5): 498–505.

iVMS: The Unmet Need

- iVMS are well documented with the use of cancer therapies and certain surgical procedures and VMS appear immediately and can be severe
- Estrogen is contraindicated for the management of VMS in patients with hormone positive (HR+) tumors, including breast and prostate tumors
- A non-hormonal treatment for the management of moderate/severe iVMS is needed to help cancer patients start and stay on critical cancer therapy
- Non-adherence to cancer therapy can shorten the time to recurrence and increase the mortality risk
- Other NK3R antagonists under development are focused on menopausal-related VMS

Development Plan

- Q1 2022: Began patient enrollment in Phase 2a, randomized, double-blind, placebo-controlled, dose-ranging trial (NCT05325775) in Q1 2022:
  - Primary objective:
    - Evaluate the safety profile of ACER-801 at different doses
    - Evaluate the pharmacokinetic (PK) profile of ACER-801 at different doses
  - Secondary objectives:
    - Evaluate the effect of ACER-801 at different doses on the frequency and severity of VMS associated w/menopause vs. placebo

- Q4 2022: Phase 2a proof of concept trial topline data anticipated[$]

acertherapeutics

$ Subject to additional capital

Overview

Disease Overview

- 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 in arteries and hollow organs (intestines, uterus, lungs, etc.)
- Often fatal: median survival in the U.S. is estimated to be 51 years of age[1]

Current Treatment Options

- No approved therapeutic options for vEDS patients
- Following the publication of the BBEST trial, celiprolol has become the primary treatment for vEDS patients in several European countries[2]

EDSIVO™ Profile

- BBEST Clinical Trial: 76% reduction in risk of arterial events observed in COL3A1+ subpopulation[3]
- Long-term Observational Study (France)[4]
  - 144 COL3A1+ patients (90% treated w/celiprolol) followed for ≤17 years
  - At end of follow-up, survival was 80.7% (95% CI: 67.8 - 93.6%) in those treated with celiprolol vs. 48.5% (95% CI: 19.7 - 77.4%) in those not treated

The Opportunity

- DiSCOVER Phase 3 decentralized (virtual) pivotal trial initiation: June 27, 2022
  - Full enrollment anticipated in mid-2023 based on current enrollment rates[$]
  - Interim analysis planned at approximately 24 months after full enrollment[$]
  - Expected to take ~3.5 years to complete once fully enrolled[$]
- NCE, Orphan Drug Designation and methods of use patents filed

acertherapeutics

1 Pepin, et al. Survival is affected by mutation type and molecular mechanism in vascular Ehlers–Danlos syndrome (EDS type IV). Genet Med. 2014 Dec;16(12):881-8.
2 https://www.ehlers-danlos.com/celiprolol-and-veds/
3 Ong K, et al. Lancet 2010; 376: 1476-84.
4 Frank M, et al. Vascular Ehlers-Danlos Syndrome: Long-Term Observational Study. J Am Coll Cardiol. 2019 Apr, 73 (15) 1948–1957
$ Additional capital required to conduct and complete the planned pivotal Phase 3 trial of EDSIVO™ beyond Q4 2022

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

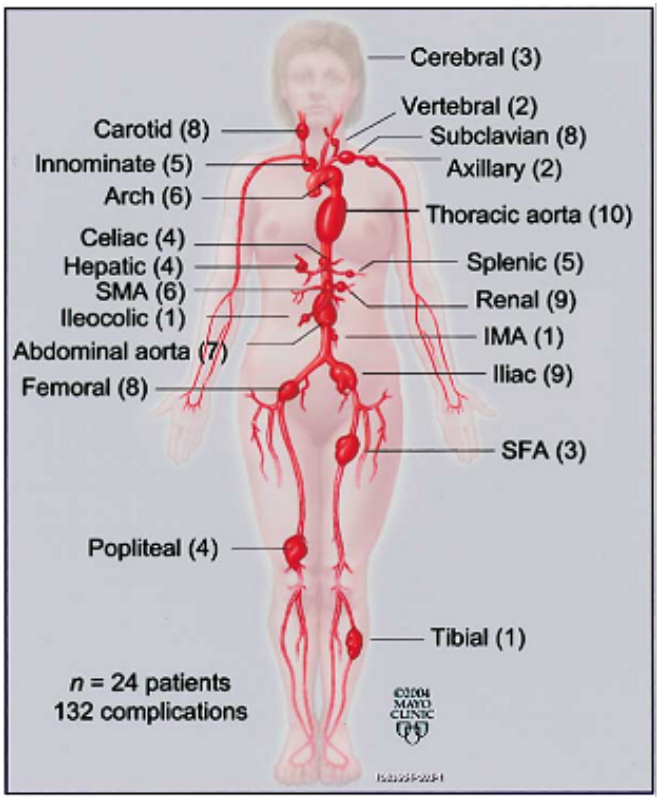


Fig. 3 Distribution of 132 vascular complications in 24 patients with a clinical diagnosis of EDS type IV. J Vasc Surg 2005;42:98-106.

acertherapeutics

1 Pepin M, et al. Genet Med. 2014 Dec;16(12):881-8.

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

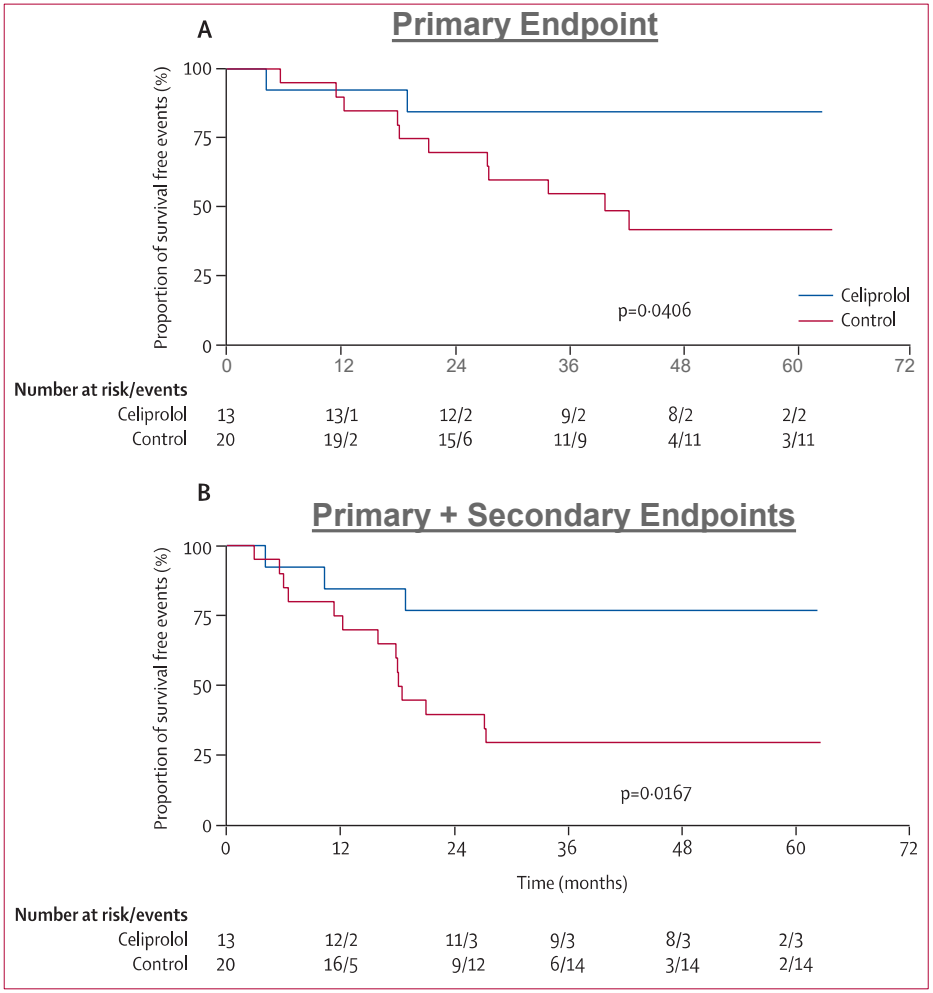


Figure 3: **Kaplan-Meier curves of event-free survival in 33 patients with positive *COL3A1* mutation**
Primary endpoint (A). Primary and secondary endpoints (B).

acertherapeutics

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

Celiprolol Pivotal Clinical Trial

- **DiSCOVER** (**D**ecentral**i**zed **S**tudy of **C**eliprolol **o**n **v**EDS-related **E**vent **R**eduction) trial design:*
  - A Phase 3, U.S.-based, randomized, double-blind, decentralized (virtual) clinical trial to compare the efficacy of celiprolol to placebo in the treatment of patients with COL3A1-positive vEDS
  - Primary objective: compare time to first occurrence of a confirmed clinical event between celiprolol group and placebo group among confirmed COL3A1-positive vEDS patients
  - Secondary objectives:
    - Safety and tolerability of celiprolol
    - Incidence rate of composite endpoint among vEDS patients treated w/celiprolol vs. placebo

- Status:
  - ✓ U.S. IND in effect
  - ✓ Granted Breakthrough Therapy designation (BTD) by FDA
  - ✓ Reached agreement with FDA under a Special Protocol Assessment (SPA)
  - ✓ Launched discoverceliprolol.com as an educational tool for interested parties
  - ✓ Initiated pivotal **DiSCOVER** trial (study NCT05432466) June 27, 2022
    - Q2 2023: Full enrollment anticipated in Mid-2023 based on current enrollment rates[$]
    - Interim analysis planned at approximately 24 months after full enrollment[$]
    - Expected to take ~3.5 years to complete once fully enrolled[$]

acertherapeutics

$ Additional capital required to conduct and complete the planned pivotal Phase 3 trial of EDSIVO™ beyond Q4 2022

Financial Overview

- Cash as of June 30, 2022: $14.5M
  - Subsequent gross proceeds of $0.6M from ATM and equity line
  - Expected to have sufficient capital to fund current operations into Q4 2022
  - If ACER-001 receives U.S. FDA approval[1] by December 31, 2022, $42.5M could be funded through loan from Marathon, extending available capital for planned operations into H2 2023*

- Capitalization as of August 10, 2022:
  - 16.1M shares of common stock outstanding
  - 21.5M shares fully diluted (includes stock options, convertible note*, and warrants*)

- $152.0M historical gross proceeds through August 10, 2022
  - ✓ $104.5M equity financings
  - ✓ $35.0M from Relief Collaboration
  - ✓ $12.5M from debt financings*

acertherapeutics

1 ACER-001 PDUFA date: January 15, 2023
* https://www.sec.gov/ix?doc=/Archives/edgar/data/0001069308/000119312522066842/d279077d8k.htm

acertherapeutics

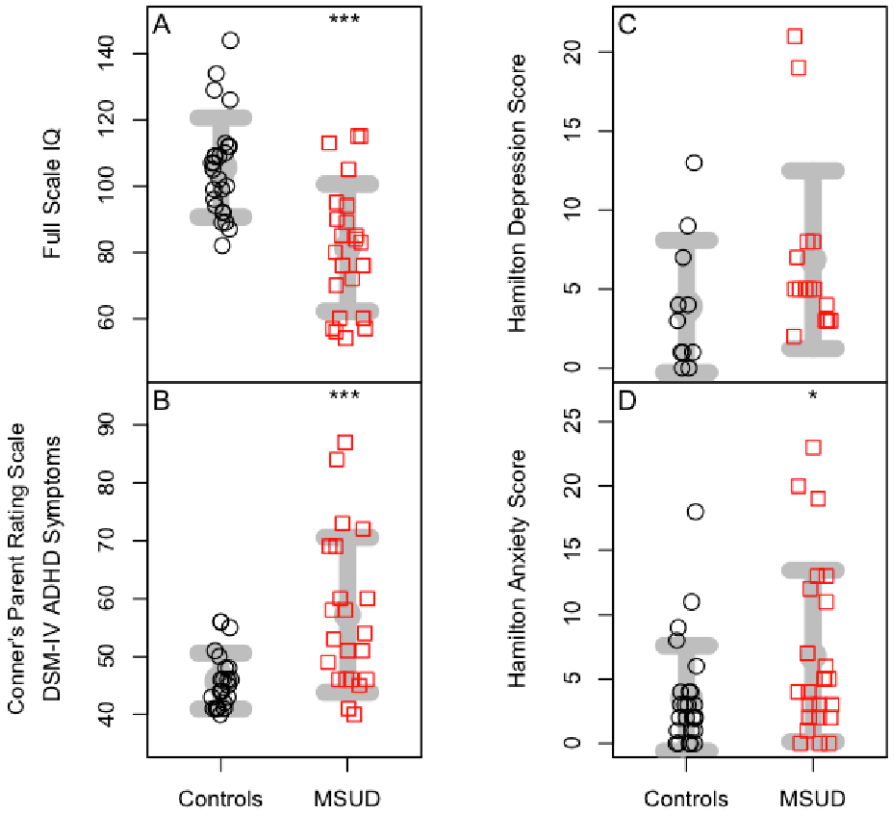
Reference Slides

Leadership Team

Chris Schelling **CEO & Founder**	• 23 years; strategic commercial dev. & orphan	BIOMARIN
Adrian Quartel, MD **Chief Medical Officer**	• 20+ years; clin. dev., medical & regulatory affairs	BIOMARIN
Tanya Hayden **Chief Operating Officer**	• 20+ years; drug dev., delivery, mfg. & alliance mgt.	Lonza
Harry Palmin **Chief Financial Officer**	• 25+ years; corporate & finance experience	Novelos
Matt Seibt **Chief Commercial Officer**	• 24 years; sales, market access & product launch	Biogen
Jeff Davis **Chief Business Officer**	• 25+ years; business & corporate development	genzyme
John Klopp **Chief Technical Officer**	• 19 years; orphan manufacturing & commercialization	BIOMARIN
Don Joseph, JD **Chief Legal Officer**	• 25+ years; general counsel & senior management	bvgh BIO Ventures for Global Health
Bernie Paul **Chief People Officer**	• 25+ years; human resources & org. development	clarisonic

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



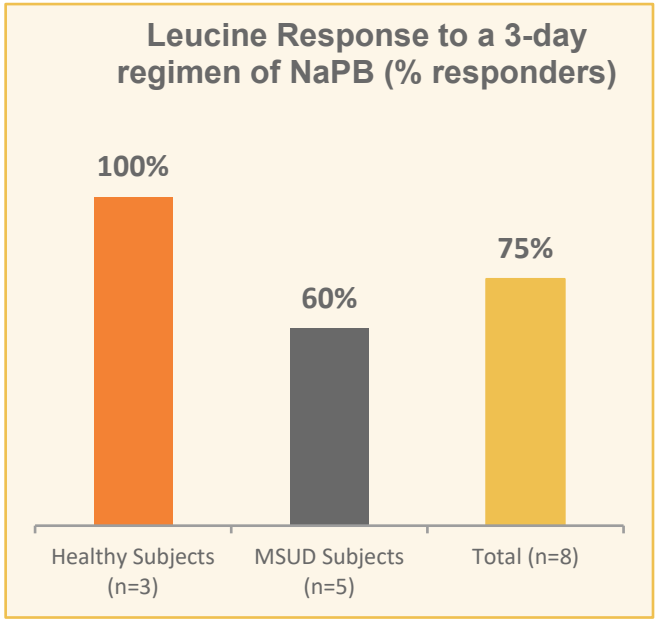
indicates p < 0.05, *** p < 0.001 compared to the control group*

acertherapeutics

* Muelly E, et al. 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

acertherapeutics

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

Overview

Disease Overview

- Potential treatment for DNA and RNA-replicating viruses, including cytomegalovirus, Zika, dengue, Ebola, COVID-19 and other viruses

Mechanism of Action

- Host-directed therapy – restores the cellular stress response, blocking ribosome biogenesis and translation-elongation of viral mRNA in infected cells

ACER-2820 Profile

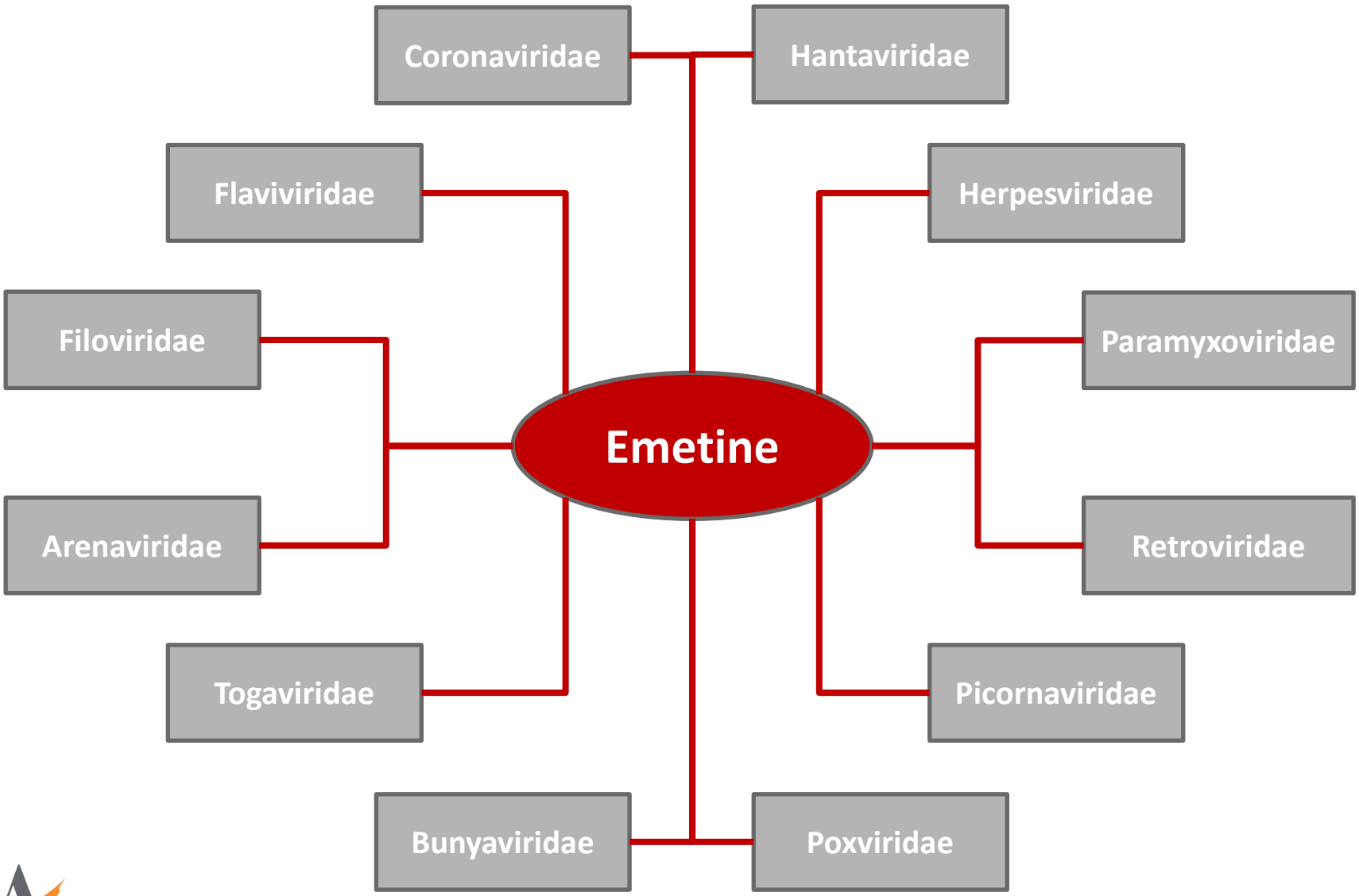
- Broad-spectrum, host-directed antiviral therapy w/ nanomolar potency in vitro against DNA and RNA-replicating viruses
- Strong in vivo efficacy data against multiple viruses

The Opportunity

- Applied for MCDC funding for Filoviruses
  - Received positive feedback and placed in “basket” if additional funding becomes available
- Further advancement of the program is dependent on ability to raise non-dilutive capital
- Composition of matter patent filed

ACER-2820

Broad-spectrum, Antiviral Activity



acertherapeutics

Nanomolar Potency In Vitro

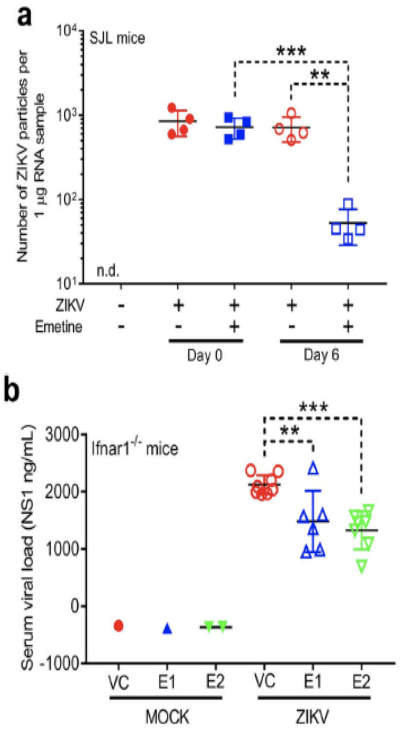
	Virus Type	Antiviral Activity*	Reference
Coronaviridae	SARS-CoV-2 (Vero-E6)	EC_{50} = 0.007	Wang et al. Molecular Biomedicine 1:14 https://doi.org/10.1186/s43556-020-00018-9 (2020).
	SARS-CoV-2 (Caco-2)	IC_{50} = 0.47	Bojkova et al. Proteomics of SARS-CoV-2 infected host cells reveals therapy targets. 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. *Viruses* **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. Viruses. 2019 Oct 18;11(10). pii: E964. doi: 10.3390/v11100964.
Paramyxoviridae	HMPV	EC_{50} = 0.14 / CC_{50} = 1	Andersen et al. Viruses. 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. Molecules. 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.

acertherapeutics

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

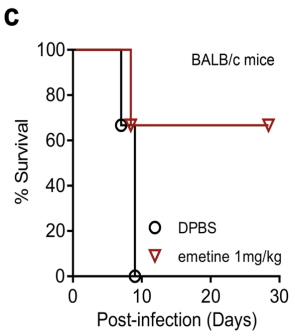
In Vivo Efficacy Data

Zika virus[1]



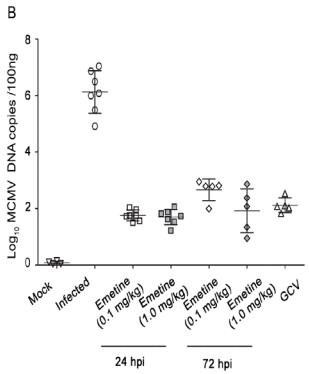
Emetine suppresses ZIKV virus load in vivo.
a Three-month-old SJL male mice were infected retro-orbitally with ZIKVBR followed by IP administration of emetine (1 mg/kg/day) for the next 6 days (N = 4 mice per group). Two groups of SJL mice (N = 4) received the same volume of vehicle buffers. Statistical 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 virus[1]



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.

Cytomegalovirus[2]



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.

Enterovirus[3]

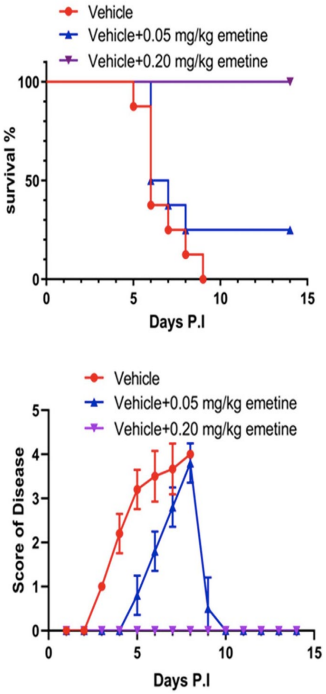


Diagram of the mice infection model (A), survival rates (B) and clinical scores (C) of two-week KM mice infected with EV-A71 GZ-CII strain and treated with emetine. The treated mice were monitored for two weeks after infection. Disease score definition as followings: Healthy, 0 point; Lethargy and inactivity,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

acertherapeutics

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.