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

Corporate Presentation

August 13, 2019

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, future financial position, future revenues, projected expenses, regulatory actions or approvals, cash position, liquidity, prospects, plans and objectives of management are forward-looking statements. Examples of such statements include, but are not limited to, statements relating to expectations regarding our capital resources; the anticipated future reduction in operating and cash conservation benefits associated with our corporate restructuring initiative; the potential for EDSIVO™ (celiprolol), ACER-001, and osanetant to safely and effectively treat diseases and to be approved for marketing; the commercial or market opportunity of any of our product candidates in any target indication; the adequacy of our capital to support our future operations and our ability to successfully initiate and complete clinical trials and regulatory submissions; our progress toward possible approval for EDSIVO™ and our other product candidates; 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, our ability to reduce our operating expenses and conserve cash on a net basis as a result of our prior or any future corporate restructuring initiative, the availability of sufficient resources to meet our business objectives and operational requirements, the fact that the results of earlier studies and trials may not be predictive of future clinical trial results, the protection and market exclusivity provided by our intellectual property, the substantial costs and diversion of management's attention and resources which could result from securities class action litigation, risks related to the drug development and the regulatory approval process, including the timing of regulatory actions, and the impact of competitive products and technological changes. We disclaim any intent or obligation to update these forward-looking statements to reflect events or circumstances that exist after the date on which they were made. You should review additional disclosures we make in our filings with the Securities and Exchange Commission, including our Quarterly Reports on Form 10-Q and our Annual Report on Form 10-K. You may access these documents for no charge at http://www.sec.gov.

Corporate Overview

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

- Headquartered: **Newton, MA**
- Headcount: **19**
- Founded: **December 2013**
- Public: **September 2017**
- Cash:
  - **$23.5M** as of June 30, 2019
  - Expected to have sufficient capital through end of 2020

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Executive Leadership Team

Chris Schelling **CEO & Founder**	• 20 years; strategic commercial development & orphan	BIOMARIN
Will Andrews, MD **Chief Medical Officer**	• 20 years; clinical development, medical affairs & orphan • M.D. Yale University School of Medicine	sunovion
Matt Seibt **Interim Head of Commercial**	• 22 years; sales, market access & product launch	Biogen
Harry Palmin **Chief Operating & Financial Officer**	• 25 years; corporate & finance experience	Novelos
Don Joseph, JD **Chief Legal Officer & Secretary**	• 25 years; general counsel & senior management • J.D. University of Texas School of Law	bvgh BIO Ventures for Global Health

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Investment Highlights

- Acer's pipeline includes three clinical-stage product candidates:
  - **EDSIVO™ (celiprolol)** for the treatment of vascular Ehlers-Danlos syndrome (vEDS) in patients with a confirmed type III collagen (COL3A1) mutation
  - **ACER-001** (a fully taste-masked, immediate release formulation of sodium phenylbutyrate) for the treatment of various inborn errors of metabolism, including urea cycle disorders (UCDs) and Maple Syrup Urine Disease (MSUD)
  - **Osanetant** for the treatment of induced Vasomotor Symptoms (iVMS) where Hormone Replacement Therapy (HRT) is likely contraindicated

- Acer's 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
  - Accelerated paths for development through specific FDA-established programs

- Multiple anticipated key regulatory milestones:
  - EDSIVO™ Type A mtg w/FDA: **Q3 2019**
  - ACER-001 (UCD) pivotal bridging & taste assessment trials initiation: **Q4 2019**
  - Osanetant IND submission: **Q4 2019**
  - ACER-001 (UCD) NDA submission*: **Mid-2020**
  - Osanetant Phase 1/2 PK/PD/safety trial initiation**: **Mid-2020**

- Expected to have sufficient capital through end of 2020

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* Assuming successful outcomes in bridging trials and NDA submission with 6 months stability data
** Subject to additional capital

Clinical Pipeline

Program / Indication	Novel MOA / Unique Characteristics	Phase 1	Phase 2	Phase 3	NDA	Market
EDSIVO™ (celiprolol)						
vascular Ehlers-Danlos syndrome (COL3A1+)*	Induces vascular dilatation and smooth muscle relaxation					
ACER-001 (reformulated sodium phenylbutyrate)						
Urea Cycle Disorders	Taste-masked formulation; evaluating comparability to Buphenyl®					
Maple Syrup Urine Disease	Inhibition of BCKD kinase to increase BCAA metabolism					
Osanetant						
Induced Vasomotor Symptoms (iVMS)	Neurokinin 3 Receptor Antagonist					

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* CRL received after market close 6/24/19

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 vasodilation and vascular smooth muscle dilation, thereby reducing the mechanical stress on collagen fibers within the arterial wall.

Product Profile

- **BBEST Pivotal 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]
- 17-year vEDS long-term observational study (n=144) published in JACC[2]

The Opportunity

- **FDA CRL received after market close June 24; conduct Type A meeting in Q3 2019**
- Corporate restructuring initiative implemented and pre-commercial activities of EDSIVO™ halted
- Seeking viable path forward with FDA which may include Formal Dispute Resolution Request

1. Ong Lancet 2010; 376: 1476-84.
2. Frank et al., J Am Coll Cardiol. 2019 Apr 23;73(15):1948-1957.

EDSIVO™: CRL and Next Steps

- Received CRL from FDA on June 24, 2019 stating that 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

- Following receipt of CRL, corporate restructuring implemented to reduce operating expenses and conserve cash, and pre-commercial activities of EDSIVO™ halted

- Acer is working with Hyman, Phelps, & McNamara (HPM) and other leading industry experts to determine the optimal path forward
  - Continue to work toward our goal of approval of EDSIVO™ for confirmed COL3A1+ vEDS patients

EDSIVO™: CRL and Next Steps

- In 2016, FDA published that from 2003-2014, of the 140 appeals accepted, 16% were granted and 84% denied.

- According to HPM, these "denials" are most often "wins"
  - While approval is not provided based on the previous NDA submission, the company is given a more favorable path forward to approval than was presented in the CRL

- Between 2015-2018, HPM worked on 9 appeals
  - FDA counted these as 12 appeals, and granted 3 (25%)
  - HPM describes that 7 of the 9 cases were given a more favorable alternative path to approval than outlined in the review (78%)

- The results of prior appeals, as well as any appeal involving a program other than EDSIVO™, should not be viewed as predictive of any appeal involving EDSIVO™

http://www.fdalawblog.net/2018/10/formal-dispute-resolution-a-different-perspective-on-wins-and-losses-2/

EDSIVO™: CRL and Next Steps

- Conduct a Type A meeting with FDA to make sure we fully understand FDA's thought process for the CRL
- Depending on outcome, consider submission of a Formal Dispute Resolution Request (FDRR)
- Depending on issues and outcomes, we may be able to resubmit our NDA, but no assurances
- The entire process will likely take many months and possibly a year or more to reach final outcome
- We will provide updates as appropriate and may discontinue the process at any point where risk/benefit no longer justifies continued resources

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
    - 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, but 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

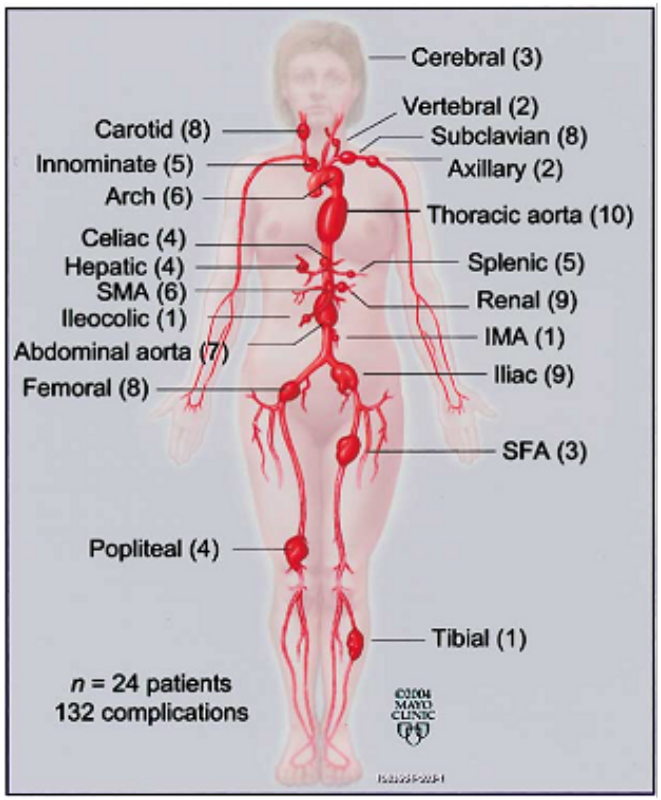

Fig. 3 Distribution of 132 vascular complications in 24 patients with a clinical diagnosis of EDS type IV. J Vasc Surg 2005;42:98-106.

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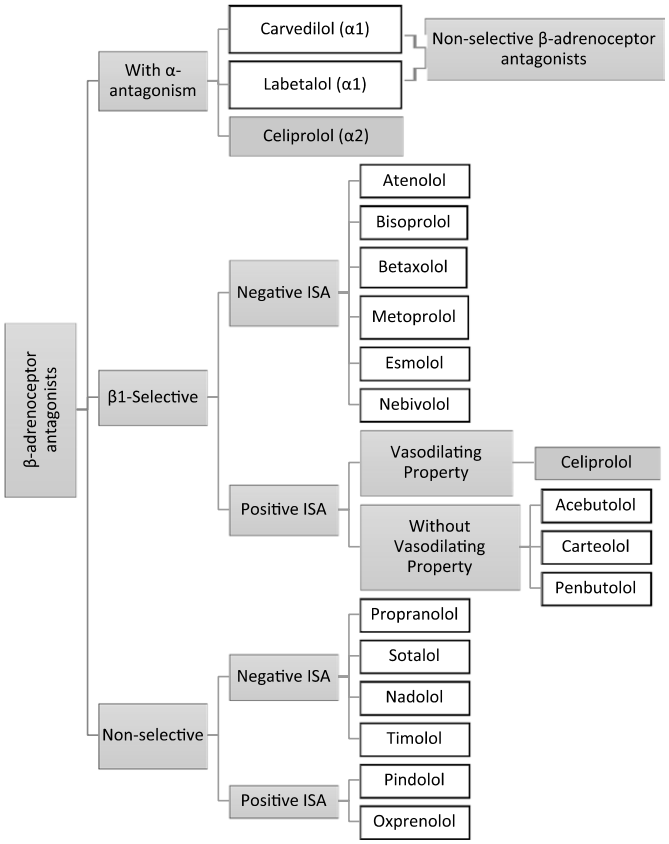
[1] Pepin Genet Med. 2014 Dec;16(12):881-8.

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™ potential beneficial effects in vEDS patients are thought to be through vasodilation and vascular smooth muscle dilation, 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 Pivotal Clinical Trial

Efficacy:

- 64% reduction in the average risk of fatal or nonfatal cardiac or arterial events in EDSIVO™ patients vs. control group over mean follow-up of 47 months
- 76% average reduction in risk of fatal or nonfatal cardiac or arterial events in COL3A1+ EDSIVO™ patients vs. control group
- Trial stopped early for clinical benefit (mean follow-up 47 months)
  - Significant differences in treatment effect were observed; consensus decision of DSMB, statisticians and principal investigator

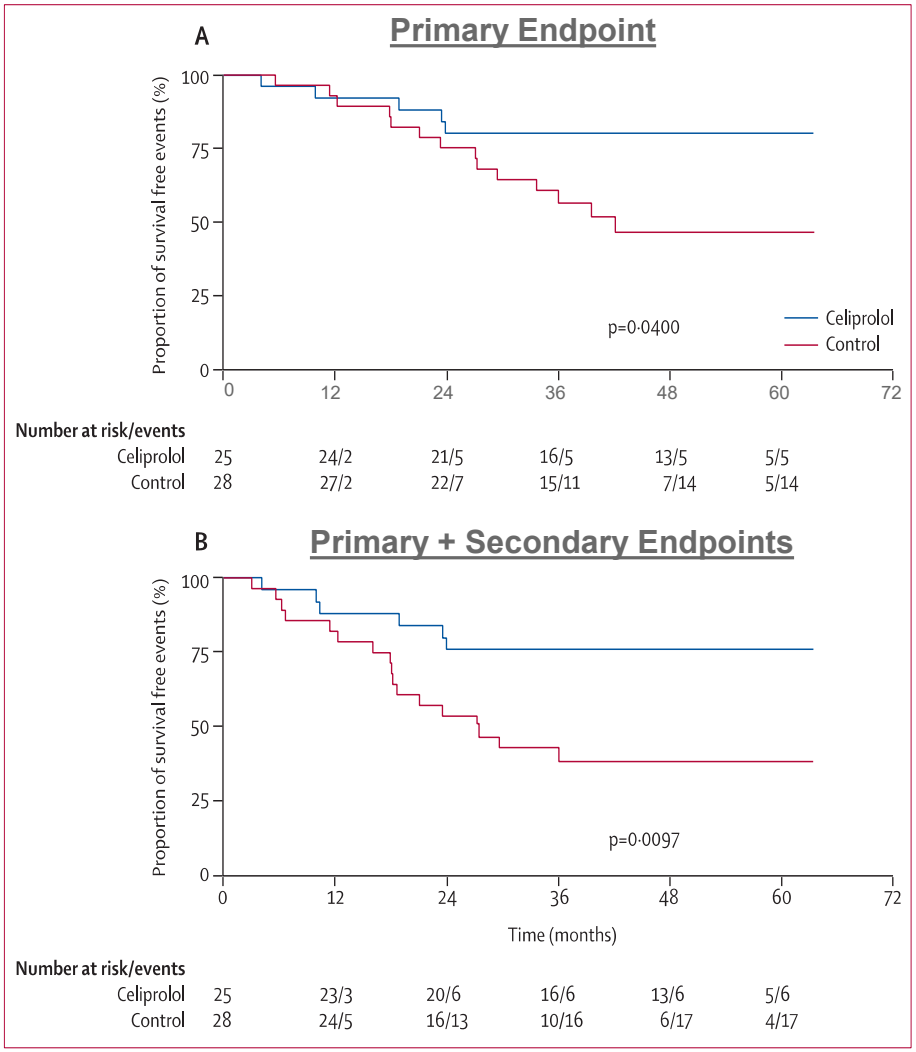

Figure 2: **Kaplan-Meier curves of event-free survival in 53 patients with vascular Ehlers-Danlos**
Primary endpoint (A). Primary and secondary endpoints (B).

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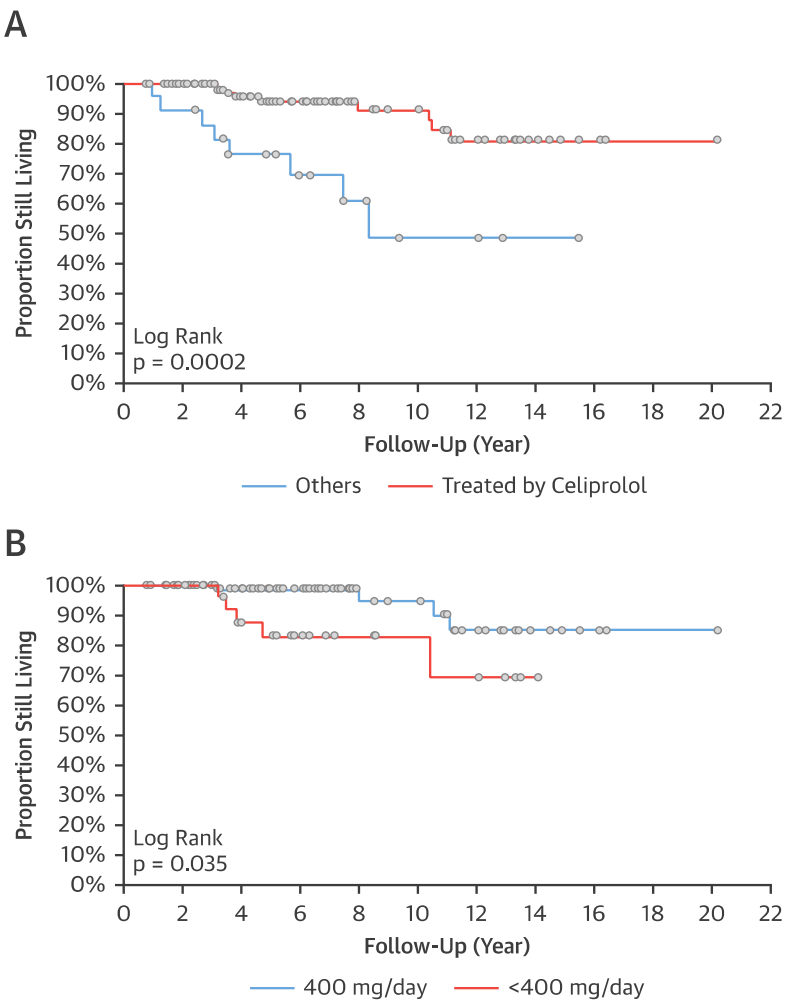
Ong Lancet 2010; 376: 1476-84.

Long-Term Observational Study

Efficacy:

- Between 2000 and 2017, 144 patients (median age at diagnosis 34.5 years; 100% COL3A1+) were included in this study
- (A) Patients not treated with celiprolol had a significantly worse survival outcome than treated patients:
  - Overall survival was 80.7% (95% CI: 67.8% to 93.6%) in those treated with celiprolol (n = 110) versus 48.5% (95% CI: 19.7% to 77.4%) in those not treated (n = 22) after 11.1 years of follow-up: p = 0.0002
- (B) Survival was significantly improved in patients taking celiprolol 400 mg/day compared with patients taking lower doses, suggesting a dose effect and that 400 mg/day should be considered the optimal treatment dose:
  - At the end of follow-up, survival was 85% (95% CI: 70.5% to 99.5%) in those patients treated with celiprolol 400 mg/day and 69.2% (95% CI: 41.4% to 97.0%) in those taking celiprolol 100 to 300 mg/day: p = 0.035
- Statistically significant reduction in rate of hospitalization for acute arterial events after systematic introduction of celiprolol treatment

FIGURE 3 Kaplan-Meier Survival Analysis of vEDS Patients in Groups I and II *COL3A1* Pathogenic Variants, According to Celiprolol Treatment



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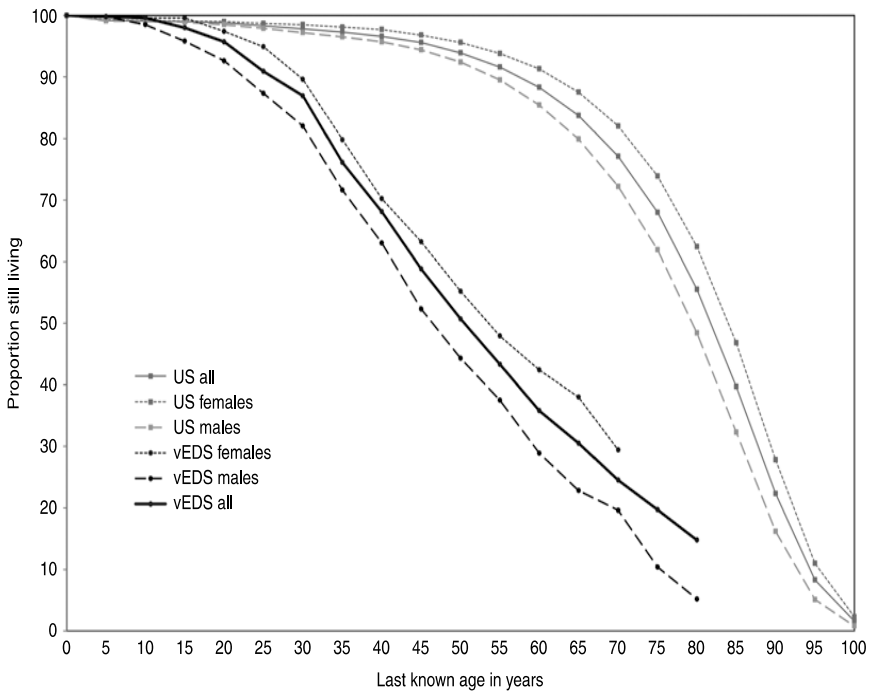
Frank et al., J Am Coll Cardiol. 2019 Apr 23;73(15):1948-1957.

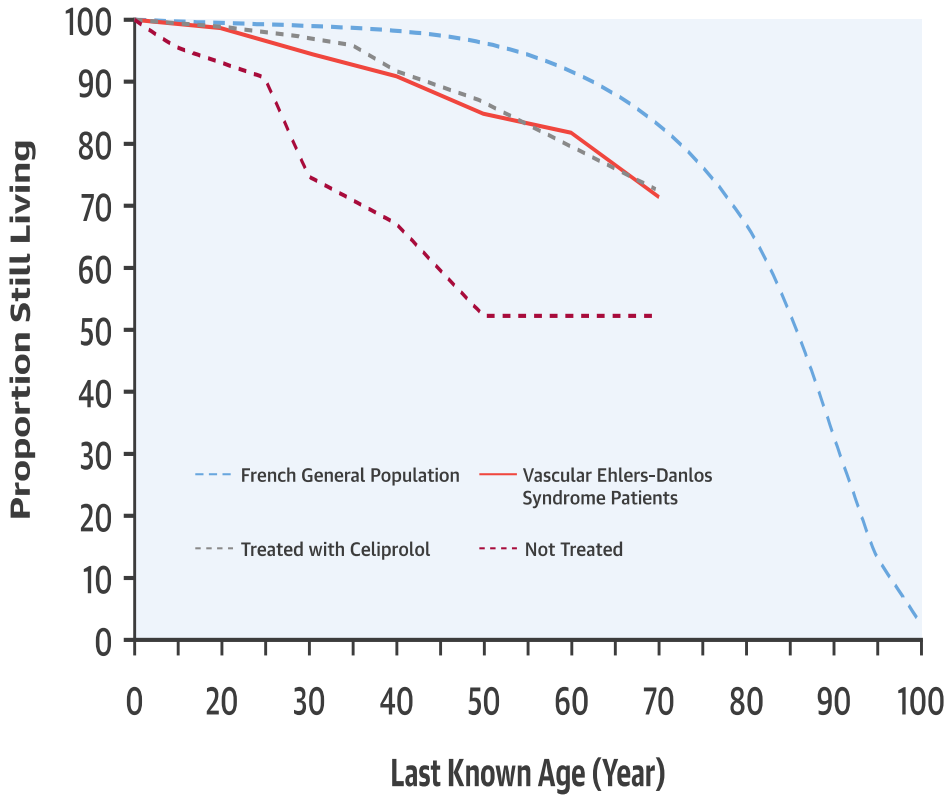
U.S. vs. French vEDS Patients

U.S. vEDS Natural History
1,231 patients (>90% COL3A1+; 630 index / 601 relatives)



Median Survival: 51 years (46 y.o. males; 54 y.o. females)

French vEDS Population
144 patients (100% COL3A1+; 91 index / 53 relatives)



Median Survival: Not Met

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Pepin Genet Med. 2014 Dec;16(12):881-8.
Frank et al., J Am Coll Cardiol. 2019 Apr 23;73(15):1948-1957.

SVM Poster: Antihypertensive Therapy

Background:

- No currently approved medications to treat vEDS
- There is no evidence supporting the use of antihypertensive medications in vEDS

Methods:

- Retrospective analysis of U.S. insurance claims identifying vEDS patients 2014-2017
- Patient data stratified based on claims for patients taking antihypertensive medications and not taking an antihypertensive medication
- Calculated and compared clinical event rates for each group

Results:

- Study suggests that minority of U.S. vEDS patients (34%) are being treated with antihypertensive medications
- Data showed no significant difference in clinical event rates in U.S. patients taking antihypertensive medications (16.5%) vs. those not taking an antihypertensive (15.6%) medication
- Underscores need for an effective treatment

Table 4. Rate of Clinical Events in vEDS Patients on Antihypertensive Therapy

vEDS Patient Group	No. Patients (%)	Rate of Clinical Events	*P*-value (vs. No Antihypertensive)
No antihypertension therapy	2,371 (65.6%)	371 (15.6%)	-
Any antihypertension therapy	1,243 (34.4%)	205 (16.5%)	0.51
Beta blocker	895 (24.8%)	146 (16.3%)	0.64
ACE inhibitor	231 (6.4%)	38 (16.5%)	0.75
ARB	228 (6.3%)	55 (24.1%)	0.999
Calcium channel blocker	254 (7.0%)	33 (13.0%)	0.27

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Tetali et al. Poster Presentation: Pilot Study to Evaluate Effect of Antihypertensive Therapy on the Rates of Clinical Events in Patients with Vascular Ehlers-Danlos Syndrome. Society for Vascular Medicine 2019 Annual Scientific Sessions, May 30, 2019

ACER-001: Overview

Mechanism of Action

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

Disease Overview

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

Product Profile

- **A taste-masked, immediate release formulation of sodium phenylbutyrate**
- **UCDs**: Will conduct a PK/BE study to show bioequivalence to Buphenyl
- **MSUD**: POC study suggests ~60% of patients have 30% reduction in Leucine

The Opportunity

- **Anticipate NDA submission for UCD mid-2020***
- **UCDs**: >2,000 patients in the U.S.; ~600 patients treated with sodium / glycerol phenylbutyrate
- **MSUD**: ~800 eligible patients in the U.S.
- Advantageous orphan pricing with robust program to support patient access and reimbursement

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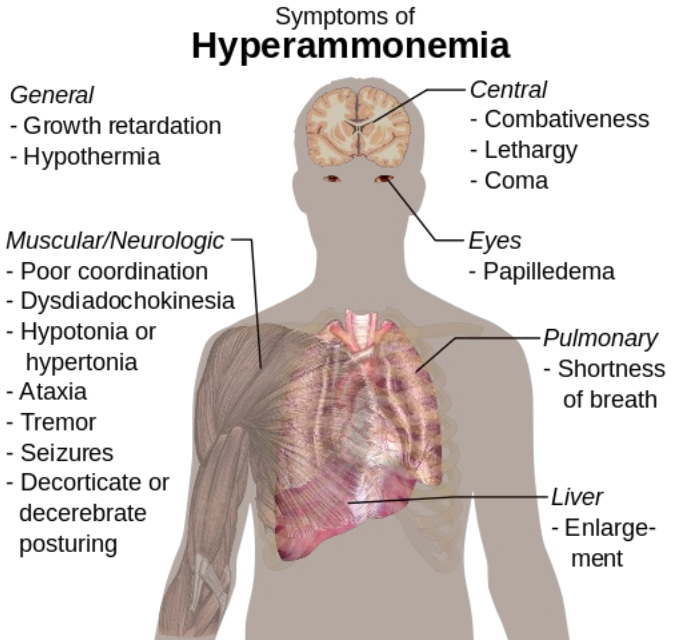
* Assumes Acer NDA submission with 6 months drug product stability data

UCDs: Clinical Manifestations

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



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: Unmet Need

- **Buphenyl®**: Foul odor and foul/bitter taste; considered unpalatable*
  - 64% of patients reported it is difficult to take because of taste
  - Physicians reported that 25-33% of patients were prescribed less than target dose due to tolerability
  - Only 25% of patients indicated that they never miss a dose
  - 46% of patients reported taste as the reason for discontinuation*
- **Ravicti®**: Tasteless/Odorless
  - Pricing has risen to levels considered challenging
  - Reports of difficult access, unaffordability, and forced switches back to sodium phenylbutyrate (NaPB)
    - For example: Buphenyl® and Ravicti® both recently removed from CVS/Caremark formulary for JPMorgan Chase plan members, effective 8/1/2019**
  - Patient groups and physicians have called for a taste-masked, affordable and accessible treatment***

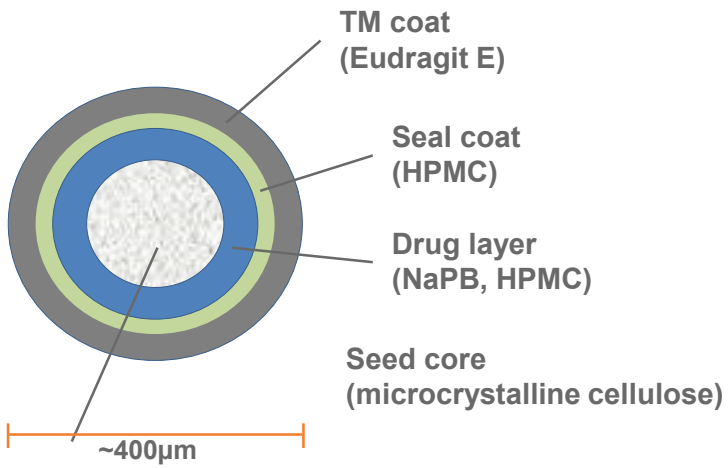
* Shchelochkov et al., Barriers to drug adherence in the treatment of urea cycle disorders: Assessment of patient, caregiver, and provider perspectives. Molecular Genetics and Metabolism Reports 8 (2016) 43-47.

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

*** Acer Market Research

ACER-001: Taste-masked, IR Formulation

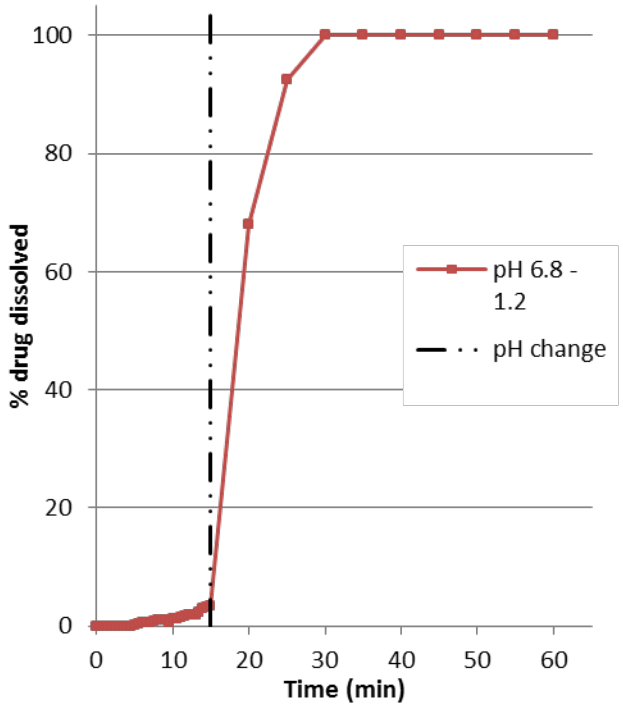
Drug Layered Core



Expected drug loading maximum ~50%

% drug dissolved Time (min) pH 6.8 – 1.2 pH change
0 10 20 30 40 50 60 80 100

Mouth → Stomach



Protection for several minutes at mouth pH followed by rapid release at stomach pH

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ACER-001: Differentiation

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

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* Subject to FDA Approval
** Molecular Genetics & Metabolism Reports 8 (2016) 43-47
*** Ravicti & Buphenyl pppy is based on patient weight and WAC price

UCDs: Clinical & Regulatory Path

- ACER-001 IND: active as of May 31st, 2019
- Pivotal bridging trial: initiation expected Q4 2019
  - Stage 1: comparison of three formulations of ACER-001 in healthy adult subjects to select optimal formulation
  - Stage 2: single-dose, fasting, comparative bioequivalence study in healthy adult subjects to establish the bioequivalence of ACER-001 to sodium phenylbutyrate
  - Up to 64 healthy volunteers
  - Multiple-day trial
  - 1 dose of sodium phenylbutyrate, 1 dose of ACER-001
- Taste assessment trial: initiation expected Q4 2019
  - Comparing ACER-001 to sodium phenylbutyrate in healthy subjects
- NDA: anticipate submitting mid-2020* pending successful outcome of bridging trials and Type C Meeting with FDA

* Assumes Acer NDA submission with 6 months drug product stability data

UCDs: Market Opportunity

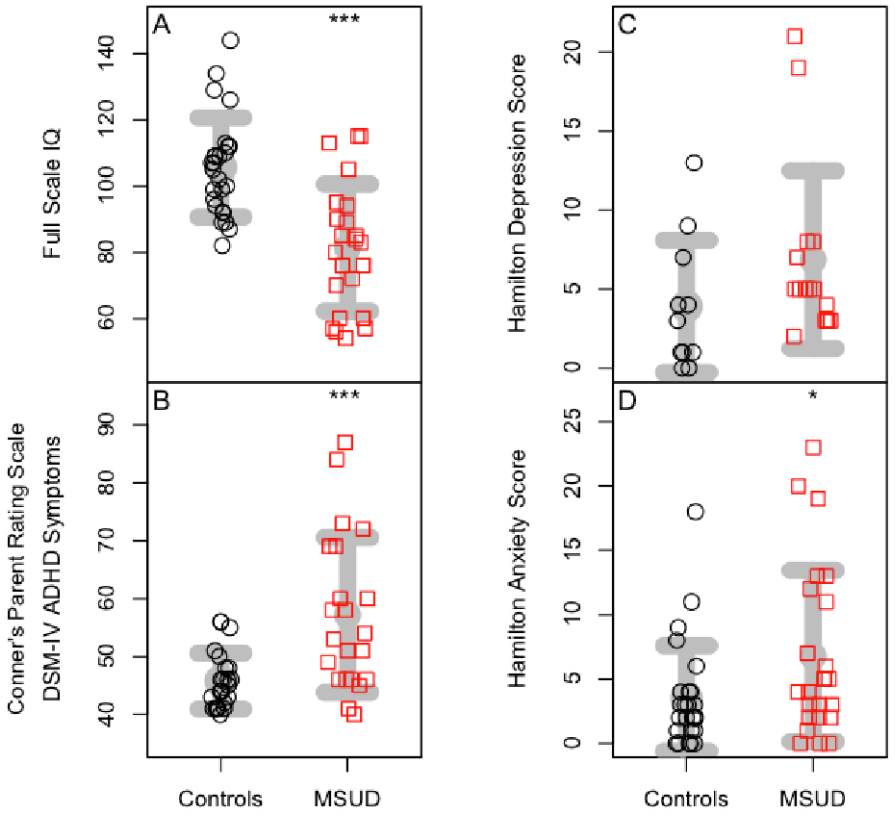
- Target existing Rx market share in UCDs
  - Currently 1,100 patients diagnosed with ~600 patients on Rx therapy*
  - 2018 U.S. Revenue for Ravicti® & Buphenyl® = $248.4M
  - Goal: transition patients from Ravicti® & Buphenyl® to ACER-001 and capture a portion of new UCD Rx

- "Transition" Value Story: A cost-effective, taste masked alternative for UCDs (assuming successful studies and FDA approval):
  - Bioequivalence to sodium phenylbutyrate
  - Greater compliance/adherence compared to Buphenyl® expected due to differentiated formulation providing taste masked alternative
  - Competitively priced vs Ravicti®
  - Payer engagement strategy to support switching

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

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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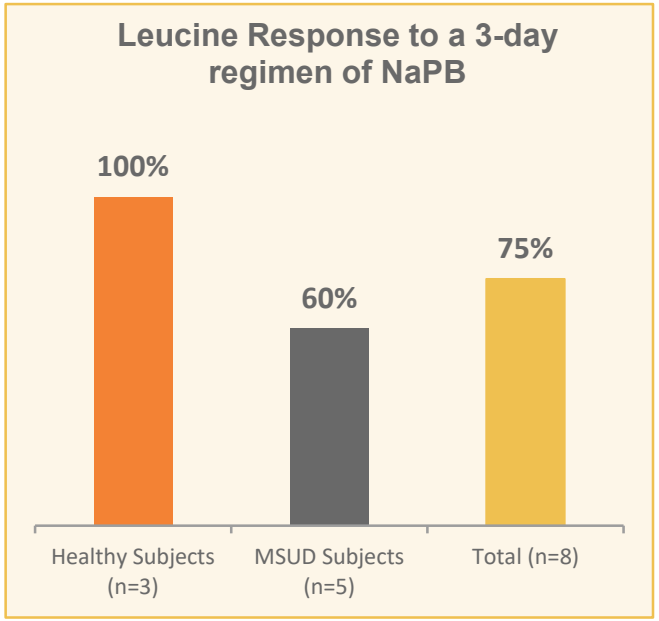
* Muelly 2011 Neuropsychiatric and Neurochemical Sequelae of MSUD.

MSUD: Clinical POC Study

- Design: Open label pilot study[1] at BCM – 3 healthy and 5 MSUD subjects with late onset disease
  - 3 days of steady-state protein diet*; then 3 days of NaPB + diet*
  - BCAAs and BCKAs determined at day 3 of each study period (4 time points)
- Results: NaPB demonstrated statistically significant leucine reduction in all 3 healthy subjects ($p < 0.05$) and 3 out of 5 MSUD patients ($p < 0.05$ in responders)
  - ~30% reduction (28-34%) in leucine in MSUD responders
  - Clinicians view >20-30% ↓ as clinically meaningful**
- Comments: Despite the short treatment duration (3 days) NaPB showed statistically significant (intra-subject) reduction in leucine in 75% of the subjects



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

[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
- ACER-001 granted U.S. Orphan Drug status by FDA
- 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**
- ACER-001 taste masked formulation may provide much needed treatment option
- Anticipate initiating Phase 2 trial in MSUD mid-2020, subject to additional capital

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* Molecular Genetics and Metabolism Reports 15 (2018)
** Acer Therapeutics: US Market Research – 2014

ACER-001: Exclusivity / IP

- Filed formulation and method of use patent application (filed Oct. 2016)
- Issued patents (US/EP): “Methods of modulation of branched chain acids and uses thereof” [US PATENT NO. 10,092,532]
  - Exclusive license rights from Baylor College of Medicine
- UCDs: 505(b)(2) application: 3 years market exclusivity from FDA approval (pending feedback from Type C Meeting)
- MSUD: Granted U.S. Orphan Drug Designation: 7 years market exclusivity from FDA approval
- Pediatric exclusivity: +6 months added (if pediatric indication study approved)

Osanetant: Overview

Mechanism of Action

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

Disease Overview

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

Product Profile

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

The Opportunity

- **Acer licensed worldwide rights to osanetant from Sanofi in January 2019**
- Anticipate submitting IND in Q4 2019
- Multiple potential orphan opportunities
- Little competition in iVMS space

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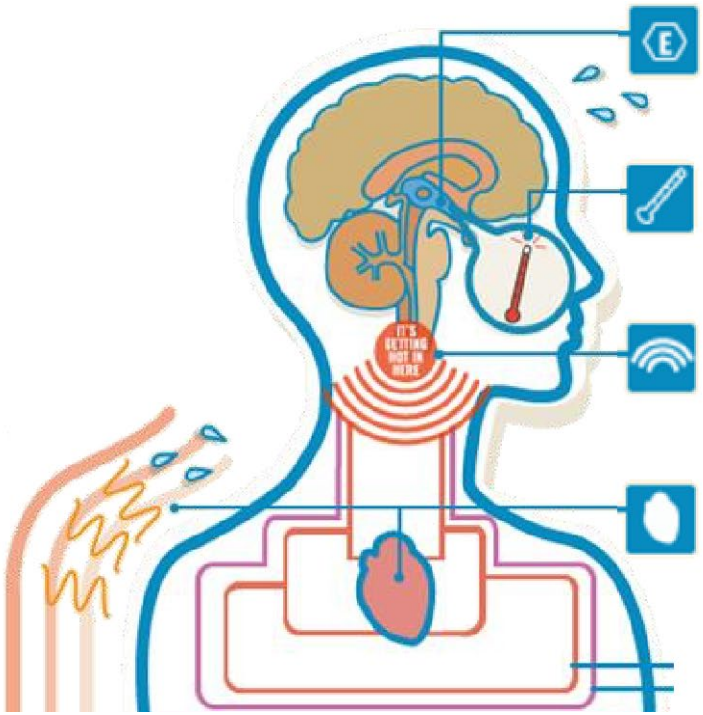
* Am J Psychiatry. 2004 Jun;161(6):975-84.

History

- Acer acquired worldwide rights to osanetant from Sanofi in January 2019
- Osanetant (SR142801) was the first selective non-peptide tachykinin NK3 receptor antagonist evaluated as a potential treatment for schizophrenia
- Clinical and laboratory safety results are available from 21 completed Phase 1 and 2 studies in which 325 healthy subjects and 665 schizophrenic patients were treated with osanetant
- No major safety concerns identified from these studies after single-dose and repeated-dose administration of up to 400 mg QD for up to 21 days, and 200 mg QD for up to 6 weeks
- In March 2005, Sanofi-Aventis discontinued the development of osanetant citing 'lack of efficacy compared with placebo' in this indication as a major reason for this decision

Vasomotor Symptoms (VMS): Overview

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



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

↓

This confuses the hypothalamus and makes it read "too hot"

↓

The brain responds by relaying an alert to cool off

↓

The body then tries to cool off by beginning to perspire

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

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 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]

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 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]

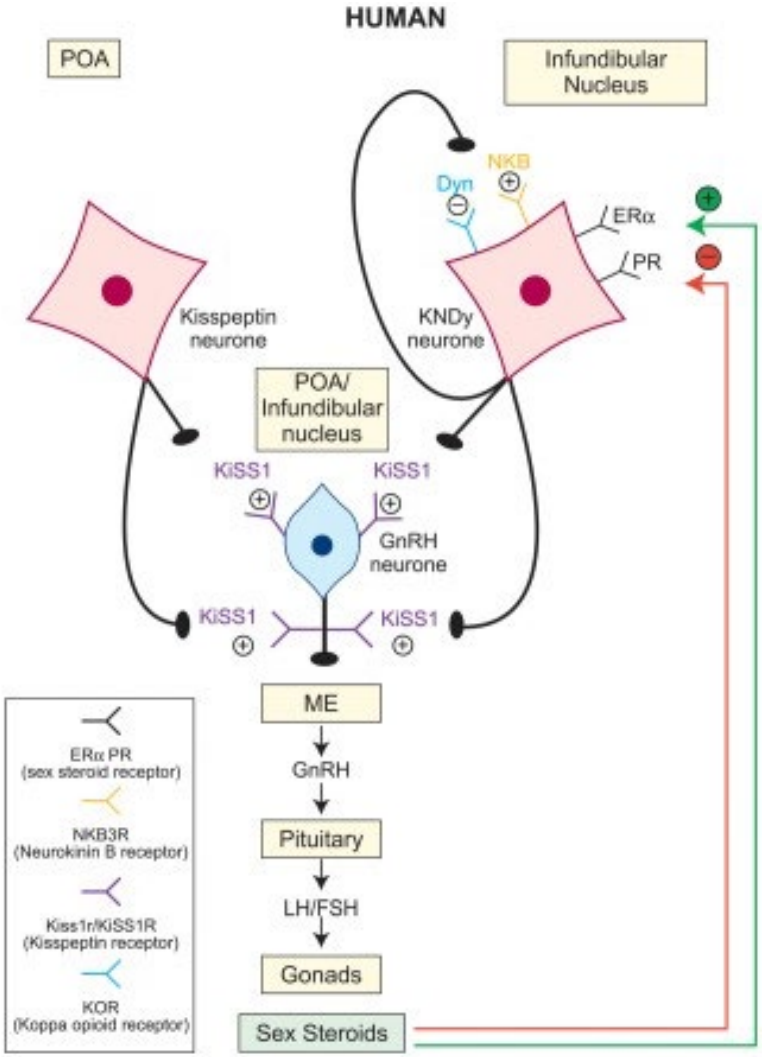
1 Moon, Z. et al., JOURNAL OF PSYCHOSOMATIC OBSTETRICS & GYNECOLOGY, 2017 VOL. 38, NO. 3, 226–235
2 Nichols, H, et al., JNCI J Natl Cancer Inst, 2015, 1–8
3 Challapalli, A, et al., Clinical and Translational Radiation Oncology 10 (2018) 29–35
4 Abildgaard, J, et al., JNCI Cancer Spectrum, 2018, Vol. 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

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

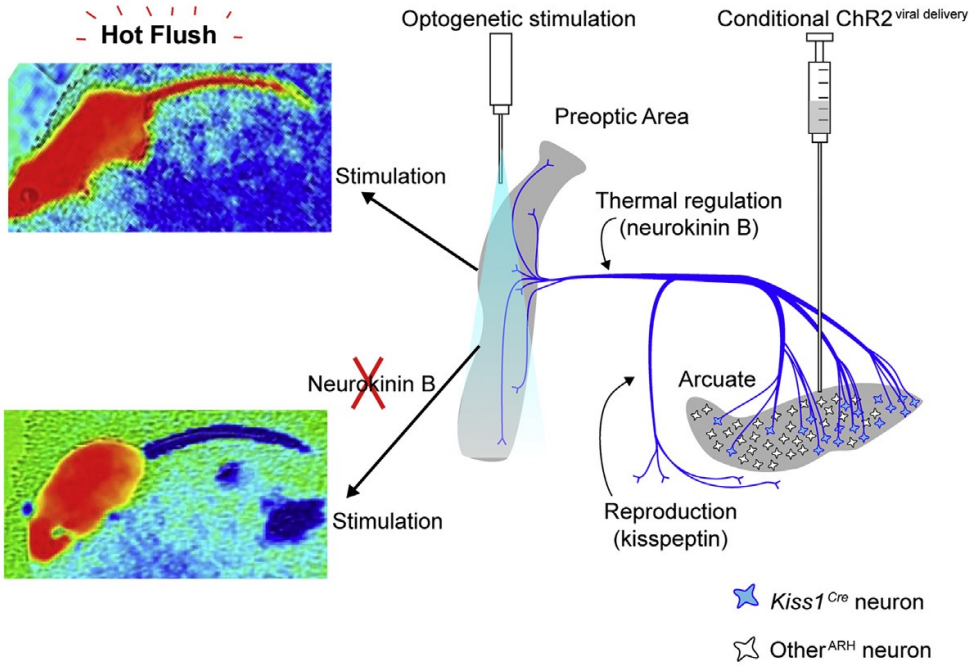
NK3 Receptor (Neurokinin B)

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



VMS: Mechanism of Action

- Neurons in the arcuate nucleus of the hypothalamus that express kisspeptin and neurokinin B (Kiss1ARH neurons) are candidates for mediating hot flushes because they are negatively regulated by sex hormones
- Transient activation of Kiss1ARH neurons following sex-hormone withdrawal contributes to the occurrence of hot flushes via NkB release in the rostral preoptic area

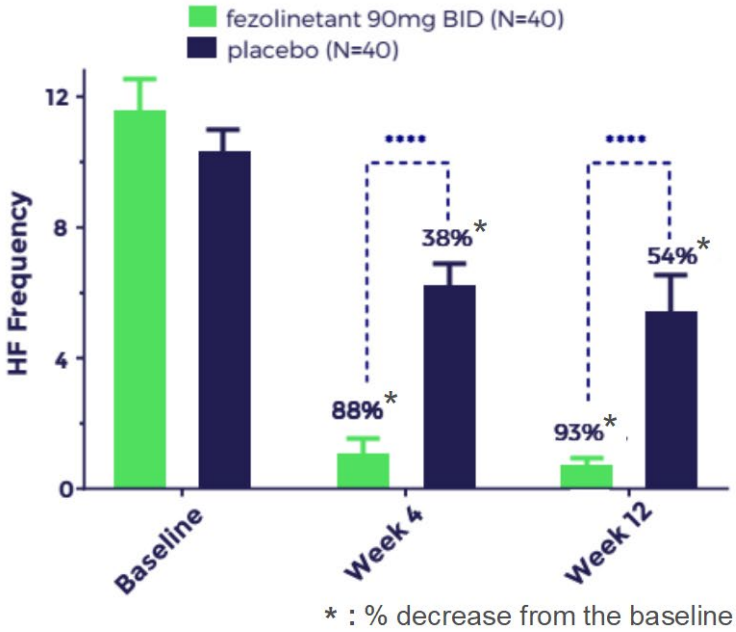


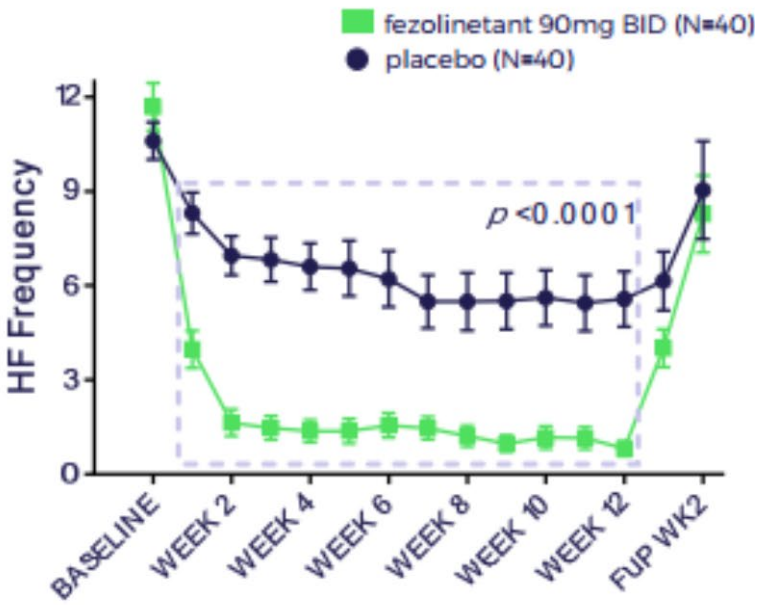
Padilla, S. et al. A Neural Circuit Underlying the Generation of Hot Flushes. Cell Reports 2018, 24, 271–277.

NK3R Antagonist Clinical POC in VMS

- Fezolinetant is a NK3R antagonist being developed by Astellas

Average Daily Hot Flash Frequency Reported as per FDA Guidance





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

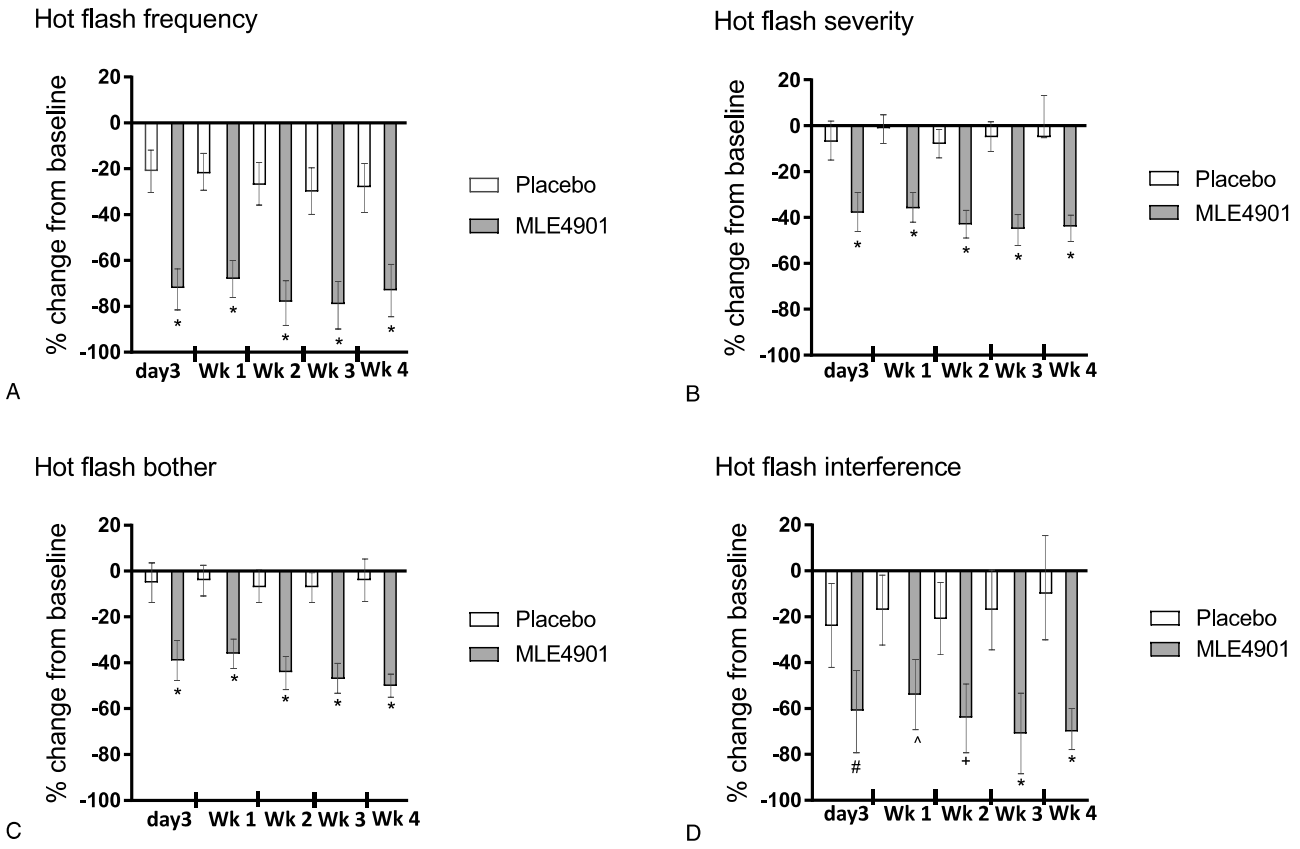

FIG. 2. Hot flash frequency (A), severity (B), bother (C), and interference (D) outcomes: results are presented as percentage change with 95% CIs from baseline at each time point during the treatment period (ie, on day 3 of treatment, and then weekly mean total for each week (wk) of the 4-week treatment 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 a leading university to design & conduct a clinical trial to evaluate osanetant in various patient populations with iVMS

- These include patients with medically or surgically iVMS (may include any/all of the following):
  - Women with HR+ Breast Cancer receiving tamoxifen
  - Men with HR+ Prostate Cancer receiving leuprolide
  - Women who are BRCA+ and have had a prophylactic bilateral oophorectomy

- This initial Phase 1/2 trial would evaluate:
  - PK/PD and Safety, including physiologic PD
  - Identify the optimal dosing strategy to advance into further efficacy studies in minimizing the iVMS symptoms

Competitive Landscape

Program / Company	Indication	MOA	Status
VERU-944 **(Veru)**	iVMS in PC on ADT	ER agonist	Ph 2
Q-122 **(Que Oncology)**	iVMS in BC on Tamoxifen or AIs	CRCX4 modulator	Ph 2
Fezolinetant **(Astellas)**	VMS – Menopause	NK3R antagonist	Ph 3
NT-814 **(KaNDy Therapeutics)**	VMS – Menopause	NK1/3R antagonist	Ph 2
FP-101 **(Fervent Pharma)**	VMS in postmenopausal	Undisclosed Non-Hormonal Therapy	Ph 2
MT-8554 **(Mitsubishi Tanabe)**	VMS	Undisclosed Non-Hormonal Therapy	Ph 2
PH80-HF **(Pherin Pharma)**	VMS	Undisclosed	Ph 2
Donesta **(Mithra)**	VMS	Native estrogen	Ph 2
AUS-131 **(Ausio Pharma)**	VMS	ERβ agonist	Ph 2

Market Opportunity and IP

- Acer acquired worldwide rights to osanetant from Sanofi in January 2019
- Data from clinical proof of concept studies with other NK3R antagonists suggest rapid and potentially clinically meaningful improvement in vasomotor symptoms
  - Ogeda SA was acquired by Astellas in 2017 for up to €800M
- Clinical and laboratory safety results are available from 21 completed Phase 1 and 2 studies in which 325 healthy subjects and 665 schizophrenic patients were treated with osanetant
- Osanetant would be a New Chemical Entity (NCE) in the US, and as such would be eligible for five years' market exclusivity from potential FDA approval
- Additional exclusivity (e.g. Orphan Drug Designation) will depend upon indication(s) and development pathway chosen
- Anticipate IND submission in Q4 2019
- Initiation of Phase 1/2 trial anticipated mid-2020, subject to additional capital

Financial Overview

- Cash:
  - $23.5M as of June 30, 2019
  - Expected to have sufficient capital through end of 2020
- Capitalization as of June 30, 2019:
  - 10.1M shares of common stock outstanding
  - 11.1M shares of common stock fully diluted
- $87M invested through August 2018

ACER

Summary

- Acer's pipeline includes three clinical-stage product candidates:
  - **EDSIVO™ (celiprolol)** for the treatment of vascular Ehlers-Danlos syndrome (vEDS) in patients with a confirmed type III collagen (COL3A1) mutation
  - **ACER-001** (a fully taste-masked, immediate release formulation of sodium phenylbutyrate) for the treatment of various inborn errors of metabolism, including urea cycle disorders (UCDs) and Maple Syrup Urine Disease (MSUD)
  - **Osanetant** for the treatment of induced Vasomotor Symptoms (iVMS) where Hormone Replacement Therapy (HRT) is likely contraindicated
- Acer's 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
  - Accelerated paths for development through specific FDA-established programs
- Multiple anticipated key regulatory milestones:
  - EDSIVO™ Type A mtg w/FDA: **Q3 2019**
  - ACER-001 (UCD) pivotal bridging & taste assessment trials initiation: **Q4 2019**
  - Osanetant IND submission: **Q4 2019**
  - ACER-001 (UCD) NDA submission*: **Mid-2020**
  - Osanetant Phase 1/2 PK/PD/safety trial initiation**: **Mid-2020**
- Expected to have sufficient capital through end of 2020

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* Assuming successful outcomes in bridging trials and NDA submission with 6 months stability data
** Subject to additional capital