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

Pipeline Update
July 31, 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 ACER-001, osanetant and EDSIVO™ (celiprolol) 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.
<table>
<thead>
<tr>
<th>Time</th>
<th>Agenda Item</th>
<th>Presenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:00am to 11:05am</td>
<td>Introduction &amp; Corporate Update</td>
<td>Chris Schelling</td>
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<td></td>
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<td>CEO &amp; Founder</td>
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<tr>
<td>11:05am to 11:30am</td>
<td>ACER-001 Overview</td>
<td>Will Andrews, MD</td>
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<td>Chief Medical Officer</td>
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<tr>
<td>11:30am to 11:50am</td>
<td>Osanetant Overview</td>
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<td>11:50am to 12:00pm</td>
<td>EDSIVO™ Update</td>
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<tr>
<td>12:00pm to 12:30pm</td>
<td>Q &amp; A</td>
<td>All</td>
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Corporate Update

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.

- On June 24th, received Complete Response Letter (CRL) on EDSIVO™
  - Acer is currently engaging with FDA

- Headcount reduced to 19 to conserve resources

- Several key milestones over next 12 months on pipeline products

- Cash: Expected to have sufficient capital through end of 2020
## Clinical Pipeline

<table>
<thead>
<tr>
<th>Program / Indication</th>
<th>Novel MOA / Unique Characteristics</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>NDA</th>
<th>Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACER-001 (reformulated sodium phenylbutyrate)</td>
<td>Taste-masked formulation; evaluating comparability to Buphenyl®</td>
<td></td>
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</tr>
<tr>
<td>Urea Cycle Disorders (UCD)</td>
<td>Inhibition of BCKD kinase to increase BCAA metabolism</td>
<td></td>
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<tr>
<td>Maple Syrup Urine Disease (MSUD)</td>
<td>Neurokinin 3 Receptor Antagonist</td>
<td></td>
<td></td>
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<tr>
<td>Osanetant</td>
<td>Induces vascular dilatation and smooth muscle relaxation</td>
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</table>

* CRL received 6/24/19; response underway
Overview

Indications

- **UCDs**: Urea Cycle Disorders
- **MSUD**: Maple Syrup Urine Disease

Mechanism of Action

- **UCDs**: Phenylbutyrate is a prodrug of Phenylacetate $\rightarrow$ a nitrogen scavenger
- **MSUD**: Phenylbutyrate is the active moiety $\rightarrow$ an allosteric inhibitor of BCKD kinase

Product Profile

- **ACER-001**: A taste-masked, immediate release multi-particulate dosage form of sodium phenylbutyrate

The Opportunity

- **Worldwide rights to ACER-001**
- **UCDs**: ~600 patients treated with sodium / glycerol phenylbutyrate in the U.S.
- **MSUD**: ~800 eligible patients in the U.S.
Urea Cycle Disorders (UCDs)

- Urea cycle disorders are a group of rare, genetic disorders caused by mutations that result in a deficiency of one of the six enzymes in the urea cycle.
- These enzymes are responsible for removing ammonia from the bloodstream.

A healthy urea cycle converts ammonia into urea, which is excreted from the body.

With a Urea Cycle Disorder (UCD), ammonia is not converted to urea, and ammonia builds up in the body.
• 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.

No matter how mild the disease, a hyperammonemic crisis can be precipitated by stressors and become a life-threatening event at any age and in any situation in life.

During acute encephalopathy, ammonia levels are typically above 200 μmol/L and often above 500-1,000 μmol/L:
- >100 μmol/L – an individual becomes symptomatic
- 200 to 400 μmol/L – in stage 2 coma
- > 500 μmol/L – in stage 3 to 4 coma

UCDs: Medical Management

- Chronic treatment options for UCDs include:
  - Restricted Diet
  - Liver Transplantation
  - Carbaglu (for treatment of NAGS only)
  - **Phenylbutyrate (Buphenyl®, Ravicti®)**

<table>
<thead>
<tr>
<th>DIFFERENTIATION</th>
<th>Sodium phenylbutyrate</th>
<th>Glycerol phenylbutyrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Powder / Tablets</td>
<td>Foul odor and bitter taste; Considered unpalatable*</td>
<td>Tasteless, odorless</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liquid (oil)</td>
</tr>
</tbody>
</table>

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

- Alternative pathway treatment diverts nitrogen from the urea cycle to alternative routes of excretion
- Both Ravicti and Buphennyl are prodrugs of phenylacetate (PAA)
- **PAA is the active moiety** – it combines with glutamine, producing phenylacetylglutamine
- Phenylacetylglutamine is excreted by the kidneys

![Metabolizing pathway and mechanism of action of GPB. GPB (glycerol phenylbutyrate); PAA (phenylacetic acid); PBA (phenylbutyric acid); PAGN (phenylacetylglutamine).](image-url)
UCDs: Unmet Need

• **Buphenyl®**: Foul odor and foul/bitter taste; consider 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 NaPB
  • Patient groups and physicians have called for a taste-masked, affordable and accessible treatment**

**Acer Market Research
ACER-001: Taste-masked, IR Formulation

Drug Layered Core

- TM coat (Eudragit E)
- Seal coat (HPMC)
- Drug layer (NaPB, HPMC)
- Seed core (microcrystalline cellulose)

Expected drug loading maximum ~50%

~400µm

Mouth → Stomach

Excellent protection for several minutes at mouth pH followed by rapid release at stomach pH

% drug dissolved vs Time (min)

pH 6.8 - 1.2

pH change
## Phenylbutyrate Formulations

<table>
<thead>
<tr>
<th></th>
<th>ACER-001*</th>
<th>RAVICTI®</th>
<th>BUPHENYL®</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy/Safety in UCDs</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Palatability / Compliance</strong></td>
<td>✓</td>
<td>✓</td>
<td>✘ **</td>
</tr>
<tr>
<td><strong>Pricing</strong></td>
<td>TBD, likely near BUPHENYL pppy</td>
<td>$158k-$1.2M**</td>
<td>$204k-$402k***</td>
</tr>
<tr>
<td><strong>Formulation</strong></td>
<td>Multi-Particulate Beads (Sachet)</td>
<td>Oil (Tablespoons)</td>
<td>Powder/Tablets (up to 40 tablets/day)</td>
</tr>
<tr>
<td><strong>Indication all ages</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

*Subject to FDA Approval
**Molecular Genetics & Metabolism Reports 8 (2016) 43-47
***Ravicti & Buphenyl pppy is based on patient weight and WAC price
ACER-001: Clinical Development Plan (UCD)

• **Clinical Bioequivalence (BE) Study**
  • In healthy volunteers
  • Compared to Buphenyl®
  • Include males and females under appropriate fed and fasting conditions
  • Expected to be adequate to support an NDA filing planned in mid-2020 (pending feedback from Type C Meeting)

• **Clinical Taste Studies**
  • To define potential taste preference/superiority to Buphenyl®
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: switch patients from Ravicti® & Buphenyl® to ACER-001 and capture a portion of new UCD Rx

- “Switch” Value Story: A cost-effective, taste masked alternative for UCDs (Assuming successful studies and FDA approval):
  - Bioequivalence to Buphenyl®
  - Greater compliance/adherence compared to Buphenyl® 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
# Competitive Landscape

<table>
<thead>
<tr>
<th>Program / Company</th>
<th>Indication</th>
<th>Admin.</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ravicti Horizon</td>
<td>UCD (CPS1, OTC, ASS, ASL, ARG, HHH)</td>
<td>Oral liquid</td>
<td>Market</td>
</tr>
<tr>
<td>Buphenyl Horizon</td>
<td>UCD (CPS1, OTC, ASS)</td>
<td>Oral powder &amp; Tablet</td>
<td>Market</td>
</tr>
<tr>
<td>Generic NaPB</td>
<td>UCD (CPS1, OTC, ASS)</td>
<td>Oral powder &amp; Tablet</td>
<td>Market</td>
</tr>
<tr>
<td>Multiple</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ammonul Valeant</td>
<td>Acute Hyperammonemia</td>
<td>Injection</td>
<td>Market</td>
</tr>
<tr>
<td>Carbaglu Recordati</td>
<td>NAGS Deficiency</td>
<td>Oral Tablet (for Suspension)</td>
<td>Market</td>
</tr>
<tr>
<td>AEB1102 Aeglea</td>
<td>Arginase I Deficiency</td>
<td>Infusion</td>
<td>Ph 3</td>
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<tr>
<td>Hepastem Promethera</td>
<td>UCD</td>
<td>Infusion</td>
<td>Ph 2</td>
</tr>
<tr>
<td>KB-195 Kaleido</td>
<td>UCD</td>
<td>Oral prebiotic</td>
<td>Ph 2</td>
</tr>
<tr>
<td>SYNB-1020 Synlogic</td>
<td>UCD</td>
<td>Oral</td>
<td>Ph 1</td>
</tr>
</tbody>
</table>

Source: product package inserts and public information
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)

* Muelly 2011 Neuropsychiatric and Neurochemical Sequelae of MSUD.
Acute metabolic decompensation is precipitated by a stressor such as:
- Infection, injury, surgery, hormonal changes, or significant dietary changes (involving increased protein intake)

Signs and symptoms:
- Brain edema
- Ataxia (unsteady, clumsy movements)
- Acute dystonia (involuntary muscle contractions)
- Mood swings, nausea, vomiting, anorexia, and hallucinations
- Altered level of consciousness
- Stroke, coma, and death
MSUD: Medical Management

- Management of metabolic decompensation
  - Stop protein intake
  - Remove accumulating BCAA by dialysis
  - IV non-protein/high-calorific fluids to reduce protein catabolism
  - Non-BCAA amino acid preparation to stimulate anabolism and exchange between the free BCAA pool
  - Treat precipitating factor(s)

- Chronic therapeutic options
  - Protein-restricted diet + formula
  - Liver transplantation
• Even if a specialized diet is strictly followed, the risk of metabolic crises still exist

• Patient Registry results:
  • 38% of patients had one of more MSUD symptom
  • 37% reported a mental health disorder, use of anti-anxiety/depressants, or use of ADHD meds
  • 37% were hospitalized in the prior year
  • Plasma leucine levels varied widely (57% with levels > 308 μmol/L)

• “Difficulty with maintenance of therapeutic plasma leucine levels was seen even in those who follow diet all of the time, reflecting the difficulties in managing MSUD. Despite treatment, there was a high rate of hospitalizations, MSUD symptoms, comorbid neuropsychological symptoms, and skin conditions.”

**NaPB: Off-Target Effect on BCAA Levels**

- Clinical observation: sodium phenylbutyrate (NaPB) reduced branched-chain amino acids (BCAAs), but not other essential amino acids, in patients with urea cycle disorders (UCD).

- Initial investigation focused on whether BCAA supplementation is required for UCD patients for optimal metabolic outcomes.

- Burrage et al. analyzed BCAA levels from 553 patients.
  - Table 2 depicts a statistically significant reduction in BCAAs levels.

- BCM and collaborators investigated this observation further by elucidation of the mechanism of action of NaPB in preclinical models and then in the MSUD clinical proof-of-concept study.

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**Table 2**

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>NaPBA (μMol/L)</th>
<th>No NaPBA (μMol/L)</th>
<th>p_corrected_value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucine</td>
<td>60 (40–85)</td>
<td>95 (72–121)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Valine</td>
<td>128 (92–169)</td>
<td>176 (142–217)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>31 (22–49)</td>
<td>49 (36–65)</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

Retrospective study of leucine levels in 5 UCD patients treated with NaPB.

Retrospective study of BCAA levels in 533 UCD patients treated with NaPB or without.

NaPB: Mechanism of Action

- BCM and collaborators demonstrated that NaPB allosterically-inhibits the BCKDC kinase responsible for phosphorylating (deactivating) the BCKDC.

- Thus, NaPB enhances metabolism of BCAAs and Branched-chain Ketoacids (BCKAs) via a novel mechanism:\(^1\):
  - NaPB targets protein phosphorylation, which regulates BCKDC.
  - Decreases protein phosphorylation of E1\(\alpha\):
    - Phosphorylated form of E1\(\alpha\) is significantly reduced in NaPB treated mice (3 days, oral) vs placebo group.
    - Increases enzymatic activity of BCKDC.
  - Phenylbutyrate is the active moiety, therefore requires high cmax of phenylbutyrate.


**Phenylbutyrate Placebo #1 #2 #3 Phospho-E1\(\alpha\) E2 Tubulin**

Western blot analysis of liver extract.
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

*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
• Pivotal studies (MSUD-001 & 002) designed similar to BioMarin’s Kuvan pivotal studies
• Primary endpoint: Leucine (clinical surrogate endpoint)
• sNDA: via 505(b)(2)
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 phenylbutyrate effectiveness, yet tolerability is a concern**

• ACER-001 taste masked formulation provides much needed Rx treatment option

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* Molecular Genetics and Metabolism Reports 15 (2018)
ACER-001: Exclusivity / IP

- Filed formulation and method of use patent application (filed Oct. 2016)

  - 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)
ACER-001: Key Expected Milestones

UCD:

✓ **2Q 2019**: IND Active

- **3Q-4Q 2019**: Type C Meeting with FDA
- **4Q 2019**: Pivotal Taste Assessment Study
- **4Q 2019**: Pivotal Bridging (Bioequivalence) Study
- **Mid-2020**: Submit NDA (assumes submission on 6-month stability data)

MSUD:

- **Mid-2020**: Initiate Phase 2 Trial in MSUD (subject to additional capital)
**Overview**

- **Indications**
  - **iVMS**: Induced Vasomotor Symptoms where Hormone Replacement Therapy is Likely Contraindicated

- **Mechanism of Action**
  - **NK3R antagonists**: block the neurokinin 3 receptor, which is the main receptor for neurokinin B (NKB), a tachykinin peptide primarily found in the arcuate nucleus (ARC) of the hypothalamus

- **Product Profile**
  - **Osanetant**: A selective, non-peptide tachykinin NK3 receptor antagonist

- **The Opportunity**
  - **Worldwide rights to osanetant**
  - Potential large orphan opportunities
  - Little competition in iVMS indications
• 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 I and II studies of whom 325 healthy subjects and 665 patients were treated with osanetant

• Data from these studies demonstrated no major safety concerns 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' as a major reason for this decision
Vasomotor Symptoms (VMS)

• Hot flashes, flushing, night sweats are known as Vasomotor symptoms (VMS), and most often occurs in women who are entering/in menopause

• VMS are causally related to decreasing estradiol concentrations, mainly in the serum and subsequently also in the hypothalamic temperature regulating center

• The lack of estrogens alters neurotransmitter activity, especially in the serotonergic and noradrenergic pathways

• Because sex steroids act as potent neuromodulators, the substitution of ovarian sex steroids by hormone replacement therapy (HRT) is the most effective treatment option for VMS

• While VMS associated with menopause can be often be treated with HRT, there are patients who experience VMS who are not in menopause, and for whom HRT is likely contraindicated
### 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\(^6\)

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VMS with Selective Estrogen Receptor Modulators

- Hormone receptor-positive breast cancers (70%) are treated with hormone therapy drugs
  - Tamoxifen is a selective estrogen receptor modulator (SERM)
    - Most widely prescribed product in this category
- Tamoxifen lowers the risk of breast cancer recurrence, breast cancer in the opposite breast and death from breast cancer
  - Cuts risk of both invasive and non-invasive breast cancer by 50%\(^1\)
  - Used in up to 40% of patients (~2.1m Rx written a year)\(^2-3\)
- Severe but non-life threatening adverse effects, such as VMS, have an important influence on a woman’s decision to start and stay on therapy
  - Hot flashes are reported in up to 80% of women taking tamoxifen\(^4\)
  - Systematic review of 30 studies demonstrated poor adherence at the end of 5 years of treatment\(^5\)
    - Adherence: 41%-72%
    - Discontinuation: 31-73%

Non-adherence with hormonal therapy can be associated with a higher risk of mortality and shorter time to recurrence of breast cancer

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\(^1\) Lin, J et al., Cancer Prev Res 2011; 4: 1360-1365
\(^2\) Symphony Prescription Data 2016
\(^3\) Clincal.com: The Top 300 Drug List 2016
VMS with ADT (Leuprolide)

- Purpose of ADT is to decrease testosterone levels
  - Typically used for high-risk localized and advanced prostate cancer

- Typical time on therapy is disease dependent
  - 4-6 months for Intermediate risk cancer
  - 2-3 years for high-risk localized prostate cancer

- Hot flashes are one of the most common and debilitating side effects of ADT therapies
  - Occurs in up to 80% of men treated with ADT (leuprolide)\(^1-3\)
    - 30%-40% having moderate to severe hot flashes\(^1-3\)
    - Symptoms do not subside over time
      - 50% of men at 5 years and at 8 years still suffer from hot flashes\(^1-3\)

Concerns over hot flashes make patients less likely to begin ADT and can lead to non-compliance with their hormonal therapy

1 Gomella LG et al BJU Int S1:25-29 2007
3 Gonzalez BD et al J Urol 194:690-695 2015
VMS with BRCA 1/2 Mutations & Oophorectomy

• Having a BRCA1 or BRCA2 mutation increases a woman’s risk for developing breast and ovarian cancer
  • Lifetime risk of developing breast cancer between 45-65%
  • Lifetime risk of developing ovarian cancer 10-70%
  • PBSO is recommended for all BRCA 1/2 mutation carriers by 35-40 years of age or after childbearing is complete
  • Uptake of prophylactic oophorectomy is estimated at nearly 60%

• Procedures surgically induce abrupt menopause
  • Vasomotor symptoms (hot flashes) show up almost immediately and tend to be more severe

• Typical hormone replace therapy is likely contraindicated for any breast cancer patient with cancer that is estrogen receptor positive (BRCA2)

PBSO will induce menopause, leading to VMS. The symptoms can be severe and impact on a women’s quality of life, as there are few non-hormonal treatment options available.

3 Staley A et al., MDEdge Gynecologic Oncology Consult: Managing Menopausal Symptoms After Risk-Reducing Salpingo-Oophorectomy, 2015
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.
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: Overview

• Vasomotor symptoms, 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
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.

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
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 $n = 37$. *$P < 0.0001$, $^aP = 0.0006$, $^bP = 0.0011$, $^cP = 0.0001$. Week 4 data adapted from Prague et al, *Lancet*, 2017."
Acer is partnering with a leading university to design & conduct a clinical study 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 study 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
## iVMS: Market Opportunity

<table>
<thead>
<tr>
<th>Population Attribute</th>
<th>Women with HR+ Breast Cancer (CaB) receiving Tamoxifen</th>
<th>Men with HR+ Prostate Cancer (CaP) receiving Lupron</th>
<th>Women who are BRCA+ and have prophylactic bilateral oophorectomy (PBSO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated Number of Patients</td>
<td>TBD&lt;sup&gt;1&lt;/sup&gt;</td>
<td>TBD&lt;sup&gt;1&lt;/sup&gt;</td>
<td>TBD&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diagnosed/Treated: May 2018-April 2019</td>
<td></td>
<td></td>
<td>Currently working with IQVIA</td>
</tr>
<tr>
<td>Therapy Indication</td>
<td>Hormone drug used to treat and prevent hormone receptor-positive breast cancers&lt;sup&gt;2&lt;/sup&gt;</td>
<td>ADT to decrease testosterone levels in high-risk localized and advanced prostate cancer&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Surgery recommended between ages of 35-40 or after childbearing completion&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Typical therapy use is 5-10 years&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Typical therapy use is 1-6 months in combination with other treatments&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Clinical Benefits</td>
<td>50% reduction in both invasive and non-invasive breast cancers&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Decreased serum testosterone to ≤50 ng/dL from week 4 through week 48 in an estimated 94% of patients&lt;sup&gt;6&lt;/sup&gt;</td>
<td>• 85%-95% reduction in incidence of ovarian cancer&lt;sup&gt;12&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 53-68% reduction in breast cancer&lt;sup&gt;12&lt;/sup&gt;</td>
</tr>
<tr>
<td>iVMS Side Effects</td>
<td>84% experience&lt;sup&gt;7&lt;/sup&gt; 60% severe</td>
<td>80% experience&lt;sup&gt;8&lt;/sup&gt; 30-40% moderate/severe</td>
<td>67% experience&lt;sup&gt;9&lt;/sup&gt;</td>
</tr>
<tr>
<td>HRT Use</td>
<td>Likely contraindicated</td>
<td>Likely contraindicated</td>
<td>Controversial; BRCA2 tend to be estrogen receptor positive</td>
</tr>
<tr>
<td>Compliance &amp; Adherence</td>
<td>• Many chose to never go on therapy due to side effects</td>
<td>Concern over hot flashes make patients less likely to begin ADT and can lead to early discontinuation&lt;sup&gt;11&lt;/sup&gt;</td>
<td>• Nearly 60% of BRCA+ women will elect a prophylactic oophorectomy&lt;sup&gt;13&lt;/sup&gt;.</td>
</tr>
<tr>
<td></td>
<td>• Almost half discontinued by 4.5 years&lt;sup&gt;10&lt;/sup&gt;</td>
<td></td>
<td>• Inducement of menopause is one of the reasons to delay or not have surgery</td>
</tr>
</tbody>
</table>

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# Competitive Landscape

<table>
<thead>
<tr>
<th>Program / Company</th>
<th>Indication</th>
<th>MOA</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VERU-944 (Veru)</strong></td>
<td>iVMS in PC on ADT</td>
<td>ER agonist</td>
<td>Ph 2</td>
</tr>
<tr>
<td><strong>Q-122 (Que Oncology)</strong></td>
<td>iVMS in BC on Tamoxifen or AIs</td>
<td>CRCX4 modulator</td>
<td>Ph 2</td>
</tr>
<tr>
<td><strong>Fezolinetant (Astellas)</strong></td>
<td>VMS – Menopause</td>
<td>NK3R antagonist</td>
<td>Ph 3</td>
</tr>
<tr>
<td><strong>NT-814 (KaNDy Therapeutics)</strong></td>
<td>VMS – Menopause</td>
<td>NK1/3R antagonist</td>
<td>Ph 2</td>
</tr>
<tr>
<td><strong>FP-101 (Fervent Pharma)</strong></td>
<td>VMS in postmenopausal</td>
<td>Undisclosed Non-Hormonal Therapy</td>
<td>Ph 2</td>
</tr>
<tr>
<td><strong>MT-8554 (Mitsubishi Tanabe)</strong></td>
<td>VMS</td>
<td>Undisclosed Non-Hormonal Therapy</td>
<td>Ph 2</td>
</tr>
<tr>
<td><strong>PH80-HF (Pherin Pharma)</strong></td>
<td>VMS</td>
<td>Undisclosed</td>
<td>Ph 2</td>
</tr>
<tr>
<td><strong>Donesta (Mithra)</strong></td>
<td>VMS</td>
<td>Native estrogen</td>
<td>Ph 2</td>
</tr>
<tr>
<td><strong>AUS-131 (Ausio Pharma)</strong></td>
<td>VMS</td>
<td>ERβ agonist</td>
<td>Ph 2</td>
</tr>
</tbody>
</table>
Osanetant will be a New Chemical Entity (NCE) in the US, and as such will be granted five years’ market exclusivity from FDA approval.

Additional exclusivity (e.g. Orphan Drug Designation) will depend upon indication(s) and development pathway chosen for initial development.

We are assessing IP and exclusivity aspects as a part of prioritizing development.

We have options to certain patent and patent applications which give us priority rights to negotiate in-license.

We will refine our strategy as we progress our development plans.
Key Expected Milestones

- **4Q 2019:** Submit IND
- **1H 2020:** Complete CMC Activities
- **Mid-2020:** Initiate Phase 1/2 Clinical Trial in iVMS (subject to additional capital)
• Received CRL from FDA after market close 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 initiative initiated on June 28, 2019 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
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 they do not provide approval 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™
Submit a Type A meeting request, 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.
Acer’s pipeline includes three clinical-stage product candidates:

- **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 various indications with Induced Vasomotor Symptoms (iVMS) where Hormone Replacement Therapy is likely Contraindicated
- **EDSIVO™ (celiprolol)** for the treatment of vascular Ehlers-Danlos syndrome (vEDS) in patients with a confirmed type III collagen (COL3A1) mutation

Multiple key milestones expected over next 12 months:

- **4Q 2019**:
  - Osanetant: Submit IND
  - ACER-001: Initiate UCD Clinical Trials (pending feedback from Type C Meeting)
  - EDSIVO™: Update on CRL
- **Mid-2020**:
  - ACER-001: (UCD) NDA submission (assumes 6-months stability data)
  - Osanetant: Initiate Phase 1/2 Trial (subject to additional capital)

Expected to have sufficient capital through end of 2020