Healthcare

Acer Therapeutics: Deriving Value By Developing Therapies For Rare Diseases

Aug. 31, 2021 6:43 PM ET | **Acer Therapeutics Inc. (ACER)** | HZNP, AYTU, AGLE... | 3 Comments | 2 Likes

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About this article

Ticker	Author rating	Price at publication	Last price	Change since publication	S&P 500
ACER	Buy	$2.66	$2.38	-10.53%	

Summary

- Acer Therapeutics is a pharmaceutical company that acquires, develops and seeks to commercialize therapies for serious, rare, and life-threatening diseases.
- Acer submitted an NDA for its lead drug candidate ACER-001 for treatment of UCDs in early August.
- Acer expects notification regarding potential acceptance for filing from the FDA approximately 60 days after NDA submission and subsequent substantive review. If approved, Acer could launch ACER-001 in mid-2022.
- Other than UCDs, Acer is developing therapies for MSUD, iVMS, vEDS, and infectious diseases. All these diseases have a market that is niche and untapped, characterized by low competition.
- Assuming a base case revenue of $40 million in 2022 and a P/S ratio of 5.0x, the company's intrinsic value would be ~$122 million or $8.70 per share, indicating an upside close to 3.5x.

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Company Overview

Acer Therapeutics (NASDAQ:ACER) is a pharmaceutical company whose goal is to acquire, develop, and commercialize therapies for serious, rare, and life-threatening diseases with substantial unmet medical needs.

The company's current product line includes four programs, namely; ACER-001 (sodium phenylbutyrate) that is being developed for the treatment of disorders such as inborn errors in metabolism, including Urea Cycle Disorders (UCDs) and Maple Syrup Urine Disease (MSUD); ACER-801 (osanetant) which is in development for the treatment of induced vasomotor symptoms (iVMS); EDSIVO™ (celiprolol) that is being developed to treat vascular Ehlers-Danlos Syndrome (vEDS) in patients that are suffering from confirmed type III collagen mutation and finally ACER-2820 (emetine), a host-directed therapy that is being developed against various infectious diseases including the likes of COVID-19.

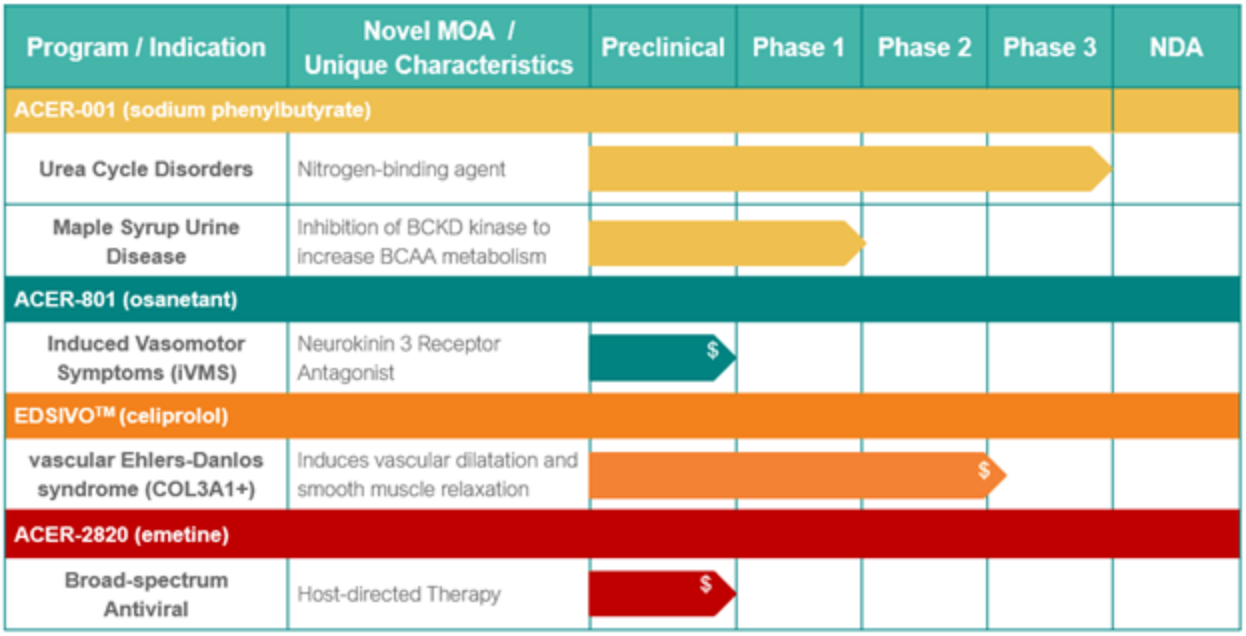

Exhibit 1: Acer Therapeutics Drug Pipeline. Source: Acer Therapeutics

ACER-001 - For UCDs and MSUD

ACER-001 is currently under development for the treatment of disorders, such as UCDs and MSUDs (different forms of inborn errors of metabolism). The drug is a nitrogen-binding agent designed with a multi-particulate dosage formulation for oral administration. The company and Relief Therapeutics have entered into a partnership for the development and worldwide commercialization of ACER-001.

Acer Therapeutics announced topline results from its second Bio-equivalence Trial of ACER-001 earlier in 2021, and introduced the submission of the New Drug Application (NDA) for ACER-001 for UCDs on August 9, 2021, through the 505(B)(2) pathway. It is expected that ACER will receive FDA notification on the potential acceptance of the NDA for filing within 60 days of submission.

ACER-001 for Urea Cycle Disorders (UCDs)

The urea cycle is a chain of biochemical reactions that take place in the liver; they convert ammonia and other nitrogenous compounds, produced in the breakdown of protein into urea, to be excreted. Urea Cycle Disorders are caused by genetic mutations, and result in excessive accumulation of ammonia in the bloodstream; this is called, hyperammonemia, which causes headaches, lethargy, confusion, cognitive defects, etc.

For patients suffering from UCDs involving carbamoyl phosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS), ACER-001 is being developed as an adjunctive therapy. ACER-001 is formulated in such a way that it has a core center and an active drug layer on top of it and a taste-masking coating which can reduce the bitter taste of the drug; it quickly dissolves in the low pH of the stomach.

Currently, NaPB is approved clinically for patients suffering from UCDs to control ammonia levels, in conjunction with the standard of care prescribed.

It is important to note that people suffering from UCDs treated with NaPB are found to have a deficiency in branched-chain amino acid (BCAA), despite the required dietary protein intake.

ACER-001 for MSUD

MSUD or Maple Syrup Urine Disease is a rare inherited disorder caused by defects in mitochondrial branched-chain ketoacid dehydrogenase complex, that results in elevated levels of branched-chain amino acids (BCAA) in blood, along with branched-chain ketoacids (BCKA). If left, MSUD can lead to mental disability, coma, or even death.

Currently, this drug is still in its investigational stage in the USA, and the FDA hasn't approved it. If ACER-001 is approved as the treatment for chronic MSUD, patients won't have to stop their standard therapy in case of an acute crisis. It is estimated that ACER-001 trials in MSUD will occur in 2022, and if these turn out to be fruitful, the company plans to seek FDA approval for commercialization of the drug ACER-001 in and outside of the United States.

Market for ACER-001

ACER believes there are about 2,100 UCDs patients in the U.S., with 1,100 patients diagnosed, and approximately 700 actively treated by one of the approved formulations of phenylbutyrate (almost entirely by Horizon's RAVICTI® and BUPHENYL®). These generated nearly $240 million in annual revenues for Horizon in 2019.

According to Horizon Therapeutics' (HZNP) recent corporate presentation (at slides 36 and 41), Horizon estimates 2,600 UCD patients in the U.S., with 1,000 patients diagnosed.

According to Coherent Market Insights, the global urea cycle disorders treatment market is estimated to be valued at US$ 1,188.9 million in 2020 and is expected to exhibit a CAGR of 3.5% during the forecast period (2020-2027).

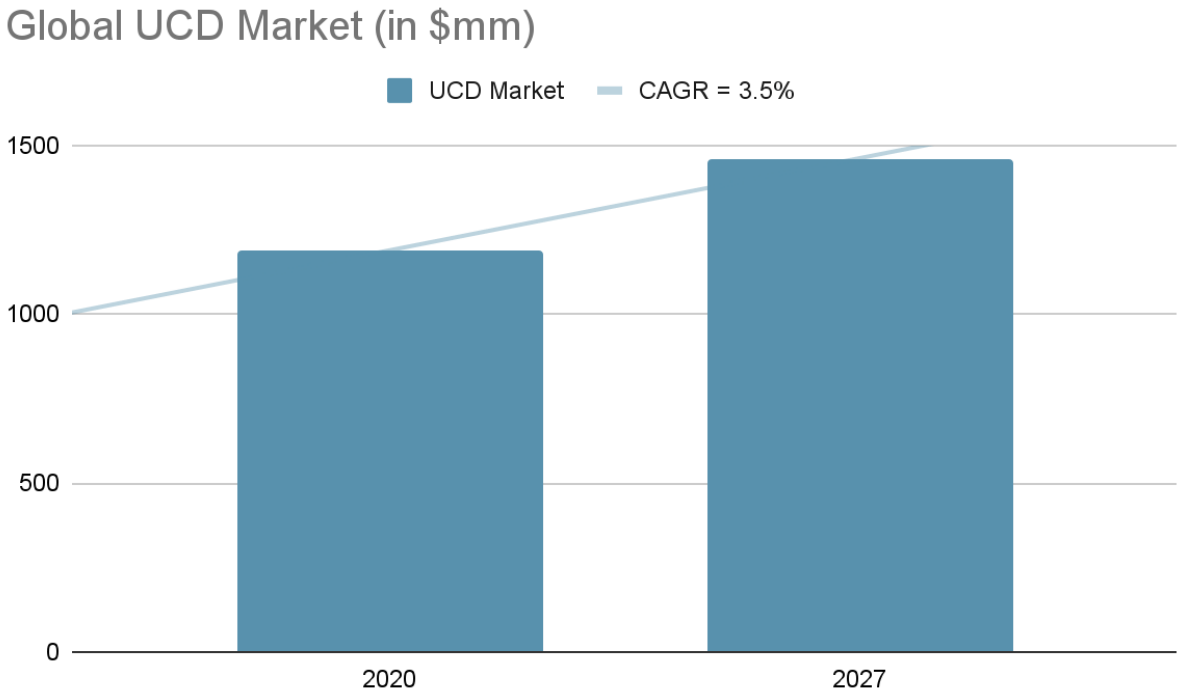

Exhibit 2: Global UCD Market. Source: Coherent Market Insights

However, the Covid-19 pandemic has negatively affected the global UCDs treatment market, hindering its research and development, thus disrupting the global supply chain, and affecting the growth of pharmaceutical companies worldwide.

Globally, North America is expected to be a major market for the treatment of UCDs, due to its continuous technological improvements heavy R&D, with respect to gene therapy by academic institutes researching cures for this disease. The rising prevalence of this disease will lead to increased demand for alternative treatment options, which will ultimately become a growth driver for companies working on such treatments. However, long-term therapy may spur health complications amongst patients, and impede future market growth.

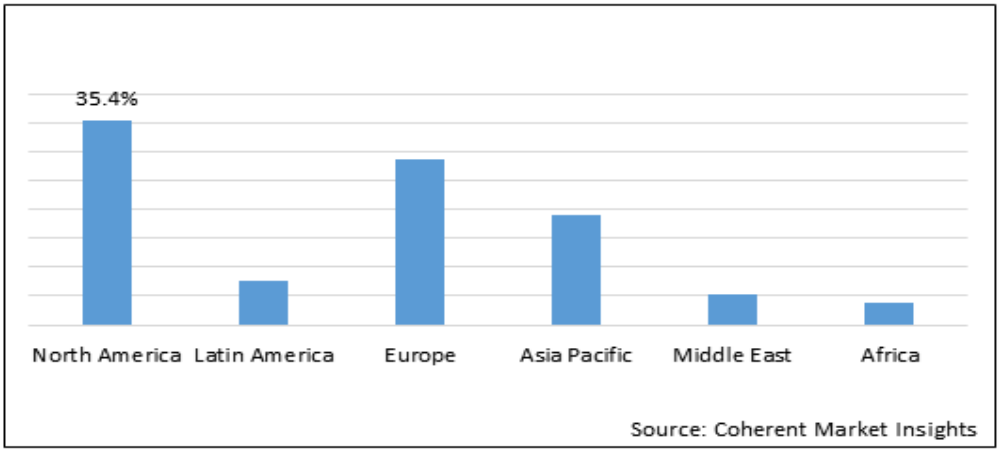

Exhibit 3: Global Market Share for UCD Treatment. Source: Coherent Market Insights

According to the Urea Cycle Disorders Consortium (UCDC), a part of the Rare Diseases Clinical Research Network (RDCRN), the combined prevalence of urea cycle disorders is around 1 in 30,000 people in the U.S in 2017.

Competition and Key Players

Horizon Therapeutics is a biopharmaceuticals company focused on researching and developing medicines that address critical needs for the people impacted by rare and rheumatic diseases. They have identified two drugs, BUPHENYL and RAVICTI that are used for long-term management of high blood levels of ammonia. RAVICTI is available in oral liquid form, whereas BUPHENYL is available in tablet and powder form. Currently, the majority of patients undergoing treatment for UCD are on either of Horizon's drugs, but both of these drugs claim shortcomings. ACER-001 has the potential to be best-in-class.

Recordati Rare Diseases Inc. is a biopharmaceutical company committed to providing typically unnoticed orphan therapies to treat rare diseases amongst underprivileged communities within the U.S. They launched an initiative, 'Check Ammonia,' in alliance with the National Urea Cycle Disorders Foundation (NUCDF). This effort aims to detect early signs of hyper ammonia, and reduce the health complications that can arise due to extremely rare and devastating diseases by providing instant therapies.

Aeglea BioTherapeutics is a clinical-stage biotech company that studies innovative human enzyme therapeutics to treat rare diseases in cancer patients. They are working on the development of Pegzilarginase, an altered form of the human enzyme arginase 1 (ARG 1), that aids in the treatment of debilitating UCD patients, who are suffering because they lack a key arginine metabolizing enzyme. The company's Phase ½ clinical trial demonstrated improvements and optimal results.

EDSIVO™ (Celiprolol) - For Vascular Ehlers-Danlos Syndrome (vEDS)

Vascular Ehlers-Danlos Syndrome (vEDS) is a severe life-threatening disease and subtype of Ehlers-Danlos Syndrome. According to market research conducted by Acer Therapeutics, it is prevalent among vEDS patients, greater than 1 in every 45,000 Americans, , and currently, no therapy has received approval. The current treatments for vEDS are mainly focused on surgical intervention.

Acer Therapeutics is developing a new chemical entity (NCE) 'EDSIVO' for the treatment of COL3A1+ vEDS patients. ADESIVOs unique construct is pharmacologically different, and contains β2 and β3 adrenergic receptor agonists with selective β1 and α2 adrenergic receptor activity. EDSIVOs biochemical process affects the dilation of vascular walls and smooth muscle relaxation which, in turn, reduces stress of collagen fibers within the arterial wall.

Efficacy and Safety Profile

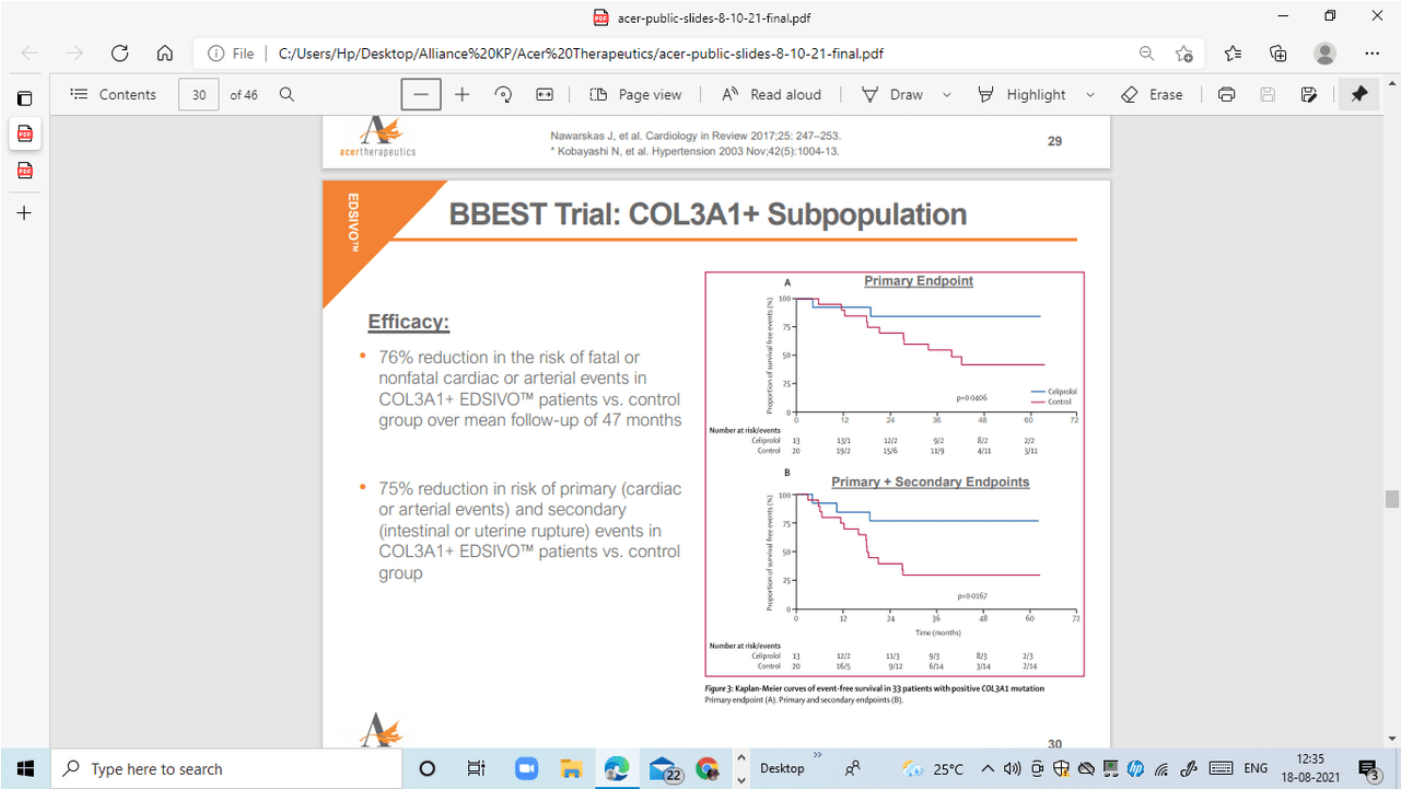

Exhibit 4: Efficacy Profile of EDSIVO. Source: Company Presentation

Results from the BBEST trial in COL3A1+ vEDS patients were promising, wherein the risk of fatal and nonfatal cardiac or arterial events was reduced by almost 75%. The company plans to initiate a pivotal Phase 3 clinical trial of approximately 200 COL3A1+ vEDS patients in the U.S., in Q1 FY22. The study is expected to take approximately 3.5 years to complete once the vEDS patients are fully enrolled.

Competitor Analysis

Aytu Biopharma, a U.S.-based specialty pharmaceutical company, announced in April 2021 that they will be conducting a clinical trial for treating vEDS patients. Under this trial, they will closely monitor the implications of a medication that sought to reduce life-threatening events among vEDS patients. Enzastaurin is an investigational oral compound that was previously utilized for over 40 human trials in the treatment of various cancers.

ACER-801 - For Induced Vasomotor Symptoms (iVMS)

Vasomotor Symptoms (VMS), commonly referred to as ‘Hot Flashes’ or ‘Flushes’ and ‘Night Sweats’ are identified in menopausal women. During the menopause stage, patients often seek treatment for VMS. It is a kind of temperature imbalance or difference in the human body that is created due to changes in gonadal hormones. In many instances, Core Body Temperature (CBT) oscillates between a certain range. Various physiological processes are responsible for maintaining temperatures, regulating temperature range, and ensuring optimal functioning of internal organs.

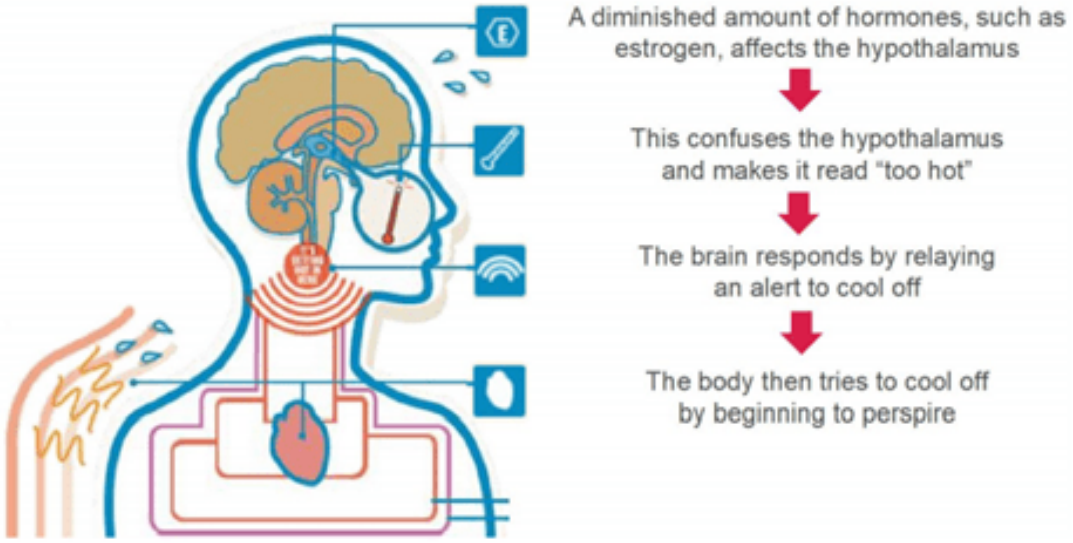

Exhibit 5: Demonstration of Vasomotor Symptoms. Source: Company Presentation

The resulting VMS that materializes due to surgical intervention or through chemical procedure is known as Induced Vasomotor Symptoms (iVMS). Tamoxifen is a potential drug that is one of the oldest hormonal therapies, but applied on a limited basis, due to its adverse side effects.

Acer signed an exclusive licensing agreement in December 2018 with Sanofi to obtain global rights to osanetant. ACER-801 is a selective, non-peptide tachykinin NK3 receptor antagonist. Acer Therapeutics believes that the NK3R antagonist could be beneficial in the treatment of several disorders involving the hypothalamus-pituitary-gonadal axis.

If ACER-801 is approved for commercialization and marketing, the drug could qualify as NCE in the U.S., and enjoy five-year exclusivity rights. This could be further extended depending on select indicators and the company's adopted development pathway.

Development Plan

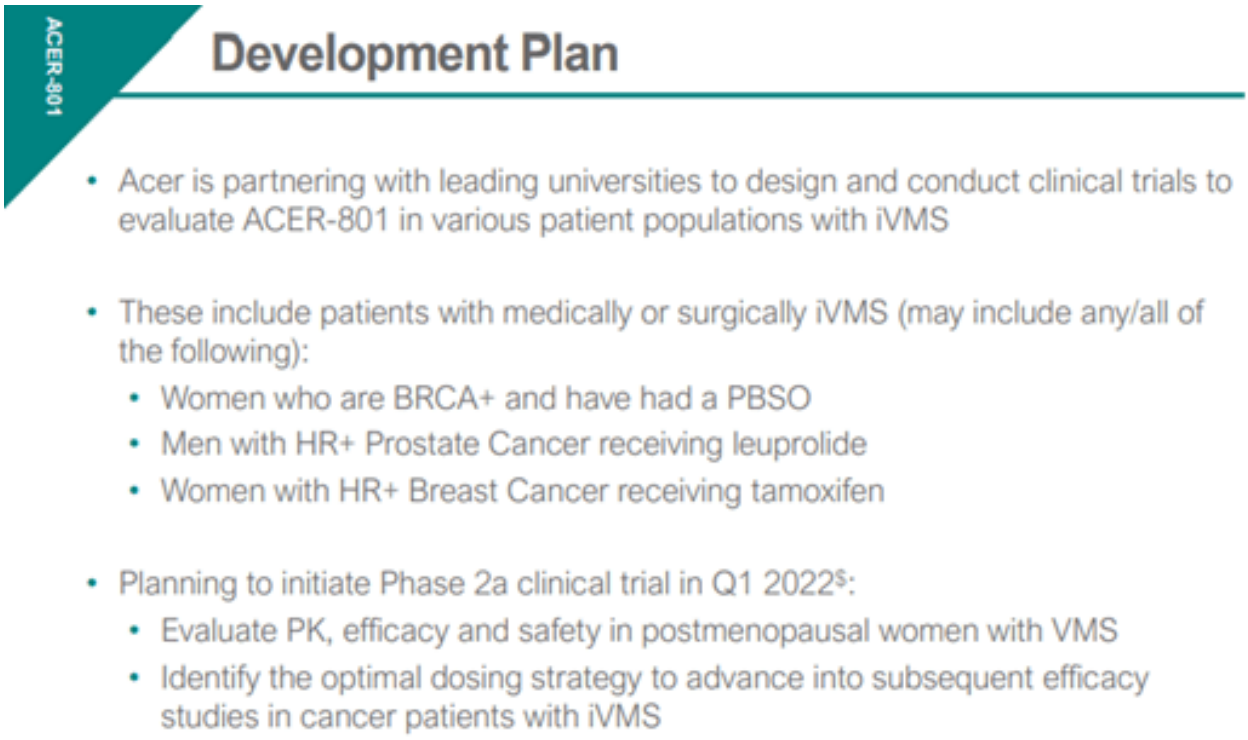

Exhibit 6: Development Plan of ACER-801. Source: Company Presentation

Competition and Key Players

Astellas Pharma Inc. conducted Phase 3 clinical trials for Fezolinetant, an investigational oral, non-hormonal compound studied for the treatment of moderate to severe VMS. The trials showed remarkable results in the reduction of the severity and frequency of VMS. Fezolinetant is not commercialized yet.

Pavinetant (MLE4901) is a drug in its initial stage of development, and produced by AstraZeneca and Millendo Therapeutics. The drug is an orally active, small molecule, selective neurokinin-3 (NK3) receptor antagonist and is used for the treatment of hot flashes and polycystic ovary syndrome (PCOS). MLE4901 was also investigated to treat schizophrenia, but discontinued due to low effectiveness. Since 2017, the drug has been administered in Phase 2 clinical trials for the treatment of hot flashes and PCOS.

ACER-2820 - For Infectious Diseases

ACER-2820 (Emetine) is one of the main alkaloids used previously as both an anti-protozoal and to instigate vomiting. It was given orally to induce emesis and as an injectable, to help in the treatment of thousands of people suffering from amebiasis. Various in-vivo studies conducted in recent years have demonstrated nano-molar potency against both DNA and RNA replicating viruses. Clinically, it has also been used in the treatment of approximately 700 patients with viral hepatitis and varicella-zoster virus. It has also been evaluated in vitro for the treatment of SARS-CoV-2. These studies show that emetine is a potent inhibitor of multiple coronaviruses with broad-spectrum efficacy.

Emetine is an investigational drug, and has not received FDA clearance for commercialization. This will be contingent upon the company's ability to raise non-dilutive capital to further fund and evaluate various infectious diseases.

The global infectious disease diagnostics market is valued at $28.1 billion and is expected to grow at a CAGR of 7.2%. Projections are to a $39.8 billion market by 2026.

The current coronavirus pandemic, awareness of infectious diseases, and opportunities in untapped markets can serve as catalysts for future market growth.

Financials

The company's three-year average annual cash burn rate is $20-22 million, with a cash balance of $22.1 million, as of June 30, 2021. If the FDA accepts Acer's ACER-001 NDA submission for filing, ACER will receive an additional $10 million as a milestone payment from Relief, which could bring its cash tally to $28-$30 million, in Q42021. This would help ACER fund its operations into mid-2022, however, the company will require additional capital to move forward with its planned ACER-801 and EDSIVO™ clinical trials. ACER is evaluating a number of non-dilutive funding sources to further extend its cash runway.

Risk Factors

- The company has incurred operating losses since inception. It is common for clinical-stage pharmaceutical companies to undergo losses initially as they research and develop a new drug.
- Small pharmaceutical companies receive the highest number of Complete Response Letters, or CRLs. A CRL indicates that the FDA is not satisfied with the review of the data in the NDA, ANDA, or BLA submission and cannot approve the application. If ACER receives any such CRLs, it may pose a significant negative effect on its share value.
- The competition in the biopharmaceutical industry is intense, and future development by competitors can render the company's main product redundant.

Valuation

Acer Therapeutics expects to receive notification from the FDA on the potential acceptance of its ACER-001 for UCDs NDA for filing in Q4 2021. The company is preparing for a potential launch, if sanctioned, in mid-2022. There are presently two drugs approved on the market to treat approximately 700 UCDs patients. ACER-001 has the potential to be best-in-class versus BUPHENYL® and RAVICTI®.

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

Exhibit 7: ACER-001 v/s competitors. Source: Investor Presentation

If approved, ACER-001 is likely to capture 55%-60% of the market with peak sales of $100-$110 million (revenue estimates are net of Relief's 40% share). ACER-001 can meet the needs of patients where both approved drugs have struggled. To forecast the company's revenue, I have assumed an average price per patient per year to be $300,000, and the total increased number of patients based on population growth and the incidence rate for new births at 1 in 8500.

		2025E Revenue (in millions)				
		$30	$35	$40	$45	$50
P/S Ratio	3x	$54.9	$64.0	$73.1	$82.2	$91.4
	4x	$73.1	$85.3	$97.5	$109.7	$121.8
	5x	$91.4	$106.6	$121.9	$137.1	$152.3
	6x	$109.7	$128.0	$146.2	$164.5	$182.7
	7x	$128.0	$149.3	$170.6	$191.9	$213.2

The above sensitivity analysis provides a brief outline of the company's valuation based on different revenue expectations and the P/S ratios. In the base case, the revenue is $40 million for 2025, while assuming a P/S of 5x and discounting for risk and time value; the intrinsic value is ~$122 million (only includes ACER's share of ACER-001) or $8.7 per share, implying an upside of ~250%.

I remain bullish on Acer Therapeutics.

This article was written by

Ari Zoldan

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