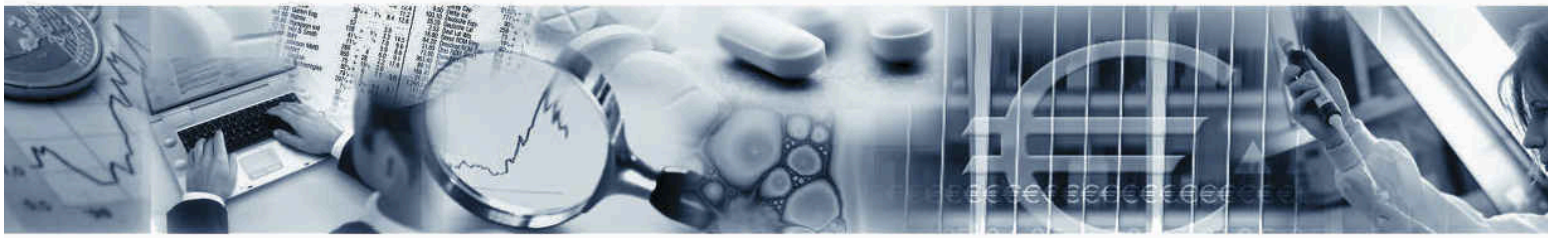

Research Note

Summit Therapeutics

Moving to the forefront in DMD

Chief Research Analyst

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Name:	**Summit Therapeutics**
Country:	**UK**
Price:	**GBp 182.11**
ISIN Code:	**GB00BN40HZ01**
Reuters Code:	**SUMM.L, NASDAQ:SMMT**
Market Cap (GBP m):	**112.6**
EV (GBP m):	**70.6**
Cash & cash eq. (GBP m):	**42.0*)**
Shares outstanding (m):	**61.8**
Volume:	**154,494**
Free float:	**100%**
52-week Range:	**82.66-262.00**

*) INCLUDING UPFRONT PAYMENT SAREPTA COLLABORATION

GBP m (ending 31/1)	2014A	2015A	2016E
Total Revenues (incl milestones)	2.148	1.451	35.000
Net (Loss)/Profit	(11.301)	(17.129)	20.000
Net loss per share (pence)	(29)	(29)	32.4
R&D costs	10.417	16.856	20.000
Cash increase/(decrease)	9.235	4.918	21.000
Cash and marketable sec.	11.265	16.304	37.304

Executive Summary

- Summit Therapeutics is a biopharmaceutical company focused on the discovery, development and commercialization of novel medicines for Duchenne muscular dystrophy (DMD) and *C. difficile* infection (CDI). Its lead programs are Ezutromid which is currently in a Phase II POC clinical trial in patients with DMD and its CDI program ridinilazole that is in a Phase II study to evaluate ridinilazole against the antibiotic fidaxomicin. Data from the CoDIFy Phase II trial demonstrated POC and statistical superiority of ridinilazole over vancomycin in the treatment of CDI.

- Summit's scientific approach for treating DMD focuses on the discovery and development of utrophin modulators. There is no marketed drug that relies on utrophin modulation whereby the production of utrophin is maintained to compensate for the lack of dystrophin for the treatment of DMD or any other indication. Summit's DMD utrophin modulation program is a treatment approach independent of the underlying mutations in the dystrophin gene that cause the disease. The major advantage is therefore that Summit is able to address 100% of the patient populations with DMD whereas the companies that are targeting dystrophin only can treat a certain percentage of patients with DMD (13% or less of the treatable population).

- DMD is one of the most prevalent rare genetic diseases globally affecting up to 1 in 3,500 boys and is universally fatal. There is currently no approved disease modifying therapy for DMD. Recent filing disappointments of DMD treatments (Santhera: Raxone, BioMarin: Drisapersen, Sarepta: Eteplirsen, PTC Therapeutics: Translarna) has reduced the potential competition for Summit considerably.

- Last month, Summit announced a substantial deal with US based Sarepta worth USD 562 million plus low to high teens royalties as a percentage of net sales in Europe. Summit gets an upfront fee of USD 40 million, but could get up to USD 522 million should testing go well, and is also in line for USD 22 million milestone upon the first dosing of the last patient in Summit's ongoing Phase II PhaseOut DMD trial.

- Following the upfront payment from Sarepta, we estimate the Company's current cash position to be GBP 49 million. This should be sufficient to carry out the further development of its pipeline. Besides, the company is already eligible to receive another milestone on or around April 1st 2017 of USD 22 million from Sarepta.

- Based on NPV based valuation, we believe that Summit Therapeutics is substantially undervalued at the current share price of GBPp 182. Using our valuation model and taking into account the Sarepta deal as well as future revenues from its late stage clinical pipeline, the company's current total value should be GBP 300 million, or GBPp 485 per share. This represents a substantial upside from the current share price.

Company Profile & Technology

Summit Therapeutics is an international biopharmaceutical company that is developing novel medicines for indications for which there are no existing or only inadequate therapies. Summit was founded in 2003 as a spin-out of the University of Oxford. Its shares are listed on the Alternative Investment Market, or AIM, of the London Stock Exchange (symbol 'SUMM') and the NASDAQ Global Market (symbol 'SMMT'). Summit is headquartered in Oxfordshire, UK and have an office in Cambridge, Massachusetts, US.

Its clinical programs are focused on the genetic disease Duchenne muscular dystrophy, or DMD, and the infectious disease Clostridium difficile infection, or CDI. Its lead DMD product candidate is ezutromid (formerly SMT C1100), an orally administered small molecule. In June 2016, Summit enrolled its first patient in a Phase II clinical trial of ezutromid in patients with DMD during 2016Q2. This trial is designed to evaluate the potential benefits of longer-term dosing of ezutromid by measuring a number of endpoints related to muscle health and muscle function, along with monitoring the safety and tolerability of long-term exposure to ezutromid. The company refers to this Phase II clinical trial as PhaseOut DMD, a Phase II proof of concept clinical trial. Summit expects to report data periodically during this trial with the first set of 24-week muscle biopsy data from the first group of patients enrolled expected to be reported in 2017Q2/Q3.

Summit's lead CDI product candidate is ridinilazole (formerly SMT19969), an orally administered small molecule antibiotic. The company reported positive top-line results from a Phase II clinical trial of ridinilazole in November 2015 and reported additional data in April 2016. Ridinilazole is designed to selectively target Clostridium difficile bacteria without causing collateral damage to the gut flora and thereby reduce CDI recurrence rates, which is the key clinical issue in this disease. The FDA has designated ridinilazole as a qualified infectious disease product, or QIDP, and the FDA granted ridinilazole fast track status in July 2015. In 2013, the Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services, or CDC, highlighted CDI as one

of three pathogens that pose an immediate public health threat and require urgent and aggressive action. CDI is a bacterial infection of the colon that produces toxins causing inflammation of the colon and severe diarrhea. CDI can also result in more serious disease complications, including pseudomembranous colitis, bowel perforation, toxic megacolon and sepsis. CDI typically develops following the use of broad spectrum antibiotics that can cause widespread damage to the natural gut flora and allow overgrowth of Clostridium difficile bacteria. CDI represents a serious healthcare issue in hospitals, long-term care homes and, increasingly, in the wider community. A study published in 2012 in Clinical Infectious Diseases, a peer reviewed journal published by the Infectious Diseases Society of America, estimated that CDI-related acute care costs total USD 4.8 billion per year in the United States alone. Summit is now preparing ridinilazole for Phase III trials.

Business Strategy & Partnerships

Summit has established partnerships with a range of philanthropic, not-for-profit organisations and government entities to support the development of its DMD and CDI programs. These entities include the Wellcome Trust and a range of DMD patient advocacy groups. hold exclusive worldwide commercialization rights for ezutromid for all indications. If ezutromid receives marketing approval, the company intends to commercialize it initially in the United States and Europe with its own specialized sales force. We feel that medical specialists treating DMD are sufficiently concentrated so that Summit will be able to effectively promote ezutromid with a targeted sales team in these and potentially other key territories. Also the established relationships with patient advocacy groups will strengthen its ability to market ezutromid. Outside of the United States and Europe, Summit plans to evaluate the potential for utilizing collaboration, distribution and other marketing arrangements with third parties to commercialize ezutromid.

Licensing Deal with Sarepta validates technology and brings in cash

In October, Summit announced a licensing deal with US based biotech company Sarepta (SRPT) granting Sarepta rights in Europe, as well as in Turkey and the Commonwealth of Independent States to Summit's utrophin pipeline, including ezutomid for the treatment of DMD. Sarepta also got an option to license Latin American rights. Summit retains the commercial rights in all other countries, including the US (the largest potential market). Under the terms of the agreement, Summit will receive an upfront fee of USD 40 million. In addition, Summit will be eligible for future ezutromid related development, regulatory and sales milestone payments totalling up to USD 522 million, including a USD 22 million milestone upon the first dosing of the last patient in Summit's PhaseOut DMD trial. This milestone is expected around April 1st 2017. Summit also will receive escalating royalties ranging from a low to high teens percentage of net sales in the licensed territory. Summit will also be eligible to receive development and regulatory milestones related to its nextgeneration utrophin modulators. Sarepta and Summit will share specified utrophin modulator-related research and development costs at a 45%/55% split, respectively, beginning in 2018. If Sarepta chooses to exercise its option for the Latin American rights, Summit would be entitled to additional fees, milestones and royalties.

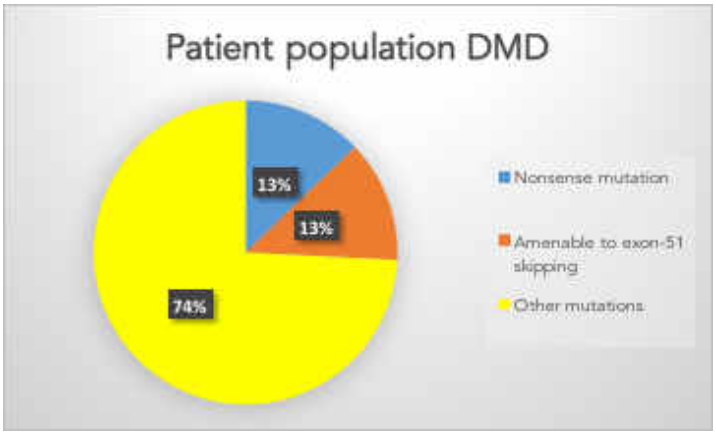
We feel that the deal is value enhancing for both parties. It will give Sarepta the badly needed access to Europe. Sarepta's lead product in DMD Exondys 51 (eteplirsen) surprisingly received approval by the FDA, however the European was cut off. Although an appeal procedure is pending, BioMarin currently has an issued and enforceable patent, which encompasses antisense oligonucleotide product/product candidates directed to exons 51 and 46 in Europe. With this agreement, Sarepta now has the possibility the access the European DMD market.

Summit receives the necessary financial backing to develop its pipeline further without the necessity to raise capital. The 50% increase in Summit's share price does however offers the potential to issue new shares at a much higher price. Besides, in our view the deal also validates Summit's utrophin modulation technology for DMD.

Utrophin versus dystrophin

Summit's approach of utilizing utrophin modulation for DMD has the potential to slow or stop the progression of DMD in all patients with the disease. Utrophin is a naturally occurring protein that is functionally and structurally similar to dystrophin. The aim of utrophin modulation is to maintain the production of utrophin in all skeletal muscles, including the diaphragm, and the heart to compensate for the lack of dystrophin in DMD patients, thereby restoring and maintaining healthy muscle function. This approach to treating DMD is independent of the underlying dystrophin gene mutation.

In a sub-population of DMD patients, synthesis of the dystrophin protein is disrupted because of mutations that may be due, among other things, to deleted exons. Exon-skipping technology seeks to allow the production of a truncated but still functional dystrophin protein. According to an article published in 2009 in the peer reviewed journal Human Mutation, skipping of the ten most common exons would treat in aggregate approximately 41% of all DMD patients. We believe that the exon-skipping therapies (Eteplirsen) and nonsense mutations therapies (Translarna) currently in clinical development would treat less than one-third of all DMD patients. A number of other companies are pursuing alternative therapeutic approaches for the treatment of DMD, including Pfizer and Bristol-Myers Squibb, which are pursuing an approach based on muscle tissue growth through myostatin inhibition.

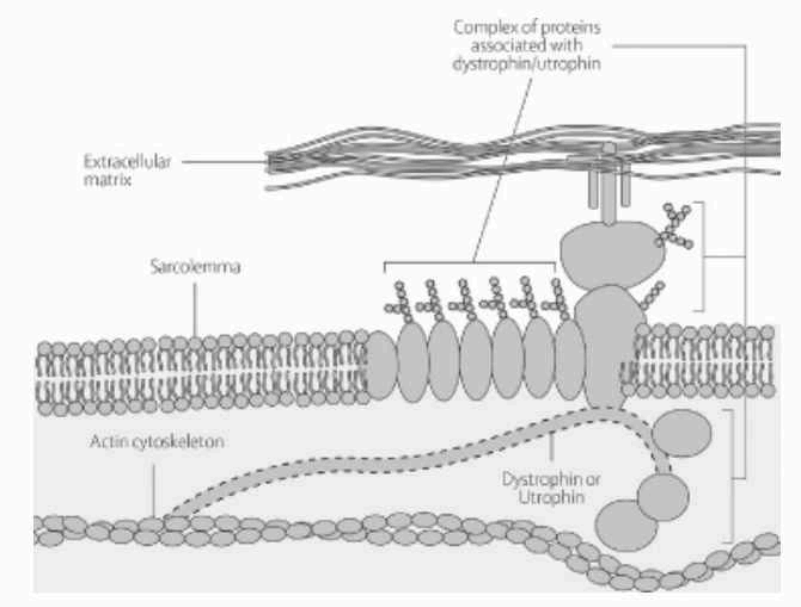


Source: Company reports, van Leeuwenhoeck Inc

We believe utrophin modulation could potentially be complementary to potential treatments for DMD based on other scientific approaches, including approaches that are focused on restoring dystrophin, such as exon-skipping and suppression of nonsense mutations. We also expect that utrophin modulation has the potential to benefit patients with Becker muscular dystrophy, a milder form of the disease in which the majority of patients produce low levels of shortened dystrophin.

The Role of Utrophin and Dystrophin in Muscle Fibers

Utrophin and dystrophin are structurally and functionally similar proteins that perform a critical role in maintaining the proper function of muscle fibers, although at different times and in different settings. The roles of utrophin and dystrophin depend on whether the muscle fibers are mature, in the development stage or in the process of being repaired and regenerated. Dystrophin plays an active role in maintaining the function of mature muscle fibers, while utrophin plays an active role in the development of new muscle fibers and in repairing damaged muscle fibers. Each muscle in the body is made up of bundles of thousands of muscle fibers. Dystrophin and a group of different proteins that bind to dystrophin, which are called the Dystrophin Associated Protein Complex, are located at specific sites along the entire length of the muscle cell membrane, referred to as the sarcolemma, of every muscle fiber. Dystrophin works by linking the actin cytoskeleton, which is a part of the muscle fiber's contractile apparatus, to the Dystrophin Associated Protein Complex in the sarcolemma. The Dystrophin Associated Protein Complex, in turn, links the sarcolemma to the extracellular matrix, which binds the bundles of muscle fibers together. This link serves as a molecular shock absorber that helps to maintain stability and elasticity of muscle fibers during contraction and relaxation. In the absence of dystrophin, this linkage is lost and muscles become damaged, which leads to continual destructive rounds of muscle degeneration and regeneration and ultimately to progressive muscle wasting. The figure below depicts the Dystrophin Associated Protein Complex and illustrates the role of dystrophin (or utrophin) and the other proteins that make up this complex.



Role of Utrophin in Developing Muscle

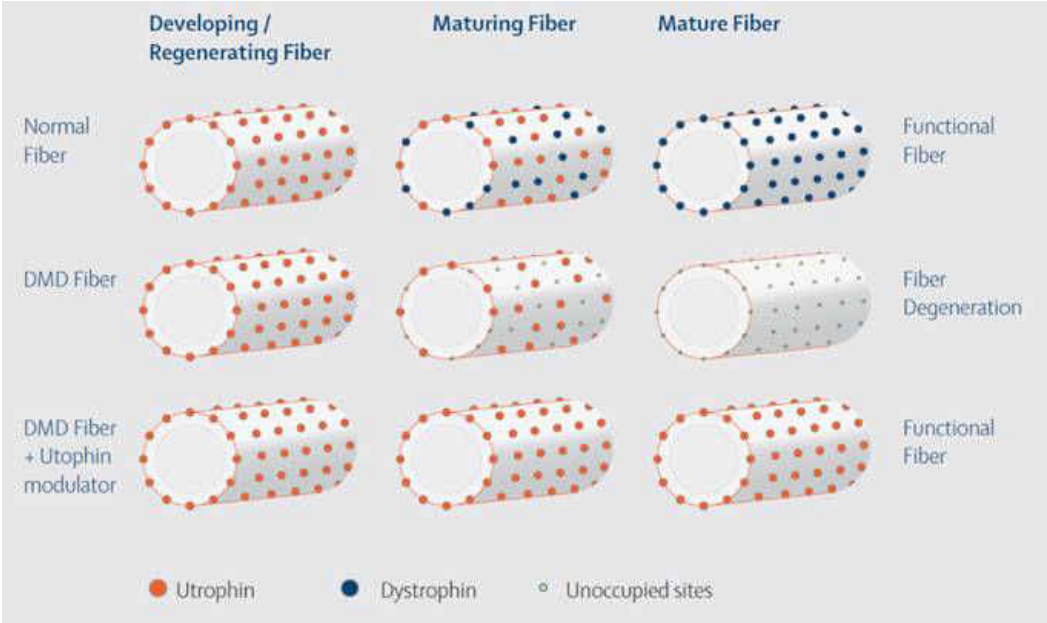
In both DMD patients and healthy individuals, utrophin and the proteins that comprise the Dystrophin Associated Protein Complex are highly localized at specific sites along the length of muscle fibers during fetal development. Utrophin production is then down regulated, or switched off, in the late stages of gestation. In the normal muscle fiber of healthy individuals, the production of dystrophin begins to replace utrophin at these sites in the maturing muscle fiber, eventually fully replacing utrophin. In the muscle fiber of DMD patients, who are unable to produce functional dystrophin to substitute for the down regulating utrophin, these sites in the muscle fiber become unoccupied, which leads to muscle degeneration as muscles mature.

Role of Utrophin in Regenerating Muscle

In both DMD patients and healthy individuals, utrophin is localized to the neuromuscular junctions, which connect nerve fibers and muscles, and myotendinous junctions, which connect tendons and muscles. The other major role of utrophin is to stabilize newly regenerating muscle fibers as part

of the natural repair process. After a muscle fiber is damaged, utrophin production switches on as needed to repair the damaged region and then switches off following successful repair.

We feel that Summit's approach of utrophin modulation can be used to maintain the production of utrophin in maturing and mature muscle fibers and compensate for the lack of dystrophin in DMD patients, thereby restoring and maintaining healthy muscle function. The figure below illustrates the transition from utrophin to dystrophin production in the normal muscle fiber of a healthy individual, the effect of the lack of dystrophin production in the muscle fiber of a DMD patient and the expected effect of utrophin modulation in the muscle fiber of a DMD patient to compensate for the lack of dystrophin production.



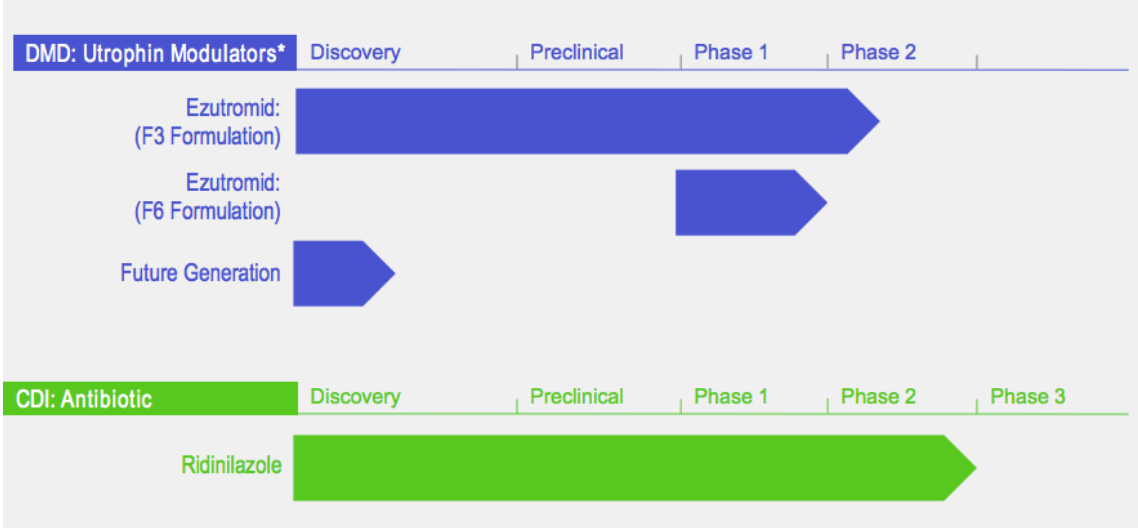
Source: Summit Therapeutics plc

Origins of Summit's Utrophin Modulation Approach

Summit's co-founder and scientific advisor, Professor Kay Davies at the University of Oxford, discovered utrophin and then developed the concept of utilizing utrophin as a treatment potentially applicable to all DMD patients. The company's DMD program was founded to develop and commercialize drugs for DMD using this approach to treatment. Professor Davies' research group at the University of Oxford developed transgenic lines of an mdx mouse that were genetically engineered to continually express utrophin protein. The mdx mouse is a naturally occurring animal model that is dystrophin deficient and is the standard disease model for studies of DMD. In these experiments, the continued expression of utrophin, even at levels just above those in a normal mdx mouse, had a meaningful, positive effect on muscle performance. Summit's utrophin modulation program uses small molecule drugs that are designed to achieve the same effect seen in the transgenic mdx mouse experiments and to continually express utrophin to protect muscle fibers against DMD.

Pipeline: Focus on DMD and CDI

Below is an overview of Summit's pipeline in Utrophin Modulators for the treatment of DMD and the antibiotic Ridinilazole for treatment of CDI.



Source: Summit Therapeutics plc

Duchenne Muscular Dystrophy: Utrophin Modulation Program

Summit's lead DMD product candidate is ezutromid (formerly SMT C1100), an orally administered small molecule. To date, the company ha conducted three Phase I clinical trials of ezutromid. Summit completed a Phase I clinical trial of ezutromid in healthy volunteers in 2012, a Phase Ib clinical trial of ezutromid in DMD patients in May 2014 and another Phase Ib clinical trial of ezutromid in DMD patients in September 2015. The second Phase Ib clinical trial of ezutromid in DMD patients evaluated the impact of diet on plasma levels of the drug. Summit refers to this second Phase Ib trial as its Phase Ib modified diet trial. This Phase Ib modified diet trial met its primary objective with patients achieving plasma levels of ezutromid that may be sufficient to modulate the production of utrophin protein and possibly result in clinical benefit while following specific dietary guidance.

Summit is currently conducting a Phase II clinical trial of ezutromid in patients with DMD. Enrolment and dosing of patients at sites in the United Kingdom is now underway, with patients expected to be enrolled into sites in the United States shortly. The Company anticipates reporting data periodically during this trial with 24-week muscle biopsy data from the first group of patients expected to be reported in 2017Q2/Q3. This trial is designed to evaluate the potential benefits of longer-term dosing of ezutromid by measuring a number of endpoints related to muscle health and muscle function, along with monitoring the safety and tolerability of long-term exposure to ezutromid. This Phase II clinical trial is referred to as PhaseOut DMD, a Phase II proof of concept clinical trial.

PhaseOut DMD aims to provide proof of concept for ezutromid and utrophin modulation by measuring muscle fat infiltration, as well as by measuring utrophin protein and muscle fibre regeneration in muscle biopsies. The primary endpoint of the open-label trial is the change from baseline in magnetic resonance imaging parameters related to fat infiltration and inflammation of the leg muscles. Exploratory endpoints include the six-minute walk distance, the North Star Ambulatory Assessment and patient reported outcomes. PhaseOut DMD is a 48-week open-label trial expected to enrol up to 40 boys ranging in age from their fifth to their tenth birthdays at sites in the UK and the US.

Phase I New Formulation Trial for Ezutromid

The company announced in August 2016 the top-line data from a Phase I clinical trial testing a new formulation of ezutromid, referred to as F6, in patients with DMD. The trial evaluated the pharmacokinetics and safety of three fixed doses (250mg, 500mg and 1,000mg twice a day) of the F6 formulation in patients aged between five and nine years who followed a modified diet. At the highest dose, the five evaluable patients achieved an average maximum concentration of 390ng/mL on day 7, the final day of dosing. This represented a greater than six-fold increase in maximum plasma levels but with a reduced oral dose compared to the current clinical formulation of ezutromid referred to as F3. In an earlier Phase I trial of the F3 formulation in patients who

followed the same modified diet, an average maximum plasma concentration of 63ng/mL (2,500mg, twice a day) on the final day of dosing (day 14) was achieved.

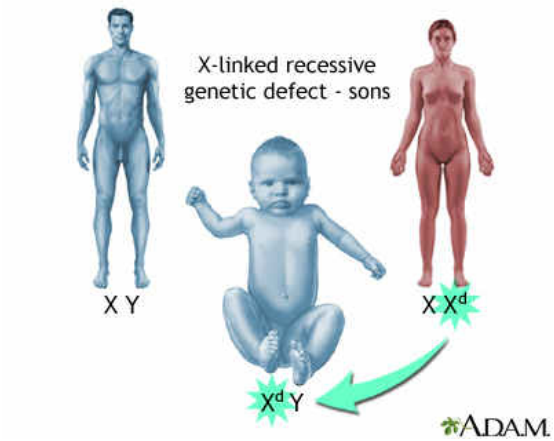
Subject to regulatory approval, Summit now plans to incorporate the F6 formulation into the ongoing PhaseOut DMD proof of concept trial. Summit anticipates testing up to ten of the 40 patients expected to be enrolled on F6 to compare the safety and efficacy of both formulations of ezutromid. This will help to determine which formulation to use in future clinical trials. These two formulations of ezutromid are expected to modulate utrophin and with a wider range in blood plasma exposure, are expected to allow Summit to further explore the potential therapeutic effect of ezutromid in patients with DMD.

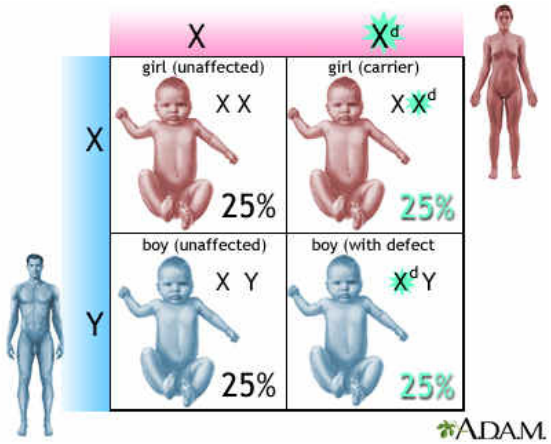
Utrophin Modulator Pipeline Update

As part of the Company's strategy to maintain its leadership position in the field of utrophin modulation, Summit has a pipeline of second and future generation utrophin modulators. The second generation molecules are structurally related to ezutromid, but are designed to have more favourable pharmaceutical properties to achieve higher plasma levels of drug. The substantial increase in ezutromid plasma levels achieved with the F6 formulation in the recently completed Phase I trial fulfilled the key objective for the second generation utrophin modulator program. In light of this progress, Summit has put the development of the second generation on hold and will switch focus to its pipeline of future generation utrophin modulators. This research is aiming to build on the promise of ezutromid to identify new, structurally distinct molecules, including ones that may have possible new utrophin related mechanisms. This research is being conducted as part of the strategic alliance with the University of Oxford.

Duchenne Muscular Distrophy (DMD): Focus on Utrophin

DMD is a fatal neuromuscular disorder caused by a recessive mutation on the X chromosome. Because the related mutation is recessive, DMD is more common in boys than in girls, as boys do not have another copy of the X chromosome to compensate for the genetic defect. DMD affects about 1 in 3,500 males. On the other hand, most girls born with DMD mutations are merely carriers, because they each possess only one mutated DMD gene on one of their two X chromosomes. Although not themselves affected by DMD, carriers can pass DMD genes on to their children.

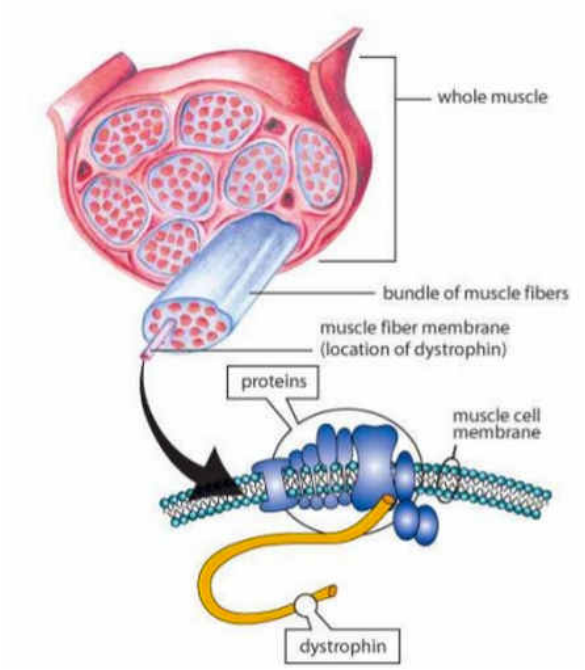




There are several X-linked (or sex-linked) recessive genetic disorders, (hemophilia,muscular dystrophy) which are inherited through a genetic defect on an X chromosome. A female has 2 X chromosomes, one she inherited from her mother and one she got from her father. A male has an X chromosome from his mother and a Y chromosome from his father. Since male offspring receive their X chromosome from their mothers, the inheritance of a defect attached to that one copy of the X will cause the disorder.

Although DMD is named after the French neurologist Duchenne de Boulogne, who first described the disorder in the late 1800s, the cause of this disease remained a medical mystery until the mid-1980s, at which time the DMD gene defect was identified. It is now known that the DMD gene encodes dystrophin, a huge muscle protein with about 4,000 amino acids that plays an integral

role in maintaining the structural integrity of muscle cells. Cells with mutated DMD genes cannot make normal dystrophin, which means that they are unable to function appropriately.



The deleterious effect of this lack of dystrophin becomes apparent early in life, although usually not immediately. In fact, most babies with DMD appear normal at birth and do not start showing their first symptoms — muscle weakness — until between the ages of three and five years. Affected children then experience increasing difficulty in performing daily tasks, such as climbing stairs and playing with their peers. Indeed, most DMD patients rely on the use of a wheelchair by their early teens, with their muscles becoming progressively weaker and more atrophied. Patients usually die from heart or respiratory problems by their twenties or thirties, if not before. Scientists have been searching for ways to treat or cure DMD for as long as they have known about the disease. Today, based on the wealth of knowledge about the underlying genetic and molecular mechanisms of DMD, researchers are actively testing a variety of different therapeutic approaches. These include

gene-based therapies (e.g., replacing a patient's faulty DMD genes with normally functioning ones), cell-based therapies (e.g., replacing dystrophin-deficient muscle cells with stem cells from healthy donors), and drugbased therapies (e.g., using drugs to compensate in other ways for the dysfunctional dystrophin protein). Most of these initiatives have not provided any definitive answers. Indeed, few of the treatments currently being developed and tested hold forth promise that they will actually be used in the future. DMD thus remains a devastating disease for which there is no cure.

There is currently no approved therapy for the treatment of DMD applicable to all DMD patients that seeks to alter the progression of the disease. Corticosteroids are the current standard of care for DMD patients, although these are symptomatic treatments that do not address the underlying cause of DMD. PTC Therapeutics is developing ataluren (Translarna), which is a small molecule that enables formation of functional dystrophin in DMD patients with nonsense mutations. DMD caused by nonsense mutations affects approximately 13% of all DMD patients. In August 2014, ataluren received market authorization from the European Commission to treat patients with nonsense mutation Duchenne muscular dystrophy. A confirmatory phase III clinical trial is ongoing. The drug does not yet have approval by the US FDA. In February 2016, FDA declined to approve or even discuss PTC Therapeutics application for ataluren because it deemed the data presented by the developer "insufficient to warrant a review". In October 2015, The National Institute for Health and Care Excellence (NICE) asked for further evidence of benefit to justify the "very high cost". NICE estimated that for a typical patient, treatment would cost GBP 220,256 per year. NICE is an executive non-departmental public body of the Department of Health in the United Kingdom. It serves both the English NHS and the Welsh NHS. The European Commission has granted conditional approval for ataluren in Europe, and PTC is commercializing ataluren in several European countries. Sarepta Therapeutics is developing treatments for DMD based on exon-skipping approaches. Sarepta recently received FDA approval for its drug Eteplirsen for patients who have a confirmed mutation of the dystrophin gene amenable to exon 51 skipping, which affects about 13 percent of the population with DMD. Another company that was developing a drug based on exon skipping, BioMarin, discontinued the development of its treatment drisapersen in May after the FDA decided in January 2016 not to approve the drug.

Near Term Milestones

In the coming 12 months we expect a number of important mile stones that can drive the stock price upwards. These are:

- Phase II results Ridinilazole vs fidaxomicin 2016Q4
- Last patient in PhaseOut DMD trial triggers milestone of USD 22 million April 2017
- First group of 24-week biopsy data: 2017Q2/Q3
- Initiating Phase III trial Ridinilazole 2017H2

Analyst: Marcel Wijma MSc
Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoeck Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.