Future Treatment Approaches for Rare Congenital and Genetic Diseases
Introduction

Many biotech and pharmaceuticals companies have prioritized drug development for rare congenital and genetic diseases over the past few years given the high unmet need, rapidly advancing science, and favorable clinical development paths. Rare congenital and genetic diseases often have severe or even fatal manifestations, with few treatments available, but emerging genetic data and new treatment modalities, such as gene therapy, are rendering monogenic diseases more tractable. What's more, regulatory and legislative initiatives such as Breakthrough Therapy designation, which makes it easier to work with the FDA on tailored trial designs, and the Orphan Drug Act, which provides seven years of regulatory exclusivity, have encouraged development in this space.

In this whitepaper, we review the current market landscape for rare congenital and genetic diseases and look forward to what treatment approaches might be available soon.
Approved therapies for rare congenital and genetic diseases

The focus of this analysis is limited to diseases that are classified as rare congenital and genetic diseases by the National Center for Advancing Translational Sciences' (part of the NIH) Genetic and Rare Diseases Information Center (GARD). According to Informa's Pharmaprojects, only 74 rare congenital or genetic diseases have an approved therapy. This accounts for less than 3% of all rare congenital and genetic diseases listed by GARD, and emphasizes the huge unmet need that exists. Diseases with the largest number of approved therapies include dwarfism, Lennox-Gastaut syndrome, and cystic fibrosis (Figure 1). However, even for these diseases the number of approved therapies is very small compared to more prevalent conditions, and the need for improved standards-of-care still remains.

Figure 1. Top 30 Rare Congenital and Genetic Diseases by Number of Approved Drugs


Source: Pharmaprojects®, July 2020
Therapies in development for rare congenital and genetic diseases

Pipeline activity for rare congenital and genetic diseases has increased considerably in the past few years, and there are now many more products in development. Specifically, there are 27 rare congenital and genetic diseases with at least 10 products in active development, and a further 153 diseases have at least one product in active development (Figure 2). Perhaps unsurprisingly, the most prevalent conditions have the greatest number of drugs in active development, but increasingly developers are also looking to address unmet need in much rarer indications. For instance, the extremely rare indications primary hyperoxaluria type 1 and Hutchinson-Gilford progeria syndrome both have products in late-stage development. Small molecules still dominate the pipeline, but more advanced modalities such as gene therapies, cell therapies, and RNAi are increasingly being trialed.

Figure 2. Top 30 Rare Congenital and Genetic Diseases by Number of Drugs in Development

Source: Pharmaprojects®, July 2020
**Key indications**

**Cystic fibrosis**

The treatment of cystic fibrosis (CF) lung disease is experiencing a period of rapid evolution, supported by well-designed clinical trials and improved understanding of the genetics and pathophysiology of the disease. Advances in physical, antibiotic, and mucolytic therapies have greatly improved the life expectancy of CF patients, while a large number of patients now also have access to novel treatments targeting the underlying genetic cause of their disease. CF transmembrane conductance regulator (CFTR) modulators are a new class of drugs that act by improving production, intracellular processing, and/or function of the defective CFTR protein.

With over 1,700 known CF-causing mutations in the CFTR gene, there is a large degree of heterogeneity, and medications that have been developed so far are effective only in people with specific mutations. There are four approved CFTR modulators for people with certain CFTR mutations: ivacaftor (Kalydeco), lumacaftor/ivacaftor (Orkambi), tezacaftor/ivacaftor (Symdeko), and elexacaftor/tezacaftor/ivacaftor (Trikafta).

All four drugs are marketed by Vertex Pharmaceuticals, which holds a dominant position after steadily increasing the number of genotypes and patients its portfolio can address. Currently, the company is riding high after the launch of Trikafta, the first triple-combination therapy, at the end of 2019. Trikafta dramatically outperformed analyst expectations by generating $895m in its first full quarter on the market. The CFTR modulator is intended to treat CF patients with at least one copy of the F508del mutation of the CFTR gene, which accounts for about 90% of all people with the disease. It has been estimated that 18,000 patients in the US are eligible for Trikafta, which has an annual list price of around $311,000, and for 6,000 of these people, this is the first time they have had a potential medicine to treat the underlying cause.

While such pricing has inhibited market access outside of the US, Vertex has finally secured a deal with NHS England for its triple-combination drug – transforming a years-long bitter stand-off into an agreement that will see patients there receive the triple therapy faster than elsewhere in Europe. England is one of the most significant markets in the world for Vertex and its portfolio of CF drugs, as it has one of the biggest populations of patients with the inherited condition.

More potential CFTR modulators are in development to address the underlying cause of the disease in people with other CF mutations, including AbbVie's ABBV-2222 and ABBV-3067.

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while Vertex is continuing to advance new combinations and treatment modalities.

The gene that causes CF was discovered in 1989; however, progress in the development of a gene therapy for the disease has been much slower than originally anticipated. This is highlighted by the 26 gene therapies for CF listed in Informa’s Pharmaprojects that are no longer in development. However, one mRNA therapy, MRT5005, in development by Translate Bio, is currently in Phase II clinical development. Additionally, there is hope that the gene-editing system CRISPR could be deployed successfully in the treatment of CF, eventually bringing corrective therapies that could be deployed to every single CF patient, regardless of genotype.

Duchenne’s muscular dystrophy (DMD)

Treatment for DMD has advanced considerably in the last five years with the approvals of three new therapies. Deflazacort (Emflaza) was the first oral corticosteroid approved by the US Food and Drug Administration (FDA) to treat the condition in 2017. Deflazacort has been found to help patients retain muscle strength as well as helping them maintain their ability to walk, although as a steroid the effect is non-specific. The other FDA-approved therapies are both exon-skipping antisense oligonucleotides marketed by Sarepta – Exondys 51 (eteplirsen), approved in 2016, and Vyondys 53 (golodirsen), approved in December 2019.

DMD is an X-linked recessive genetic disorder caused by a lack of the protein dystrophin which leads to muscle weakness and early death. Exon skipping works by allowing a smaller but still functional dystrophin protein to be produced, although the size of the dystrophin gene and range of potential mutations mean that this is not a “one size fits all” solution. That being said, data suggest that over 80% of DMD patients have genotypes responsive to exon skipping, with potentially 14% responsive to exon 51 skipping, 10% responsive to exon 53 skipping, and 9% responsive to skipping exon 45. Sarepta also plans to expand its DMD portfolio with casimersen, an exon 45 skipping therapeutic, which is currently in late-stage development.

Although these therapies have seen considerable commercial success – albeit with contentious clinical benefit – their sales could be usurped by a potentially curative DMD gene therapy. There are several gene therapies in development for DMD which have the potential to revolutionize treatment, and Sarepta’s SRP-9001 is currently leading the pack. The considerable potential of this drug is illustrated by the sum Roche invested solely for ex-US rights; a considerable $750m upfront fee was supported by Roche taking a $400m equity stake in Sarepta. In addition, Roche will fund half of SRP-9001’s global clinical development costs, invest up to $1.7bn in regulatory and sales milestone fees, and pay

royalties estimated to be a mid-teens percentage of the product’s ex-US sales. Sarepta’s gene therapy is not the only one in development, and Pfizer is a competitor with its gene therapy, PF-06939926. However, this therapy continues to fall behind SRP-9001, with disappointing Phase Ib efficacy data and safety concerns prompting a study halt.

**Huntington’s disease**

Unmet need in Huntington’s disease is huge, and the launch of a disease-modifying drug would be a game changer. The only two FDA-approved therapies, Lundbeck’s Xenazine and Teva’s Austedo, target vesicular monoamine transporters and can help control the abnormal movements associated with Huntington’s, but can’t treat the underlying disease. Research strategies to develop efficacious therapeutics to treat Huntington’s include gene silencing therapies to reduce or prevent the abnormal huntingtin (HTT) protein from being made, and therapies that aim to prevent the damage to and death of nerve cells in the brain due to toxic HTT protein accumulation.

A particularly promising therapy in development is tominersen (previously known as IONIS-HTTRx and RG6042), developed by Ionis Pharmaceuticals and later acquired by Roche. It is an antisense oligonucleotide designed to target and destroy all forms of mutated HTT protein. The investigational therapy is not tailored to individual HTT mutations, and because of that it has the potential to treat all Huntington’s patients. Tominersen drove a 40% reduction in the mutant protein in a Phase I/II trial, and a Phase III trial is ongoing to evaluate its effect on Huntington’s disease progression. Tominersen has been awarded PRIME designation by the European Medicines Agency (EMA), a designation aimed to enhance support for the development of medicines that target an unmet medical need. Meanwhile, another antisense oligonucleotide, WVE-120102, is in development by WAVE Life Sciences. However, WVE-120102 recently demonstrated just a 12.4% placebo-adjusted reduction in mutant HTT protein, which, while a statistically significant result, was unfavorable in comparison to tominersen’s 30–52% effect on this surrogate efficacy marker.

VX15/2503, another promising therapy being developed by Vaccinex, is an antibody against the protein SEMA4D. SEMA4D is involved in signaling processes leading to neuroinflammation and cell death, and VX15/2503 is designed to specifically bind to and block the activity of SEMA4D. A Phase II clinical trial called SIGNAL is currently ongoing in the US, with initial results suggesting that the treatment is safe and may be effective in preserving brain structure in Huntington’s patients.

Spinal muscular atrophy (SMA)

There are currently two approved therapies for SMA, Biogen’s Spinraza (nusinersen) and Novartis’s gene therapy Zolgensma, with Roche’s risdiplam waiting in the wings. The RNA interference drug Spinraza is priced at $750,000 for the first year and $375,000 for each year afterwards, while Novartis’s Zolgensma, a one-shot gene therapy, is priced at $2.1m, making it the industry’s most expensive one-time treatment.

The FDA’s positive decision for Biogen and Ionis Pharmaceuticals’ Spinraza in December 2016 came five months ahead of schedule, reflecting the urgency at the agency to approve the first treatment for SMA. The FDA was also very generous with Spinraza’s label, allowing the drug in all three subtypes of the disease – and in both pediatric and adult patients – again emphasizing the lack of treatment for the rare genetic disorder. Spinraza, which corrects RNA splicing of the SMN2 gene and increases SMN protein levels, got off to a strong start. Even though its $125,000-per-injection price tag initially drew some unwanted public attention, payers were on board, and as of Q4 2019, Spinraza revenues had reached $243m in the US and $300m abroad.

However, Spinraza is now feeling the pressure from Novartis’s adeno-associated viral (AAV) vector-based gene therapy Zolgensma, which was approved in May 2019 and comes with the promise of a potential cure with just one injection. In the US, the drug, through intravenous delivery, is currently only approved in type 1 children younger than two years old, but Novartis is aiming to reach older patients with an intrathecal formulation. Zolgensma is expected to become the standard of care for newborn-screened and young type 2 SMA patients, and the treatment has so far exceeded analyst expectations. Novartis noted that full-year sales for 2019 were $361m, with $186m coming in the fourth quarter when 100 new patients were treated.

In May 2020, Japan’s regulatory authorities decided to grant reimbursement to Zolgensma under the National Health Insurance scheme at the equivalent of around $1.56m per administration, marking a watershed in drug pricing in the country. Novartis has also secured conditional approval in Europe for patients with a clinical diagnosis of SMA type 1, the most severe form of the disease, or patients with up to three copies of the SMN2 gene for babies and young children up to 21kg with SMA.

Companies operating in the rare congenital and genetic diseases space

The largest pharma companies dominate the commercial landscape despite the lower development and marketing costs associated with targeting rare diseases. Takeda, Pfizer, Sanofi, GlaxoSmithKline, and Novartis each have at least eight approved therapies for rare congenital and genetic diseases (Figure 3). However, increasingly, it is the smaller, more specialist players such as Sarepta Therapeutics, Vertex Pharmaceuticals, and Ionis Pharmaceuticals that are developing the new products (Figure 4). Their prominence in the pipeline makes these companies perennial acquisition targets in a similar vein to Shire, whose $62bn takeout propelled Takeda to the top of Figure 3.

Figure 3: Top 30 Rare Congenital and Genetic Diseases Developers by Number of Approved Drugs

Source: Phamarproject®, July 2020
Figure 4: Top 30 Rare Congenital and Genetic Diseases Developers by Number of Drugs in Development

Source: Pharmaprojects®, July 2020
Sarepta Therapeutics bills itself as “the leader in precision genetic medicine for rare diseases”, and the company has built an impressive and competitive position in DMD, as well as more recently expanding into limb-girdle muscular dystrophy (LGMD), Charcot-Marie-Tooth disease, and CNS-related disorders. In total, Sarepta has 22 products in development for rare genetic conditions. The company's programs span across several therapeutic modalities, including RNA, gene therapy, and gene editing.

Sarepta has achieved FDA approval for two DMD therapies: Exondys 51 (eteplirsen), and most recently for Vyondys 53 (golodirsen). The approval of Vyondys 53 marked a remarkable four-month journey from FDA rejection to approval, a turnaround made possible by a formal dispute resolution which Sarepta filed with the agency. In addition, Sarepta has a further DMD therapy in late-stage development – a rolling NDA submission for casimersen was announced in January 2020 (see above analysis).

Sarepta originally made a name for itself in the field of RNA therapeutics, but is increasingly pivoting towards gene therapy and gene editing in the longer term. In order to achieve this, Sarepta has been busy in the deal-making space in the last year and has focused on agreements that center around AAV vectors. In 2019, Sarepta and StrideBio agreed to collaborate on the development of AAV-based therapies for up to eight CNS and neuromuscular disease targets, while Sarepta also acquired the private, neuromuscular-focused gene therapy startup Myonexus Therapeutics and its pipeline of potential gene therapies for LGMDs. Myonexus’ approach uses the rh.74 AAV vector system designed to systemically deliver a corrective copy of the appropriate deficient gene to cardiac and skeletal muscle, including the diaphragm, without crossing the blood-brain barrier. Furthermore, most recently, in May 2020, Sarepta announced an agreement with Dyno Therapeutics, a biotech applying artificial intelligence to gene therapy, to develop next-generation AAV vectors for muscle diseases using Dyno’s CapsidMap platform.

Sarepta is also putting its hope in LYS-SAF302 (SAF301), a gene therapy for the treatment of mucopolysaccharidosis type IIIA (Sanfilippo A syndrome) under development by Lysogene. Sarepta licensed exclusive worldwide commercialization (except in Europe) and manufacturing rights from Lysogene in 2018. LYS-SAF302 uses the AAVrh10 virus to replace the faulty SGSH gene with a healthy copy of the gene. A global Phase II/III clinical study is ongoing.

Novartis
With the acquisition of The Medicines Company and the RNAi asset inclisiran in November 2019, Novartis becomes the only Big Pharma with presence across four advanced therapy platforms: cell, gene, radioligand, and RNA therapies. The desire to diversify and minimize reliance on single products and technologies is undoubtedly a driver behind the acquisition, but it also allows Novartis to operate within cardiovascular population health. Novartis has
submitted filings to the FDA and EMA for the use of inclisiran in hyperlipidemia, but the drug is also in Phase III development for homozygous familial hypercholesterolemia, an inherited condition which leads to very high cholesterol levels.

As discussed in the above analysis, Novartis is responsible for marketing the world’s most expensive one-shot treatment, as its SMA gene therapy Zolgensma is priced at $2.1m in the US. In addition, Novartis received conditional approval for Zolgensma in Europe in May 2020, and has hit the ground running with access programs for the closely watched gene therapy. Novartis is also interested in developing gene therapies for ocular diseases, led by its licensing of ex-US commercial rights to Luxturna (voretigene neparvovec), approved for the curative treatment of certain inherited retinal diseases. Like Sarepta Therapeutics, Novartis has also formed a collaboration with Dyno Therapeutics to develop improved AAV vectors, but this collaboration will focus on their use in gene therapies for ocular diseases.

**Vertex Pharmaceuticals**

As well as being a key player in the CF market (see above analysis), like Sarepta and Novartis, Vertex is investing in AAV technology, and in April 2020 it entered into a strategic research collaboration with Affinia Therapeutics to engineer novel AAV capsids to deliver genetic therapies. The collaboration will leverage Affinia’s capsid engineering expertise and proprietary AAVSmartLibrary alongside Vertex’s scientific, clinical, and regulatory capabilities to accelerate the development of genetic therapies.

Vertex is also looking to expand beyond CF into severe neuromuscular disease, and in June 2019 the company announced that it plans to enhance its gene editing capabilities and develop therapies for DMD and myotonic dystrophy type 1 (DM1). To achieve this, Vertex bought privately held Exonics Therapeutics for $245m up front and extended and expanded a 2015 collaboration with CRISPR Therapeutics.
As part of this analysis we have picked out 10 of the most anticipated new drug launches for rare congenital and genetic diseases – in particular, we have focused on drugs that have the potential to treat patient populations not currently served by available therapies.

**Table 1: Key upcoming approvals for rare congenital and genetic diseases**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Company</th>
<th>Indication</th>
<th>US status</th>
<th>Likelihood of US approval</th>
<th>Modality</th>
<th>Estimated US approval date</th>
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<tr>
<td>Viltolarsen</td>
<td>Nippon Shinyaku</td>
<td>Duchenne's muscular dystrophy</td>
<td>NDA</td>
<td>90%</td>
<td>Antisense oligonucleotide</td>
<td>July to September 2020</td>
</tr>
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<td>Risdiplam</td>
<td>Roche</td>
<td>Spinal muscular atrophy</td>
<td>NDA</td>
<td>99%</td>
<td>Small molecule</td>
<td>24 August 2020</td>
</tr>
<tr>
<td>Zokinvy</td>
<td>Eiger BioPharmaceuticals</td>
<td>Hutchinson-Gilford progeria syndrome</td>
<td>NDA</td>
<td>89%</td>
<td>Small molecule</td>
<td>20 November 2020</td>
</tr>
<tr>
<td>Lumasiran</td>
<td>Alnylam</td>
<td>Hyperoxaluria</td>
<td>NDA</td>
<td>98%</td>
<td>siRNA</td>
<td>3 December 2020</td>
</tr>
<tr>
<td>Casimersen</td>
<td>Sarepta Therapeutics</td>
<td>Duchenne's muscular dystrophy</td>
<td>NDA</td>
<td>90%</td>
<td>Antisense oligonucleotide</td>
<td>25 June 2021</td>
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<td>Arimoclomol</td>
<td>Orphazyme</td>
<td>Niemann-Pick disease</td>
<td>NDA</td>
<td>92%</td>
<td>Small molecule</td>
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<td>Fosdenopterin</td>
<td>BridgeBio Pharma</td>
<td>Molybdenum cofactor deficiency</td>
<td>NDA</td>
<td>89%</td>
<td>Small molecule</td>
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<td>FCX-007</td>
<td>Castle Creek Biosciences</td>
<td>Epidermolysis bullosa</td>
<td>III</td>
<td>66%</td>
<td>Cell-based gene therapy</td>
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<tr>
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<td>Minoryx Therapeutics</td>
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<tr>
<td>PXT3003</td>
<td>Pharnext</td>
<td>Charcot-Marie-Tooth disease</td>
<td>III</td>
<td>60%</td>
<td>Small molecule</td>
<td>N/A</td>
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</tbody>
</table>

*Source: Biomedtracker®, July 2020*
Viltolarsen
Viltolarsen is an exon-skipping therapy in development for DMD by NS Pharma with its parent company Nippon Shinyaku. Viltolarsen is intended to treat the 10% of DMD patients with mutations amenable to exon 53 skipping. While exon skipping is not a cure for DMD, it has the potential to lessen the severe muscle weakness and atrophy that is the hallmark of the disease, and as such exon skipping therapies have been able to command high price points. Sarepta's Vyondys 53, which works in the same way as viltolarsen, is already on the US market, priced at an annual cost of $300,00012,13.

Risdiplam
Risdiplam, an SMN2 splicing modifier in development by Roche, is likely to be the first oral treatment for people with SMA as both Spinraza and Zolgensma are injectables. Applications to market Roche's SMA drug have already been submitted in eight countries including the US, where a decision is expected on 24 August 2020. Its initial target population is expected to include both newborns with type 1 SMA and type 2–3 patients up to the age of 25 years, providing a broad commercial and competitive opportunity. Furthermore, Roche has suggested that it plans to undercut both Biogen and Novartis on price in order to make up for being third-to-market. However, given that Zolgensma and Spinraza are two of the most expensive drugs in the world, risdiplam is still expected to be very costly14.

Zokinvy
Zokinvy (lonafarnib) is an orally active inhibitor of farnesyltransferase in late-stage development for Hutchinson-Gilford progeria syndrome, an ultra-rare condition in which children age too quickly and for which there are no approved therapies. Current treatments focus on managing symptoms, but Zokinvy is hypothesized to address the course of the genetic disease. Eiger BioPharmaceuticals' unconventional NDA includes data from two single-arm, open-label studies with a combined 63 patients that received Zokinvy and a historical control group of 103 untreated patients. After two years, mortality among Zokinvy patients was 3.7% compared to 33.3% for the untreated group, equivalent to a risk reduction of 88%15. Zokinvy has been granted Orphan Drug designation for progeria by the FDA and EMA, as well as Breakthrough Therapy and Rare Pediatric Disease designations by the FDA.

Lumasiran
Lumasiran, an RNAi in development by Alnylam, is slated to be the first drug approved specifically for the ultra-rare kidney disorder primary hyperoxaluria type 1. Lumasiran has been shown to help patients clear a toxic substance called oxalate from their kidneys and other vital organs.

In the Phase III ILLUMINATE-A trial, Alnylam’s drug met the primary objective of a significant reduction compared to placebo in urinary oxalate excretion over 24 hours, averaged across months three to six. If approved, lumasiran would become Alnylam’s third approved RNAi product, further validating the clinical success of its drug discovery platform.

**Casimersen**
Casimersen is another exon skipping therapy which is being developed by Sarepta Therapeutics to treat DMD patients with mutations amenable to exon 45 skipping. Casimersen would be the first available therapy to treat the 9% of DMD patients amenable to exon 45 skipping, and similarly to Vyondys 53 and Exondys 51 it is expected to be very expensive. With the potential approval of casimersen in June 2021, Sarepta would be able to target its portfolio to approximately one third of DMD patients. Similarly to its predecessor brands, Sarepta will face competition in the form of exon 45 skipping pipeline drugs, as Daiichi Sankyo has progressed its candidate (DS-5141b) into Phase II development.

**Arimoclomol**
Arimoclomol has the potential to be the first ever drug approved for the treatment of Niemann-Pick disease type C in the US. Arimoclomol acts by targeting heat-shock protein 70 (HSP70). It is thought that increased HSP70 expression assists in the correct folding of mutant NPC1 and NPC2 proteins, thus allowing them to process the accumulation of lipids. It is this abnormal build-up of cholesterol and other fats within various tissues in the body, including the brain, that drives the pathophysiology of the disease. Orphazyme announced in May 2020 that it has initiated the submission of its NDA for a rolling review by the FDA.

**Fosdenopterin**
Fosdenopterin is a cyclic pyranopterin monophosphate replacement therapy in development to treat patients with molybdenum cofactor deficiency (MoCD) type A. Currently, there are no approved therapies that alter the course of the disease, which results in severe and irreversible neurological injury. Fosdenopterin aims to reduce the build-up of toxic sulfites and alleviate CNS symptoms in infants and children with MoCD type A. BridgeBio Pharma subsidiary Origin Biosciences has initiated a rolling submission of an NDA with the FDA while two global clinical trials are ongoing, although until these produce data little is known publicly about the drug’s clinical profile.

**FCX-007**
FCX-007 is a genetically modified autologous fibroblast cell therapy that encodes the COL7

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gene, which is defective in patients with recessive dystrophic epidermolysis bullosa. Fibroblasts are harvested from the affected patient and transfected to encode functioning COL7 before being cultured and injected back into wound sites to aid in the healing process. FCX-007 has received several FDA designations including Orphan Drug, Fast Track, RMAT, and Rare Pediatric Disease. Fibrocell, now part of Castle Creek Pharmaceuticals, projects enrollment and dosing of patients will be completed in the Phase III trial of FCX-007 in Q3 2020, and that data collection for the primary endpoint will be completed in the fourth quarter of 2020.

**Leriglitazone**

Leriglitazone, developed by Minoryx Therapeutics, is an experimental oral medication for the treatment of adrenoleukodystrophy (ALD). While PPAR gamma agonists are best known for promoting peripheral insulin sensitivity in type 2 diabetes, leriglitazone has the ability to cross the protective blood-brain barrier and enter the CNS. Once there, it aims to prevent processes associated with ALD, including inflammation and oxidative stress, protecting nerve cells from damage. The EMA granted leriglitazone Orphan Drug designation in 2016, and the FDA followed suit in 2017. The FDA also granted leriglitazone Fast Track designation in January 2020. Currently, the efficacy and safety of leriglitazone is being evaluated in a Phase II/III clinical trial, with top-line results expected to be announced in Q4 2020. Additional evaluation within Friedreich's ataxia is also ongoing, owing to the drug's potential broad neuroprotective effect.

**PXT3003**

PXT3003 is an investigational combination therapy of baclofen, naltrexone, and sorbitol – three approved treatments that act on the nervous system – and is formulated as an oral solution that is given twice a day. PXT3003 is in development for the treatment of Charcot-Marie-Tooth disease type 1A (CMT1A), an inherited genetic disease in which the motor and/or sensory peripheral nerves are affected, resulting in muscle weakness and wasting, as well as sensory loss. There is currently no cure for CMT1A, and treatments include physiotherapy, splints, occupational therapy, and sometimes surgery. While its developers Pharnext have already established treatment efficacy in a Phase III trial, PLEO-CMT, a second confirmatory trial was requested by the FDA to address the formation of crystals in its high-dose formulation. Provided this additional clinical expense can be funded, PXT3003 is likely to become the first treatment specifically approved for patients with CMT1A.
Conclusion

The industry is increasingly focused on narrowly defined diseases and scientific advancements, and incentives for focusing on rare congenital and genetic diseases have led to the development of many new therapies that have the potential to transform patient outcomes. Yet as more high-priced therapies are approved, they continue to challenge affordability and access. Collectively, rare congenital and genetic diseases affect a considerable proportion of the population, and health systems are not equipped to keep paying the high prices associated with many recently approved therapies. If payers increasingly restrict treatment to certain subgroups, such as those who benefit most in trials, this may have a detrimental impact on innovation and development in the rare congenital and genetic diseases space.

About The Author

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Anna forms part of the leadership team at Informa Pharma Custom Intelligence, a team which specializes in pharmaceutical and healthcare consultancy. Anna's team informs investment, clinical development, and commercial planning decisions across the product lifecycle for top-tier and mid-cap pharmaceutical companies, as well as biotech and medtech companies.

Anna has a keen interest in rare diseases and has led multiple projects in this area including opportunity assessments, market landscapes, patient-based forecasts, and indication and product prioritization exercises.

Prior to joining the Custom Intelligence team, Anna was an analyst at Informa Pharmaprojects. Here, she expertly curated the drug development database, provided research support to clients and produced custom analytics projects, transforming clinical study data and drug data into actionable insights. Anna’s strong scientific background enables her to fully understand the therapeutic potential of developmental therapies. Before joining Informa, Anna completed the Wellcome Trust PhD training program in Infection and Immunology at Imperial College London, and she holds a first-class degree in Molecular Biology from the University of York.

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Accurate and timely intelligence about the drug development pipeline is vital to understanding the opportunities and risks in today’s biopharmaceutical marketplace—whether you are targeting an unmet medical need, investigating promising new therapies or researching drug development historical trends and treatment patterns. If you are providing contract research or other services in the pharma industry, you need to stand out. A solid understanding of your potential clients’ pipelines and competition will help you leave a lasting impression.

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