

An integrated patient-centric development plan, when applied to rare and orphan medicinal products (OMPs), can accelerate time to market by 12 to 36 months

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If I'm a person with a rare or orphan condition . . .

I might not know about my condition

The burden for patients suffering from any form of a rare disease typically starts with a late diagnosis. Finding and engaging these patients early with a sophisticated, robust, cheap and easy diagnostic workflow remains the challenge. Engagement with patient groups ensures that diseases don't go misdiagnosed or underappreciated.

Read the blog entry about Ehlers-Danlos syndrome (EDS) called *Thirty doctors have been wrong for 12 years: the medical odyssey of Denise B.*

“Yes, EDS has no cure, but getting diagnosed changed me a lot—for example, my attitude towards doctors, as well as towards myself. The most important thing was: I knew I wasn't crazy. My illness was not just in my head! I was able to cope with my condition in a completely different way.”



I might be the only one in my country with this rare disease ... ultra rare

In most cases, this disease is a mystery to researchers, as there are no models or guidance, no trials performed on patients and clear lack of natural history. Partnering with patient advocacy groups for advice and finding a patient to participate in the trial are common occurrences for these patients. Their help is important to the OMP life cycle.

Michael has hereditary spastic paraplegia type 50 (SPG50). Children afflicted with this genetic disorder present with a variety of symptoms, including global developmental delay, microcephaly, seizures, malformation of the brain and hypotonia.

“They told us Michael had this ultra-rare condition, and he was the only child in Canada with this condition. Honestly, our world fell apart.”



My family and I need constant physiological and physical support

Many patients with a rare disease face chronic disease involving multi-system dysfunction, without effective treatment, and require complex care. Multiple factors are leading to additional physical and psychological impairments for patients and families.

Harlem Globetrotters star Zeus McClurkin brought a belated birthday surprise to 10-year-old Ethan, who has a rare disease called ectrodactyly ectodermal dysplasia.



I may encounter social and emotional challenges unique to my condition

With complex or rare diseases, late diagnoses and misdiagnoses occur very often, which causes mental and physical burdens for patients and families. Most individuals will not be cured in their lifetimes. Identifying ways to improve QoL is crucial to patient-centered care in rare diseases.

Brothers Richard, 5, and Lennon McDonald, 6, have the rare condition ectodermal dysplasia (ED), which causes their hair, teeth and nails to grow abnormally.

“Sometimes it's truly heartbreaking. My son asked for hair for his birthday, which was difficult to hear, but they understand their condition now.”



My physician may lack understanding about my condition

The low prevalence of rare disease identification is due to the lack of knowledge of healthcare providers, which causes challenges for people with rare diseases. Relevance of the ability to acknowledge the patient's active role as an informed and involved partner in the treatment process is high.

Perez and her husband, Walter, found out their son has progressive familial intrahepatic cholestasis—an ultra-rare genetic liver disease that affects one in every 50,000 to 100,000 children born around the world. At first, they thought Armando might have an allergy.

“I tried different laundry detergents and different body washes, but he was still itchy. Then he turned yellow. I was like, ‘Well, that's not normal.’”



I value medical advancements that can empower my children

Availability of cyber-based health information and online groups has led to the emergence of the “expert” patient, who seeks a collaborative relationship with the physician. Patient-led communication and patient discovery of treatment via online research tends to be the norm for many people with rare diseases. Their role in their therapy and diagnosis changes the dynamic of the typical doctor-patient relationship.

Late infantile Batten disease, which is inherited through an extremely rare recessive gene, affects only one to three children in the UK each year. Most of those do not live to see their 20s.

Ellie Mae, six, and her four-year-old brother Caleb want to experience as much as they can before the devastating disease claims their speech, eyesight and mobility.

After being handed the heartbreaking diagnosis, the siblings' parents, Lynsey and Duncan, created the ultimate bucket list to make every second count before it is too late.



I might not have research treatment during my life

The volume of new treatments is a substantial improvement for patients, but most rare diseases do not yet have ongoing drug development and will not have a treatment available by 2030, highlighting a need for continued incentives to address research and treatment gaps.

Jeanie Stich, who has idiopathic pulmonary fibrosis (IPF), and her husband, Elfie, have constantly been on the move throughout their 32 years of marriage.

“Elfie and I spent that weekend after diagnosis praying, crying and trying to figure out what had just happened to our perfect life. I was devastated by the thought of no longer sharing a life with my husband, my kids and my seven grandkids.”

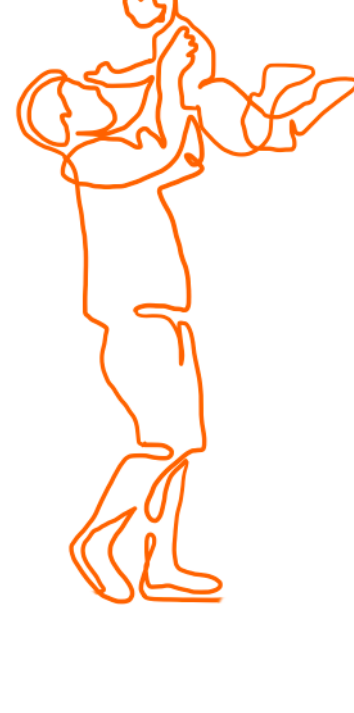


I may not have authorized treatment

Reimbursement has a strong impact on patients' effective access to orphan drugs, which may be restricted by difficulties with assessing the clinical value of these drugs as well as pricing issues. Prescribing restrictions and drug delivery systems influence the ease of supply for reimbursed orphan drugs.

At 8 months of age, through genetic testing, Paige was diagnosed with Dravet syndrome, which is a rare and catastrophic form of intractable epilepsy.

“This is my beautiful daughter Paige, otherwise known as the Princess Warrior. She is very deserving of the ‘warrior’ title as she has been through more in her 4 years of life than any adult should ever have to endure. She will never outgrow this condition and it affects every aspect of her daily life, along with our family's as well.”

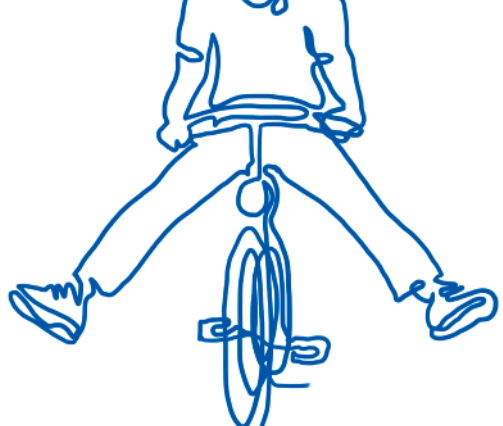


I want to help others with my condition

Patient involvement improves discovery, development and evaluation of new effective medicines, based on the collaborative identification and understanding of unmet needs and research priorities, the optimization of clinical study design, and the incorporation of patient views in regulatory activities.

Sam Clarke was two years old when he was diagnosed with Alport syndrome—a rare, genetic kidney disease that causes hearing loss, eye abnormalities and kidney failure. Sam, now 31, says:

“Throughout my twenties, I struggled psychologically with the concept of my kidneys failing, because of the uncertainty of when it would happen. My doctor recently told me that my kidneys will soon fail considering the rate at which they are declining. While I'm still fairly fit and able, I want to use this time to share my story, to raise money and awareness by doing this challenge.”



I want to engage

Opportunities for patient, family and patient organization involvement exist throughout the orphan drug life cycle. Improved patient involvement can drive a more relevant and impactful patient outcome and make medicine development faster, more efficient and more productive.

Samuel has osteogenesis imperfecta, also known as brittle bones disease.

“My son is truly one of the happiest kids you'll ever meet. He is funny, smart, silly, and always full of laughter and conversation. He is a social little boy with an infectious personality. He is stronger emotionally and physically than anyone I have ever met, and his resilience is astounding. But behind his smiles and tough exterior lies an unbreakable spirit determined to live each day to the fullest, refusing to let his rare condition define his life.”



The ADAPT model has 51 tangible and easily implemented levers with easily defined expected outcomes and resource requirements. To reflect ADAPT in everyday practice, we developed an integrated operational solution



Accelerate time to market by applying and implementing one or a combination of the efficiencies, opportunities and incentives available in the Rare and Orphan space tailored per specific asset, therapeutic area and patient needs and expectations

Accelerate Levers	Days / Months / Years
Agreed consensus on definitions and diagnosis	2 years
Innovative feasibility	8-12 weeks
Medicines adaptive pathways	1-2 months
Adaptive trial design	6 months +
Faster, smaller, targeted clinical development	Up to 3 years
Integrated PIP / Waiver	6 months +
Accelerated regulatory pathways & early access tools	6 months to 3 years
Early scientific advice	49 to 210 days
Accelerated assessment	60 days
Priority review	4 months
Conditional MA	~ 4 years
Agreed regulatory-grade RWE	6 months - 2 years
CUP, NPP, EAP	5-36 months

Leading and managing asset integration will accelerate our operational efficiencies by 20%.

Drive data collection and generate the evidence required at each inflection point for the asset during the life cycle to support acceleration in time

Drive Levers Examples

- Integrated evidence for success criteria in ODD
- Quantifying the potential substantial benefit of early access to inform stakeholders and expedite CMA/MAA and P&R
- Efficient integrated post-approval and follow-up measures
- OMP value and differentiation in a hyperdynamic competitive landscape

Anticipate risks, unknowns, complexities, new information in disease progression and flow, constant revision of experience with new market realities and future trends, shifts in stakeholder needs, digital data and technology updates

Anticipate Levers Examples

- Evidence vs. access conundrum
- Regular review of the investment vs OMP value and cost-effectiveness
- Disease/OMP budget impact vs. preferences: society/family/patient
- High upfront costs vs. downstream health benefits regular analysis
- Implementing short-term vs. long-term views and solutions for dynamic results

Partner with all key stakeholders early and through OMP lifetime/life cycle

Partner Levers Examples

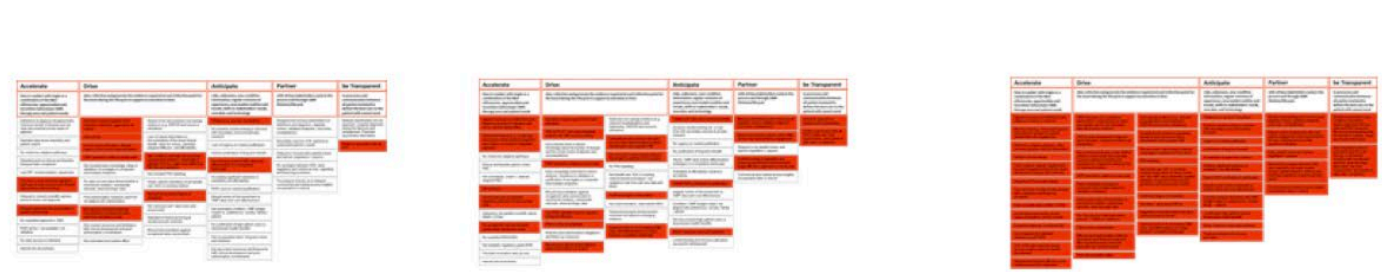
- Early patient engagement
- Having multiple stakeholders early in the development will create mutual understanding and consensus of eligibility criteria, validated endpoints, outcomes, comparator(s)
- Maximize the synergies between ODD, early regulatory and early market access
- Regulators and payers parallel consultation procedure

Transparent processes and communication between all parties involved

Transparent Levers Examples

- Incorporating the insights of multiple stakeholders early in the process, regular alignment during the life cycle and arrangement for the benefit of a patient
- Integrated evidence generation plan

Depending on current strategy, our analysis suggests an opportunity to accelerate time to market by 12 to 36 months



Each OMP after ADAPT diagnostics has:

- Identified potential differentiator in being first, best or different
- Detailed barriers to overcome to approval, reimbursement and use
- 5 main CSFs required in the development and commercialization
- Preliminary guiding strategy that needs to be executed per CSF in Regulatory, Clinical, RWE and Commercialization
- Opportunities to:
 - Accelerate time to market (months/years)
 - Drive required data collection and evidence generation
 - Anticipate risks, complexities in competition and potential unknowns
 - Partner with key stakeholders
 - Be transparent in competition and communication



ADAPT is our commitment to patients, bringing clinical and commercial together for superior innovation in the field.