Orphan drug development remains a specialised segment with limited players

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Recently, Syngene International was involved in the development of a drug for a rare disease that affects children. Dr Mahesh Bhalgat, COO, Syngene International, shares more details about the project, its impact, progress, potential and challenges in orphan drug development, evolving role of CROs in drug development and more, in an exclusive interaction with Lakshmipriya Nair

How has the COVID-19 pandemic transformed the industry's approach to drug development? What are the imperatives that led to this change? What have been the lessons in drug development over the past two years?

Drug development has seen acceleration, partly due to the agility displayed by the regulatory bodies around the world. Regulators have put together the required machinery for swifter and parallel approvals. However, given the need of the hour, this has been more targetted towards COVID-related drugs. So, has there been a broader benefit? Not quite as much, as the world was primarily focussed on fighting the pandemic.

While drugs related to COVID have benefitted from the acceleration, non-COVID drugs have two contributory aspects – firstly, organisations that didn't have the bandwidth to handle multiple programmes, have not been able to pursue non-COVID drugs at the same pace. We have seen some regulatory bodies around the world having to put things on hold; for example, FDA inspections of sites, which is a key step in the approval process, couldn't be pursued at the same pace. Secondly, we have also witnessed pharma and biotech companies increasingly outsourcing their drug development activities to CROs in various parts of the world, India being one of the key markets. By outsourcing, these companies could leverage the skills and expertise available in other markets to maintain their research pipelines.

Recently, you were involved in the development of a drug for a rare disease that affects children. Can you tell us more about the project?

I would like to use this opportunity to delve deeper into our approach to drive programmes and projects. Clients collaborate with us for our scientific expertise and approach, which includes our sharp focus on quality, infusion of cutting-edge technology and access to skilled scientists. As a strategic partner to our clients, often working as an extension of their internal scientific teams, we continue to bring them innovative solutions for complex scientific challenges. This approach isn't specific to any disease, drug or client. It is who we are, and it remains uniform across the discovery, development and manufacturing spectrum.

Let me offer an example of what I mean by this particular rare disease drug, which is approved for the treatment of pruritus in all subtypes of Progressive Familial Intrahepatic Cholestasis (PFIC). Similarly, Syngene has also received FDA approval to manufacture the drug Brexafemme (Ibrexafungerp tablets), which is useful for the treatment of life-threatening fungal infections. In both scenarios, the indications were different. The target population for a rare disease drug is different from that of a broad treatment targetting a therapeutic drug. For us, the approach is to ensure that we find the right solutions and get the drug through the next stage of the development pipeline or in them commercialisation pipeline, irrespective of the indication or target population it serves. The approach to solutions we provide changes as per the science it needs and the patient population that is targetted. Given our broad expertise in many diverse areas, whether it is a small molecule or a large molecule, whether it is a peptide or protein or an oligonucleotide, whether it's an oral formulation or an injectable formulation, regardless of any of these modalities, Syngene is able to provide the required services through its scientific staff effectively.

How was the process of developing this drug different from the drug development of diseases that affect larger masses? What were the major challenges faced and how were they overcome?

One of the key components related to the time required for developing treatments for rare diseases is getting the status of an orphan drug for accelerated assessment in the system. This status reduces the timeline for the regulatory approvals. For example, the EMA accelerated assessment means that the medicine is of major interest for public health. So, its time frame for review is 150 days rather than 210 days. Therefore, as the manufacturing partner for this drug, Syngene had to produce limited quantities of the drug substance to support the trial and meet tight timelines. The opportunity to do so lies through finding the most optimal routes for synthesis and also flawless execution.

Since, with orphan drugs, the patient population is limited, the trial size is not as large as with other traditional drugs, making data generation more manageable.

What is the current landscape of orphan drug development? What are the key learnings you would like to share with the industry stakeholders to improve the current scenario and help advance potential treatments for rare diseases?

In my opinion, the whole area of orphan drug development is a specialised area. If a company is committed to a blockbuster drug being launched in the market, then it also requires selling a large volume of that drug, and, therefore, needs a combination of unit cost and volume to meet its objectives. Orphan drugs are produced in smaller volumes and yet need to be affordable, which calls for the application of innovative solutions to managing costs at low volumes. This is certainly a different challenge than what is faced for drugs being pursued for diseases such as cardiovascular, diabetes, neurology, oncology, bone disease, and so on. Patient recruitment is an additional challenge that needs to be addressed since the disease prevalence is low.

On the other hand, any company that decides to work on an orphan drug also benefits from lesser competition in this space. Once the drug receives the orphan status and gets a priority review, the approval and launch can be accelerated leading to benefits for patients.

However, despite the pros and cons, this remains a specialised segment with limited players.

Are rare diseases finally gaining priority in the pharma industry's agenda? Is it going to be a focus area for Syngene in the coming years?

At Syngene, our focus and commitment is to deliver cutting-edge science to our clients and help them advance their product pipeline. Our clients come to us knowing that we apply our scientific expertise to problem-solving and that we add value by critiquing and challenging their scientific ideas, bringing our own expertise to the table. So, that's the opportunity, and it's also the marginal driver for long-term growth. It's about the intellectual added value that we can bring, which segues perfectly.

This approach remains consistent for all areas of our work, it can be a drug for a rare disease or can be for a highly prevalent disease. So, I don't think there is really any change for us in the need to focus more on rare diseases because the toolkit is what we continue to equip well for bringing strong scientific contribution. Through this approach, we provide support to the complete stream of drug discovery, development andmanufacturing aspects, leading to the launch of client products on the market for patients.

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