OUTLOOK FOR RARE DISEASE AND ORPHAN DRUG RESEARCH

Collectively rare diseases comprise a large segment of the global population. Developing effective treatments to combat these diseases demand heavy resources from biopharmaceutical companies — both monetary and scientific. Even though these diseases are singularly rare, the combination of governmental incentives to develop compounds for potential success, combined with public support to find cures for these diseases make the practice of R&D for Rare Diseases-Orphan Drug one of the fastest growing segments in the biopharmaceutical industry.

As a response to limited R&D activity in the early 1970's international regulatory bodies, assisted by patient advocacy groups lobbied for incentives to drive innovation in this area. As a result of the 1983 Orphan Drug Act in the US and the EU Regulation on Orphan Medicinal Products, 1999 the Rare Disease Orphan Drug awareness and activity has spurred new development. In the US, incentives include extended patent protection, tax credits on clinical research costs, annual grant funding, waiver in Prescription Drug User Fee Act (PDUFA) filing fees, and premium pricing for companies - to name a few. Similar incentives exist globally and are considered a priority as evidenced by the Joint European Medicines Agency (EMA), US Food and Drug Administration (FDA), and Japanese Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA) orphan medicinal product workshop in March 2014.

THE PIPELINE IS GROWING

With over 7,000 rare diseases registered, there are 452 compounds currently in development. Approximately 350 million people worldwide suffer from a rare disease. 50% of these patients are children. Growth in R&D for rare disease is growing at twice the rate of common diseases. The majority of rare diseases are in the areas of cancers and genetic disorders.[1]

THE DISEASES ARE COMPLEX

A major factor in orphan drug development is the complexity of the disease profile itself. Understanding the epidemiology of the disease and translating that to clinical trial design is daunting. Personalized medicine and genomic mapping have lent new insights in the origin of these diseases. These new tools allow researchers to identify narrow patient populations through genetic mapping, a critical step to overcoming the challenge of patient recruitment in these rare diseases.

CHALLENGING FEASIBILITIES AND STUDY DESIGN

Rare diseases in the US are classified as one patient in 200,000. This number varies globally, with most countries defining rare disease as one with a low prevalence in an existing sample size. However one issue is constant. Rare diseases make patient recruitment difficult. These small sample sizes challenge traditional clinical development feasibilities geographically, affecting site selection and patient enrollment.

CHALLENGING REGULATORY CLIMATE

Regulatory practice is by nature, inflexible. Before legislation was enacted to address rare disease, researchers and patients were left with few options. Traditional approaches to clinical studies for drug development were not well suited for the accelerated development and adaptive methods needed to address the issue of rare disease and the challenges imposed.

Many of the regulatory barriers to this research have been addressed. In the US, the FDA has addressed the need for accelerated review timelines; fast track and accelerated approval processes to facilitate development and review; priority review; and expanded access of patients to investigational products.

Strides are being made with regard to evaluation of new methods for clinical trial design, developing educational programs for researchers, and increasing communication with stakeholder groups — both in academia and advocacy. This outreach provides new hope for these patients.

Orchestrating regulatory issues across the globe will continue to be challenging, however, most regulatory authorities are addressing this important area.[2]

STAKEHOLDER GROUPS HOLD THE KEYS

The combination of patient scarcity for a disease, coupled with a high pediatric concentration makes enrollment a significant hurdle to overcome for study feasibility. The need to develop solutions given accelerated timelines have given rise to a new era of collaboration.

PATIENT ADVOCACY GROUPS

At the center of any disease is the patient. Before regulatory authorities recognized the importance of drug development for rare disease — 1980, US — only 10 compounds were approved. Globally, organizations such as the National Organization of Rare Disease (NORD), US; CORD — Canada; and EURORDIS, Europe, have been active to help establish an international focus on rare disease, which in turn has resulted in regulatory action to expedite research.[3]

These groups have driven international cooperation between regulatory bodies, investigators, researchers, and patients to develop common guidance for study approach, registries building, and other key tools to connect researchers and patients. Patients with rare diseases can find support systems, patient communities and news about their disease. Researchers can understand the challenges these patients face and adapt programs to drive enrollment and retention.

ESTABLISHED DISEASE REGISTRIES

Many rare diseases have established international registries. These registries include regulatory driven natural disease histories, benefiting researchers, and encouraging collaboration. These databases can provide invaluable insight into disease profiles and epidemiology, key biomarkers and other diagnostic methods for study support. In addition, working with these agencies can aid in overcoming the regulatory hurdles that exist.

ESTABLISHING PATIENT REGISTRIES

Organized systems using observational study methods to collect uniform data and establish agreed upon outcomes are vital. Best practices include ensured geographic reach, links to corresponding collaborative bio banks, minimum established Common Data Elements (CDC), and combined input by both patients and investigators.*

SUMMARY

The need is great and time is of the essence in rare disease studies. Taken disease by disease, the road ahead is challenging. However with the existence of new tools from cross disciplinary teams — applying innovation in study design, use of patient registries, and partnering with patient advocacy groups - the work for effective therapies continues. Harnessing of the power of these groups in conjunction with the patients who live with the disease each day will enable researchers to understand the way forward for improved treatments and therapies to combat rare diseases in the patient's lifetime.

REFERENCES

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