Navigating Innovation To Deliver For Patients

Christelle Huguet, Head of R&D at Ipsen, discusses how External Innovation is central to Ipsen's R&D strategy and provides a spotlight on Rare Disease, where the portfolio has seen strong movement in 2023.

Innovation is "really accelerating" in the pharmaceutical R&D space right now, according to Christelle Huguet, Head of R&D at Ipsen. There is greater connectivity and collaboration, enabling companies to bring together their expertise in different fields, as well as many exciting developments in biotech and academia that will certainly change the treatment landscape for patients in the future. However, we continue to see "changes and challenges" in the regulatory environment and so, if we want to really harness this innovation, then as an industry it is crucial that we connect the right incentives to scientific progress. Bridging that gap is far from easy but the team at Ipsen remains committed to working collaboratively to help move towards this collective goal. Ipsen's strategy is to exclusively source the best scientific innovation from biotech and academic institutions. Ipsen then helps to accelerate research and development by providing commercialization expertise across their key focus areas: Oncology, Rare Disease and Neuroscience.

"We are building a diverse and sustainable pipeline at every stage and through acquisitions, partnerships and collaborations, have expanded across early development, clinical programs, and also commercial assets," Huguet says. "Our expertise is used to complement the strengths of our partner. We add most value by using our internal know-how to translate early science into a clinical candidate molecule and take it through development all the way to patients."

New technologies are helping Ipsen continue to develop novel treatment solutions, she adds, including real-world evidence and digital technology and the use of artificial intelligence (AI) in clinical trial design to mine data more deeply. Ipsen has also used model-informed drug development (MIDD) to analyze data and work out how a new treatment could benefit more patients. Exploring the potential role for novel technologies remains a strong focus for Ipsen, while recognizing that it must add the right value, contributing to clinical development and the regulatory process to ultimately deliver innovations to patients.

Open Dialogue With Regulatory Agencies

"At Ipsen, we welcome the opportunity to work with global regulators as early as possible, including within our early development portfolio, to shape and prepare for clinical development with the aim of a submission following the completion of a rigorous development program," Huguet says. However, there are some circumstances where the regulatory environment could discourage innovation. "It could impact the types of indications that the industry might invest in. There are pressures on some geographies where the patient ultimately loses out, and that is concerning," Huguet says.

Open dialogue with authorities and regulators is paramount and must continue, she adds. More than that, "we need to continue to foster greater collaboration in the ecosystem between industry, regulators, and patient organizations, so we can encourage continued innovation and bring more options to patients." For Ipsen, the voice of the patient is particularly crucial, and it will continue to keep them at the center of its investment and focus.

To address the evolution of regulatory pressures, Ipsen has: invested in the requisite skills as well as in digital and AI; strengthened its regulatory group; kept in constant dialogue with regulators at all stages of medicine development. This helps Ipsen to understand the agencies' needs and where they can work more effectively with them.

"We have a dedicated team with cutting edge skill sets that complement our more traditional drug development capabilities, so that we can apply new technology where it's going to have the biggest impact," Huguet says. "We want to ensure our 'heritage' expertise remains equally advanced, so we train our people in all aspects of clinical development, trial design, and using predictive toxicology more in non-clinical drug safety."

Driving Progress In Rare Disease

Rare disease is one of Ipsen's three strategic therapeutic areas and the company has seen strong expansion in recent years through acquisitions and partnerships with both biotech and academic institutions. In particular, the rare disease clinical pipeline has more than doubled since 2020 with eight investigational programs in development, including in rare bone and rare liver diseases. The company defines rare diseases as those affecting up to six in every 10,000 people globally, but also in terms of whether patients can access treatments and how the treatment paradigm differs in different geographies.

A key consideration when developing treatments for rare and ultra-rare diseases is "to work carefully on endpoints and trial design" in Huguet's view. Endpoints that are well validated for larger indications are often not appropriate for rare diseases, where there is often no precedent in initiating clinical development programs. Ipsen works closely with regulators, patient associations, and healthcare professionals to refine endpoints that are both meaningful for patients and accepted by the regulators.

"Thinking about alternative trial design, we would like to see greater use of natural history and real-world evidence. For a rare disease where a child is born with a defect so severe that their life expectancy will be six to twelve months, there is no way we could use a traditional placebo-arm approach here," says Huguet.

Accelerated approval mechanisms have helped in such cases, enabling drug developers to quickly bring solutions to patients in need, sometimes defining the endpoint as development progresses. In the case of palovarotene "the first global Phase III trial crossed futility, largely due to the selection of an inappropriate statistical methodology. But the raw data clearly showed there was efficacy and so we worked with the FDA to look at the strength of the totality of the data, assess the risk-benefit profile, and listen to the voice of the fibrodysplasia ossificans progressiva (FOP) community. In the end, palovarotene was approved in the U.S. for people living with FOP.[1] That was trailblazing, and a true collaboration across all stakeholders from industry, regulators, clinical experts, and the patient community." Although this is not always possible, Huguet adds, it shows what can be achieved.

More generally, Huguet notes, there is more openness to using, as yet, unvalidated endpoints in rare disease research. There are also more opportunities for earlier discussions with regulators and modified trial designs in consultation with both regulators and patients. All this gives Ipsen the confidence to expand into new areas. The ultra-rare disease space, by contrast, is much harder to operate in. "It's going to need a different societal approach and a much longer conversation, but with commitment and drive across the ecosystem we can be successful."

CHRISTELLE HUGUET, HEAD OF R&D, IPSEN

Key Learnings

Distilling her experience of regulatory filing processes in rare diseases into advice for those developing programs today, Huguet says: "Talk early and often with the regulators. Work very, very closely with healthcare professionals on the endpoint itself. Really listen to the patients – what do they need?" The biggest impact may come from preventing disease progression, though this may be a long time coming because endpoints in slow-progressing diseases are very difficult to establish.

Other endpoints that should be considered, in her view, include quality of life – for the patient's family as well as the patient – because of the demands placed on them as caregivers. Drug developers should also think about the economic landscape and payers, so that insurers can understand what will make a big difference for the patient and what they should consider themselves.

Data are much less available in rare diseases than in other areas, such as oncology. Ipsen seeks to extract the most value by combining multiple data sets, including registry data, real-world evidence, and data collected by prospective studies sponsored by patient organizations. "All of these matter in terms of the rare disease environment and how we can best serve the patient," Huguet observes.

She believes that regulators are interested in 'new' forms of data but there is more dialogue to be had before they are used more widely. The field is evolving, and regulators may be taking it into account more in the oncology space, where accelerated approval is not always being followed by traditional confirmatory evidence. "It's piquing their interest, but we're not there yet in terms of truly using those datasets as a body of evidence on their own."

Future Potential

Looking forward, Huguet is resolute that the courage to pioneer science and trial design, alongside prioritizing listening to the patient, will be vital to drive drug development in the rare disease space. These foundations are not just limited to Ipsen's work in rare disease, but are at the core of the company's approach to their three therapeutic focus areas. "We believe that the best science is delivered by biotech and academic centers and are excited by the continued scientific progress we see across oncology, rare disease and the neuroscience landscape," explains Huguet. "We are confident that by uniting expertise through exclusively building our pipeline through external innovation, we can harness Ipsen's end-to-end excellence to convert today's molecule into tomorrow's medicine for patients around the world."

[1] Sohonos (palovarotene) is approved in the U.S. and Canada for the reduction in volume of new heterotopic ossification in adults and pediatric patients aged 8 years and older for females and 10 years and older for males with fibrodysplasia ossificans progressiva (FOP)