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By fostering collaboration among the government, industry stakeholders, and patient advocacy groups, we can create policies that promote early diagnosis and ensure a brighter future for patients

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Nicolas Linares of Ultragenyx Pharmaceutical Mexico highlights the company's commitment to developing innovative treatments for rare and ultra-rare diseases. He emphasizes the importance of collaboration with healthcare systems and the need for a focused approach to address the unique challenges faced by patients in Mexico.

What can you tell us about Ultragenyx, its mission, and the company’s focus on rare diseases?

Ultragenyx is a biotech company dedicated to developing treatments for rare and ultra-rare diseases that have never been treated before, founded less than 15 years ago by our CEO, a pediatric geneticist and clinical physician with extensive experience in rare disease research. His involvement in creating the first enzyme replacement therapy for MPS1 (Mucopolysaccharidosis Type I),sparked his passion for tackling the unmet medical needs of patients with rare conditions. This commitment to patients is at the core of Ultragenyx’s mission to transform the lives of people with rare disease.

Since its establishment, the company has become the most productive rare disease company in the industry, with three FDA-approved treatments: one for X-linked hypophosphatemia (XLH) and tumor-induced osteomalacia (TIO), another for Mucopolysaccharidosis type VII (Sly syndrome), and

a third for long-chain fatty acid oxidation disorders (LC-FAOD). These treatments are already commercially available in the U.S., and we expanded our footprint into Latin America within six or seven years of U.S. launch, recognizing the region as a key market with patients in need of these therapies.

Ultragenyx's approach to treatment development is distinguished by its flexibility in using the most suitable modality for each disease. We work with various platforms, including monoclonal antibodies, enzyme replacement therapies, small molecules, and gene therapy. Our approach has led to the delivery of multiple first-ever rare disease treatments at a faster speed than the industry average. While much of our work is still in the research and development stage, we have an exciting pipeline, with plans for additional commercial launches in the future. Our goal is to bring transformative therapies to patients as quickly as possible.

What motivated Ultragenyx to expand into Latin America, given the regulatory complexities and challenges in markets like Mexico?

The decision to expand into Latin America, particularly Mexico, was primarily driven by the unmet medical needs in the region. One of the early indicators of this need was the involvement of Mexican and Brazilian patients in our clinical trials. These patients were excellent candidates for our therapies, which highlighted the demand for these treatments in Latin America.

While there are undoubtedly regulatory challenges and market access hurdles in the region, the opportunity is undeniable. Other rare disease companies have demonstrated that, despite the complexities, it is possible to succeed with the right strategy. Over time, the market has become more receptive to treating rare diseases. If you develop a well-thought-out plan, it is possible to enter the market earlier than anticipated.

Our launch of the treatment for XLH across Latin America has been a great success, proving that the region offers tremendous potential. When you consider the major markets like Brazil, Mexico, Argentina, and Colombia, the population exceeds 400 million, making Latin America a highly significant and strategic region for rare disease therapies.

How does Ultragenyx navigate the challenges of diagnosing rare diseases in Mexico, given the complexities in clinician expertise and diagnostic resources?

Addressing the challenges of rare disease diagnosis in Mexico requires a multifaceted approach. One of our primary efforts has been to raise disease awareness and ensure that clinicians are equipped to identify and refer patients. Mexico's healthcare system, with its three levels of care, plays a crucial role in this process. Complex cases typically reach third-level hospitals, such as the national health institutes, the Unidades Médicas de Alta Especialidad (UMAE) within IMSS, and national centers within ISSSTE. These institutions are pivotal in diagnosing rare diseases, and by establishing strong medical education programs, we can enhance the ability of clinicians to recognize and manage such conditions.

Another critical gap we are addressing is the lack of molecular diagnostic testing, which is essential for confirming rare disease diagnoses. Through public-private partnerships, we support diagnostic testing services to fill this void. Once a patient is screened and there's a strong suspicion of a rare condition, a test to confirm the diagnosis, particularly focusing on genetic mutations, is provided. This process ensures that when payers are asked to reimburse treatments, they have full confidence in the accuracy of the diagnosis. By combining focused medical education and accessible diagnostic services, we ensure that patients are properly identified and receive the care they need.

What is the current state of Mexico's regulatory framework for rare diseases, and what improvements are needed to align it with global standards?

Mexico's regulatory framework for rare diseases is still developing, and while there is a legal definition in place, there isn't a comprehensive, detailed framework. At present, the process functions through exception mechanisms that provide orphan drug recognition. Although this approach allows us to bring our therapies to market, it lacks the structured clarity that would make the pathway smoother, especially as more complex therapies like gene and cell therapies emerge. Organizations such as the Asociación Mexicana de Industrias de Investigación Farmacéutica (AMIF) are actively working with COFEPRIS (Mexico's regulatory agency) to refine and develop more specific guidelines for rare diseases and advanced therapies.

A positive aspect of the current system is the ability to base submissions on data from international regulators like the U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMA), which is crucial for rare diseases, where building local data can be challenging due to small patient populations. Additionally, Mexico allows us to bring international product presentations, such as those used in the U.S. or EU, without the need for a specifically tailored Mexican version. This

flexibility helps with production and demand planning However, while these mechanisms are helpful, they are not part of a formal regulatory framework, and it would be more efficient to have a clearer, standardized process.

While flexibility is important, particularly in data recognition, the key challenge moving forward is ensuring that the regulatory framework remains balanced—rigorous enough to ensure quality but not so complex that it deters investment in the rare disease sector. Striking that balance will be crucial for encouraging continued innovation and market entry in Mexico, to ultimately ensure that families facing a rare disease diagnosis can access the medicines they need

How does the regulatory framework for rare diseases in Mexico influence Ultragenyx's efforts to bring treatments to the region, and what progress has been made in expanding across Latin America?

Mexico's regulatory framework for rare diseases has presented both opportunities and challenges as we work to bring treatments to the region. The ability to use global regulatory data has been a significant advantage that has allowed us to streamline the process and enter the market much sooner than we would have been able to otherwise. In terms of progress, in Mexico our treatments for XLH MPS VII, and LC-FAOD have all been approved by COFEPRIS and included in the national reimbursement list. In Central America, we are in the early stages of expansion, working with a distribution partner. Our focus is on submitting regulatory dossiers for the XLH product next year, starting with Costa Rica, Guatemala, and Panama as key markets for growth.

How did Ultragenyx achieve success in Mexico, particularly with having your entire portfolio reimbursed, and what were the challenges in securing reimbursement?

I'm very proud of what we've accomplished in Mexico. It's the only country in the world where we are commercially selling all four of our medicines. This is particularly exciting because, in other regions like Europe, not all of these products are available. Achieving this success in Mexico has been the result of strong partnerships—working closely with the government, the medical community, physicians, hospitals, and payers to ensure that the value of treating rare diseases early with innovative therapies is clearly understood. Building a community around the patients.

What has made our story compelling is the real, life-changing impact of our treatments. For example, with XLH, children suffering from the disease experience phosphorus loss, leading to

bowed legs (rickets). Early intervention can reverse this damage, and after months or years of treatment, children who once had bowed legs may be able to lead normal lives. When you can show such clear, transformative results, it becomes a powerful value proposition. It’s not just about managing the disease—it’s about delivering disease-modifying treatments. This has resonated strongly with payers, physicians, and patients, making them eager to embrace these treatments.

Our approach goes beyond just submitting regulatory dossiers. We’ve made sure that all stakeholders are deeply involved. Physicians, for example, see the clinical benefits firsthand and become advocates for the therapies, pushing institutions to provide access. Their advocacy creates a virtuous cycle, where it’s not just us requesting approval but also physicians highlighting the urgent need for these treatments.

At the same time, the healthcare system in Mexico has become more open to evaluating rare diseases and orphan drugs quickly. This includes not only the regulatory bodies and HTA agencies but also healthcare institutions. While the patient population may be small, the understanding that these patients have no other treatment options has created a sense of urgency. All these elements combined have been key to our success in securing reimbursement and bringing our products to market.

How does Mexico, with its limited healthcare spending, approach the treatment of rare diseases, and what role do physicians and patient advocacy groups play in this process?

Despite Mexico’s limited healthcare spending, the small number of patients with rare diseases helps to balance the overall cost. While the individual cost of treatment may be higher than for more common conditions, the limited patient population means the financial impact on the system is relatively low. The challenge lies in allocating resources to these few patients when hospitals face larger numbers of patients with other conditions.

In Mexico, the main advocates for rare disease treatments are physicians. Unlike in some countries, patients themselves are not directly involved in the reimbursement process, particularly within the public healthcare system. Physicians play a crucial role by advocating on behalf of their patients—submitting cases, pushing for budget allocation, and navigating the complex bureaucratic processes. If a physician is truly committed to securing the best treatment for their patient, they will often drive the entire process forward, ensuring the necessary approvals are eventually obtained.

Patient advocacy groups, while active, tend to focus on broader issues such as raising awareness, influencing public policy, and advocating for legislative changes related to rare diseases. They are not yet directly involved in the reimbursement process on a case-by-case basis.. However, there is potential for this to change in the future, especially as Mexico evolves its approach to healthcare. In Europe, for example, patient groups are integral to discussions with regulators, particularly for advanced therapies like gene therapy, and this model could be beneficial in Mexico as well.

Moreover, these advocacy groups play an essential role in pushing for initiatives like newborn screening, which is critical for early diagnosis. Early detection can significantly improve outcomes, even in cases where treatments may not yet be available. As Mexico's healthcare landscape continues to develop, the involvement of patient groups in shaping policies and driving initiatives like screening will be increasingly important.

For now, physicians remain the key advocates, but the role of patient groups is expected to grow as the system evolves.

How does the pricing negotiation process work for rare disease treatments in Mexico once a product is included in the national reimbursement list, and are there mechanisms for ongoing discussions?

One of our core values at Ultragenyx is responsible pricing, which has been crucial to our success in Mexico. We recognize that pricing for rare diseases and orphan drugs can be complex. Our primary focus is to ensure that as many patients as possible can access these life-changing treatments.

Once a product is listed in the national compendium, there are opportunities for further discussions. The government may reach out to renegotiate during the national contract review process. These discussions are essential for determining how many patients they can treat and what their budget allows. Our approach is always collaborative, with the goal of ensuring that innovation reaches the patients who need it most. Price increases are very rare, even for inflation, but we remain open to ongoing conversations about how we can work together to expand access.

Ultimately, our aim is to ensure that once we achieve orphan drug recognition and inclusion in the national compendium, patients are receiving the treatments they need. If patients aren't being treated, then we haven't fulfilled our purpose. This is why maintaining open and constructive dialogue with payers is key to ensuring the best outcomes for patients.

How is Ultragenyx addressing data collection and patient follow-up, particularly as you move into advanced therapies like gene and cell therapies, and what challenges do you anticipate in Mexico regarding data and reimbursement?

Data collection is essential, especially as we shift towards more innovative therapies like gene and cell therapies. At Ultragenyx, we recognize that providing value goes beyond pricing or diagnostics—it's about ensuring that treatments deliver the expected outcomes. To support this, we collaborate with healthcare institutions and payers to implement real-world evidence generation. For instance, when a therapy is accepted, we propose follow-up studies that track patient outcomes at key milestones, such as 40 or 80 weeks, allowing institutions to compare their own data with clinical trials. We are already working with IMSS (Instituto Mexicano del Seguro Social) on this and have initiated a cross-collaboration between AMIF (Asociación Mexicana de Industrias de Investigación Farmacéutica) and IMSS to ensure ongoing data collection and research partnerships.

When it comes to more complex therapies, such as gene therapy, the challenges become even more pronounced. For example, although the first gene therapy has been approved in Mexico, reimbursement is still an open question. This is where innovative pricing and access models will play a critical role. Many of these therapies propose long-term benefits, but with limited data on their durability. This raises important questions: What happens if the therapy's effects diminish over time? Should payments be structured over time, or should there be refunds if the therapy fails after a certain period? These are the kinds of discussions that will shape the future of healthcare, and while no standard model exists yet, these conversations are already beginning to take place.

Mexico's smaller patient population actually presents a unique opportunity to lead in data collection. With a more manageable number of patients, we can potentially move ahead of other countries, even in emerging regions, by building comprehensive datasets. As more advanced therapies—such as CRISPR and other gene-editing technologies—enter the market, it will challenge not only the industry but also regulators and payers.

What is the future vision for Ultragenyx in Latin America, and how do you see the company evolving over the next few years?

Our vision is clear: to lead the future of rare disease medicine. This involves not only building a strong pipeline but ensuring that our treatments are accessible to the patients who need them. The real challenge lies in bridging the gap between innovation and patient access. We don't want to develop cutting-edge therapies only for them to be out of reach. It's crucial that we work within healthcare systems to ensure these therapies are delivered to patients.

Looking forward, we're moving toward commercialization of our late-stage clinical pipeline. Our vision is truly global, and that includes a strong focus on Latin America. We see the region, particularly Mexico, as a key driver in our growth strategy. Mexico's increasing regulatory predictability is giving companies more confidence to invest and plan for long-term success. Scientifically, Mexico is incredibly diverse in terms of genetics, with unique populations, such as the Mennonites in the north and indigenous groups in Oaxaca and Jalisco, offering valuable insights into rare diseases. This genetic diversity makes Mexico a vital region for research and clinical trials.

Do you see Mexico becoming more involved in clinical trials, especially in aligning with international standards?

Mexico has enormous potential to become a key player in global clinical trials, but this will require aligning its regulatory framework with international standards like those set by the International Council for Harmonisation (ICH). We've had discussions with stakeholders, including AMIIF (Asociación Mexicana de Industrias de Investigación Farmacéutica), about the opportunities this could unlock. Currently, we're losing trial sites to countries like Guatemala and Argentina because our processes aren't as agile as they need to be.

The opportunity is not just in healthcare but also in economic growth. If Mexico can streamline its regulatory processes, it could attract significant investment—potentially increasing clinical trial investments from $240 million to as much as $4 billion. For smaller companies like Ultragenyx, the bureaucratic delays are already a major hurdle, and this challenge is even greater for larger pharmaceutical companies. If we can improve these systems, Mexico could not only retain existing trials but also attract more advanced stages, such as phase 2 and phase 3 trials, bringing significant benefits to the country.

What have been your key learnings during your journey with Ultragenyx, and how prepared do you feel to advance in the rare disease market?

Reflecting on my journey with Ultragenyx, I've encountered various challenges, yet each presented an opportunity to discern effective strategies and potential pitfalls as we built our presence from the ground up.

A cornerstone of our success has been our steadfast commitment to keeping patients at the forefront of our efforts. This patient-centric approach ensures that every aspect of our strategy aligns with their needs, which is vital for driving positive outcomes. Furthermore, the team we have assembled has been instrumental in our achievements. Attracting dedicated professionals who are passionate about our mission has allowed us to foster a collaborative environment where everyone engages in cross-functional activities, gaining a deeper understanding of the healthcare ecosystem.

Our strategy hinges on crafting a compelling value narrative that resonates across various stakeholders. This is often overlooked, as many organizations prioritize developing immaculate health economic dossiers. However, if the value proposition of our treatments isn't communicated effectively to physicians, it ultimately fails to resonate. When physicians advocate for our therapies to representatives from IMSS (Instituto Mexicano del Seguro Social), it initiates a crucial alignment of interests.

In contrast to the traditional silos often seen in larger pharmaceutical companies, where departments such as health economics, sales, and medical affairs operate independently, we have succeeded in integrating these functions. By collaboratively sharing our value story with payers, health economic reviewers, physicians, and institutions, we ensure that all parties involved understand our mission, including the patients themselves.

This holistic approach has not only been effective for our current therapies but will also serve as a guiding principle as we expand into new indications. The lessons learned throughout these five years at Ultragenyx in Mexico have equipped us with the insights necessary to navigate the complexities of the rare disease market, positioning us for continued growth and impact.

What additional insights do you have regarding the future of Ultragenyx in Mexico, especially in relation to the new government and the challenges faced by rare diseases?

As we look to the future, a primary concern is how to collaborate effectively with the new government to improve the purchasing process for rare diseases and orphan drugs. Recent challenges, such as delays in contract executions and transition of many decision makers, have

resulted in some patients going without necessary therapies for extended periods—sometimes as long as five to six months. It is imperative that we establish a more efficient purchasing system to ensure consistent access to treatments for our patient community.

In the short term, we are eager to engage with the new health authorities to elevate the focus on rare diseases. This initiative aligns with the broader trend in the pharmaceutical industry, where many companies are increasingly targeting niche conditions in their research and development efforts. To navigate this evolving landscape, we must work alongside the healthcare system to enhance the overall ecosystem, ensuring it is prepared to accommodate and treat patients effectively.

We have made significant strides in raising awareness, securing reimbursements, and improving access to diagnostics—especially as the costs of genetic testing have decreased, making these services more accessible. However, the broader healthcare agenda continues to predominantly spotlight conditions such as diabetes, hypertension, HIV, and oncology.

We believe it is crucial to establish a dedicated focus on rare diseases within the healthcare framework, complete with specific programs and funding to address these conditions. In Mexico, an estimated six to seven million people are affected by rare diseases, underscoring the need for a distinct framework that prioritizes their treatment. By fostering collaboration among the government, industry stakeholders, and patient advocacy groups, we can create policies and initiatives that promote early diagnosis, newborn screening, and other critical areas. This collaborative effort will ultimately ensure a brighter future for patients and enhance access to the innovative therapies we can provide.

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