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Shaping the Future of Drug Delivery: Orexo's AmorphOX® Unlocks New Possibilities for Critical Medicines

Formulating therapeutics as powders offers significant advantages over liquids, particularly for stabilizing fragile compounds that degrade under varying environmental conditions. This approach enhances molecular stability, extends shelf life, and eliminates the need for cold chain logistics. Orexo has emerged as a leader in the intranasal delivery of powder-based medications thanks to its proprietary AmorphOX technology. To learn more about powder-based drugs, their transformative qualities, the advantages of intranasal delivery, and the characteristics of AmorphOX, we spoke with Orexo's Senior Vice President and Head of Research and Development, Robert Rönn.

What is powder-based formulation technology?

Robert Rönn, Senior Vice President and Head of Research and Development

Formulating powder-based products involves converting active pharmaceutical ingredients into fine, dry particles that can for example be delivered by inhalation or intranasally. In practice, this can be done by either spray drying or freeze drying using specific stabilizing excipients. Unlike traditional nasal liquid spray formulations, powders may not require preservatives, reducing formulation complexity and making them purer for patients.

Nasal drug-delivery enables rapid absorption through the mucosal membranes, offering a non-invasive, needle-free alternative to injections. The fast absorption makes nasal products ideal for emergency treatments and therapies requiring immediate effect.

What are the transformative aspects of powder-based formulation technologies?

Powder-based formulation technologies have clear advantages over traditional liquid-based systems. One of the most critical benefits is thermal stability, allowing medicines to withstand fluctuating temperatures without degradation. This eliminates reliance on cold chain logistics, simplifying global distribution and making it far easier to reach patients in remote or resource-limited settings.

> **"Powder formulations may also extend shelf life and preserve therapeutic efficacy over time.**

Powder formulations may also extend shelf life and preserve therapeutic efficacy over time, which is especially crucial for sensitive compounds including vaccines, biologics, and emergency medicines such as epinephrine. In addition, the dry format reduces the risk of microbial contamination and improves handling flexibility. These qualities make powder-based delivery especially well-suited for mass deployment in emergency or pandemic scenarios.

While the advantages are compelling, the transition to powder formats comes with its own set of challenges, particularly around scalability and advanced manufacturing techniques. At Orexo, we have invested in manufacturing technologies and partnerships to ensure robust, scalable production of powder-based products for nasal delivery. We need to ensure that the benefits of these drugs can be realized at a global scale.

Could you elaborate on how AmorphOX® was developed?

It all started with the development of OX124, our nasal naloxone rescue medication, formulated to save the lives of people experiencing overdoses caused by powerful synthetic opioids. We knew that developing a liquid spray would probably be simpler, but we could see the potential and benefits of using a nasal powder instead.

We started by evaluating different concepts of formulating a dry powder and after thorough assessment, we decided to proceed with a monoparticulate powder – we wanted to bring all the materials needed for each product into a single particle. Monoparticulate powders overcome one of the biggest challenges with more traditional dry powder blends, which is that particles of various sizes separate and can cause manufacturing issues.

With AmorphOX, we dissolve all the materials into a solution and then spray dry the product to create a monoparticulate powder. Spray drying is an established, scalable manufacturing process.

It's taken us 8 years of research, during which time we've experimented with the AmorphOX technology across more than 500 formulations, using more than 20 different molecules and conducted 5 successful clinical studies.[1] All this knowledge features in our researchers´ daily work as we apply AmorphOX to new molecules and explore different therapeutic areas.

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What challenges have you experienced during your research?

A key challenge we faced was to identify suitable excipients and the appropriate combination with different active ingredients. This contributes to critical attributes of the powder, such as chemical and physical stability, dissolution speed and ultimately pharmacokinetic properties once delivered to patients.

It's taken us time to work through the spray-drying process to produce a powder with the desired properties, such as a controlled particle size. This is especially important when you want to administer the powder in the nose and know that it will stay there and not go into the lungs. We're delighted to have established a robust manufacturing process, even at commercial scale, through our significant investments into research and development.[2]

Another challenge we have faced during the development has been to protect the powder from coming into contact with moisture, which we've achieved through the development of a robust secondary packaging.

Regulatory processes for novel, groundbreaking formulation technologies are complex, particularly when it comes to emergency use combination products that integrate both a drug and a device. In the

development of OX124, which is currently in the regulatory review phase with the FDA, we've had to learn the hard way about all the governance and manufacturing requirements that are needed for approval. It's something we take seriously as ultimately it's to protect the safety of patients and prescribers.

What makes AmorphOX® powder technology innovative?

Superior stability is the most significant advancement over liquid-based products. During research, we saw very early on in our data that the powder form improves the stability of small molecules. We've researched this extensively, testing different formulations and APIs, including large, biologically sensitive molecules, for example proteins and vaccines. To put this into perspective, proteins and vaccines in liquid form are often stored at -80 degrees centigrade and need to be kept under cold conditions at every step of the supply chain, but when combined with AmorphOX in a powder form, this requirement disappears.

For OX640, our adrenaline product in the clinical development phase, the stability and dose conformity are outstanding compared to today´s standard treatments. The amount of the drug in a typical autoinjector product actually reduces as it moves closer to the expiry date. When it's first issued, there's around 115% of 0.3mgs epinephrine available, and by the time it goes out of date, it may be around 80%, which is only 0.24mgs. With OX640, our nasal epinephrine product, the dose starts at 2mgs and remains at 2mgs for the duration of the product lifecycle because it has better stability and dose conformity.[3]

We have recently successfully completed an in-vivo proof-of-concept study of a vaccine in partnership with Abera Bioscience. The data demonstrates the potential of AmorphOX for the development of powder-based vaccines with transformative benefits for patients, clinicians and healthcare systems globally.[4]

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What are the advantages of nasal administration?

Perhaps the most significant advantage for many patients is that it's needle-free. Not only does this make it a more comfortable option, it also gives patients with needle-phobia an alternative treatment choice. Needle fear is widespread and associated with avoidance behaviours, even where the injection is needed to treat a severe medical condition.[5]

For vaccines, which are commonly administered through injections by a healthcare professional in a clinical setting, powder-based nasal products could be self-administered at home, empowering patients to use them wherever they are in the world. This would save healthcare professionals valuable time and resources and reduce carbon emissions across supply chains. It's an exciting and growing opportunity space, although it needs more research.

Another important advantage of the nasal administration route for vaccines is that it has been proven to provide better protection than with injectable vaccines. This is because, while both nasal and injected products stimulate a systemic immune response, when you vaccinate in the nose, the body also creates

a local immune response. As many viruses enter the body through your mucosae, including those in the nose, the local immune response that's triggered in the respiratory tract may provide patients with a first line of defence. [6]

What is the long-term strategy with AmorphOX®?

Orexo was founded over 30 years ago with a clear vision to develop innovative drugs using proprietary drug-delivery technologies. With AmorphOX, we are continuing that legacy as the platform is the backbone of our future product pipeline.

Unlocking the full potential of AmorphOX is central to our growth strategy. Powder-based medications are advancing rapidly, and the versatility of this technology opens up a wide range of opportunities.

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We're well positioned to drive this forward at Orexo, but we also see significant value in partnering with other pharmaceutical companies, where our technology can enable exciting new possibilities for their product candidates.

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About Orexo
Orexo is a Swedish pharmaceutical company with 30 years of experience developing improved pharmaceuticals based on proprietary formulation technologies that meet large medical needs. On the US market, Orexo provides innovative treatment solutions for patients suffering from opioid use disorder. Products targeting other therapeutic areas are developed and commercialized worldwide with leading partners. Total net sales in 2024 amounted to SEK 590 million, and the number of employees 110. Orexo is listed on Nasdaq Stockholm's main list and is available as ADRs (ORXOY) on the OTCQX market in the US.

For more information on Orexo, visit www.orexo.com. You can also follow Orexo on X, LinkedIn, and YouTube.

[1] OX124: Positive results from human PK study assessing Orexo's new intranasal naloxone formulations for opioid overdose reversal; link PR. Orexo announces positive results from pivotal trial for its leading pharmaceutical pipeline asset OX124; link PR.
OX125: Positive results from human PK study assessing Orexo's intranasal nalmefene formulations for opioid overdose reversal; link PR.
OX640: Orexo announces positive data from phase 1 clinical study for OX640 - a nasal epinephrine rescue medication for allergic reactions; link PR. Orexo announces positive topline data from clinical study of OX640 in subjects with and without allergic rhinitis; link PR

[2] Henriques, P., Fortuna, A., Doktorovová, S. (2022). Spray dried powders for nasal delivery: Process and formulation considerations. *European Journal of Pharmaceutics and Biopharmaceutics*. **176**, 1-20.

[3] OX640: Epinephrine Nasal Powder - a sustainable and reliable option for the treatment of anaphylaxis; link https://orexo.com/media/o50cci0y/eaaci-2025-nasal-epinephrine-stability-final-1.pdf. Bioavailability and Stability of Epinephrine Nasal Powder Formulations for Treatment of Anaphylaxis; https://orexo.com/media/k1vhowgj/ox640-001_aaaai_poster-feb-2024-1.png.

[4] Vaccine in vivo study: Orexo announces positive data for powder-based intranasal vaccine formulated with the AmorphOX technology; link PR.

[5] https://pmc.ncbi.nlm.nih.gov/articles/PMC9678288/#:~:text=Utilizing%20non%2Dinvasive%20alternatives%20(94.1,non%2Ddevice%2Drelated%20approaches.

[6] Kiyono, H., Ernst, P.B. Nasal vaccines for respiratory infections. *Nature* **641**, 321–330 (2025). https://doi.org/10.1038/s41586-025-08910-6.