SMI TECHNOLOGY

How Soft Mist Inhalers Support Improved Biopharma Drug Delivery

By: Nicolas Buchmann, PhD

INTRODUCTION

Worldwide, rising cases of chronic lung conditions, such as asthma, cystic fibrosis, pulmonary arterial hypertension (PAH), and chronic obstructive pulmonary disease (COPD), are driving demand for inhalation drug delivery devices.

Some 262 million people were living with asthma and 212.3 million with COPD globally in 2019, and case rates for these conditions are expected to rise by 7% and 23% respectively over the next 20 years.[1-3] It is estimated that up to 50-70 million individuals, almost 1% of the world's population, are affected by PAH worldwide — a figure that is expected to rise over the next few decades as the global population grows and ages.[4] According to estimates, 162,428 people are living with cystic fibrosis worldwide.[5]

Inhalation is the ideal route for delivering drugs to the target site within the lungs to tackle these pulmonary conditions. It is no surprise, then, that the inhalation drug delivery market is forecast to reach a value of $18.6 billion by 2029, growing at a compound annual growth rate (CAGR) of 3%.[6]

This is not the only factor in the growth of inhalation as a delivery route. One of the most significant factors is the rapid rise of the biopharma segment — expected to enjoy a CAGR of 7.8% from 2022 to reach $719.84 billion by 2030.[7]

Traditionally, biologics have been delivered parenterally to avoid the gastrointestinal route. However, an intravenous injection can be unpleasant for patients, as 20%-50% of adults have a fear of needles, leading to a high rejection percentage of needle-based therapies. Administration of these treatments is often limited to a clinical setting, further increasing patient burden while impacting the limited resources of healthcare professionals (HCPs).[8]

Developments in inhalation delivery technologies, such as soft mist inhalers, mean that inhalation is now a viable alternative delivery method for many biologic formulations.[9]

The Resyca® Soft Mist Inhaler.

MARKET OPPORTUNITIES FOR BIOPHARMA

As the biopharmaceutical industry grows, it is becoming increasingly competitive. Several blockbuster biologic therapies are due to lose their exclusivity in the next few years, including four of the best-selling biopharmaceutical drugs of 2020: Humira, Revlimid, Eliquis, and Keytruda.[10] These patent expiries are, in part, driving the expansion of the biosimilars market — the segment is expected to reach a value of $75 billion by the end of the decade, with a CAGR of 15% between 2020 and 2030.[11]

Faced with the possibility of new rivals entering the market, product originators need to reconsider the life cycle of their therapies to maximize the value of their investments. Reformulation into inhaled treatments can offer the potential to support drug developers in extending their product life cycle while enhancing the lives of the patients using the therapies.

NASAL ADMINISTRATION RISING UP THE BIOPHARMA AGENDA

The nasal administration route is also being considered increasingly for the reformulation of biologics. Recent studies have highlighted the benefits of the nasal route for a wide range of biopharmaceutical formulations compared with the traditional parenteral route.[12]

There are unique advantages to using the nasal cavity for the systemic delivery of a variety of protein and peptide drugs, thanks to its large, 150 cm^2 absorption area, which is highly vascularized, with a similar permeability to the small intestinal mucosa. Nasal inhalation is also easy and non-invasive to administer, offers rapid onset of action and avoids gastrointestinal degradation and hepatic first-pass effects.[11]

Studies have shown that the delivery of insulin from the nose to the distal regions of the brain is enhanced via nasal administration.[11] In addition, mucosal delivery of vaccines has been found to offer a more pronounced and longer-lasting effect than traditional injection.[13] Harnessing this route triggers a strong protective immune response at the principal sites of pathogen infection. The induction of adaptive immunity at mucosal sites, involving secretory antibody responses and tissue-resident T cells, can prevent an infection. This is particularly the case for vaccines against viruses, such as influenza and coronavirus, that can stop establishing infection in the first place, rather than only curtailing infection and protecting against the development of disease symptoms. For these reasons, the nasal vaccine segment is expected to grow particularly well in the next few years to reach $250.91 million by 2029, up from $122.29 million in 2021.[14]

In addition, nasal delivery offers an exciting advantage for the reformulation of biologics about to lose their exclusivity. It opens up a new avenue for drug developers to breathe new life into their products, providing a distinct new format for their intellectual property that also offers enhanced convenience for patients. The nasal route also has regulatory advantages for reformulated products compared with parenteral administration. Due to its non-invasive nature and target delivery with fewer side effects, the path to regulatory approval can be significantly streamlined.

OVERCOMING THE CHALLENGES OF NASAL DRUG DEVELOPMENT

With all of these benefits in mind, it is clear nasal delivery offers a unique alternative route for biopharmaceutical innovators to consider. Nevertheless, developing an effective final nasal drug product does pose challenges that need to be overcome.

For example, biologic formulations can be fragile and prone to damage from delivery devices during nebulizing or spraying. Lipid nanoparticles of the kind used in mRNA vaccines can be damaged by nebulizers for oral inhalation, according to a study by the University of Amsterdam.[15]

Preservatives traditionally used in nasal devices, such as benzalkonium chloride, also cannot be used in biological formulations as they are incompatible with the actives. This complicates the development of nasal biopharmaceutical treatments, mandating delivery devices that can ensure sterility of the biopharmaceutical during use.

In addition, the area of the nasal cavity that needs to be dosed, as well as the dose volume, are critical for drug efficacy. This makes the selection of the nasal inhalation device vitally important. For instance, a traditional nasal spray often features a swirl nozzle with a spray cone angle of between 60° and 90°. Rather than allowing the treatment to penetrate deep into the nasal cavity, this can result in most of the formulation being deposited on the walls of the nose, undermining dose uniformity.

The need for an effective turn-key nasal delivery device platform for biopharmaceuticals is another challenge that needs to be addressed. An appropriate platform would not only address the issues around the sensitivity of the active to shear forces during administration and the restrictions on preservatives — it would also be easy to source and use with minimal time-consuming customization.

Nasal spray design has evolved significantly in recent years, overcoming many of these challenges for biopharmaceutical developers. Partnerships between specialist device developers have been integral in spearheading this innovation, helping to establish nasal delivery as a viable option for biopharmaceutical development.

THE ROLE OF PARTNERSHIPS IN INHALED & NASAL DEVICE INNOVATION

A network of strategic collaboration partners is fast becoming an important element of many device developers' strategies to meet the needs of the pharmaceutical industry and address drug delivery trends in healthcare. Working together, device experts can share knowledge and technology to create new inhalation and nasal device platforms that offer improved performance for biologics and enhance patient convenience. Due to this collaboration, there has been an increase in the variety of inhaled and nasal spray technologies available to drug developers in recent years.

Each device has unique benefits that make it suitable for particular applications. However, many devices often require considerable design customization to ensure they are effective at delivering biologic formulations at the required dose. This can add time and cost to any inhaled or nasal biologic reformulation project.

COLLABORATION ENABLES DEVICE DEVELOPMENT EFFICIENCIES

A new generation of inhaled and nasal devices has recently entered the market due to collaboration between specialist developers — soft mist inhaled and nasal sprays. They offer unique design advantages both for new biologics projects and for the reformulation of existing drugs. They can significantly reduce the customization required to ensure the device is suitable for the formulation, minimizing the time and cost of development.

Related to the soft mist inhaler (SMI) for oral delivery, the soft mist nasal spray is a liquid sprayer that creates a slow-moving aerosol cloud designed to optimize drug delivery to the nasal cavity while minimizing the inspiratory effort required by the patient.

Partnerships between device specialists have enabled further enhancement to the design of soft mist nasal spray devices that have made them ideal for the delivery of sensitive biologic formulations.

Large suppliers that offer full integration of device development, pharmaceutical product development, and manufacturing can enable collaboration between internal experts in each aspect of the development journey. Supporting every aspect of a project, from the sourcing of clinical material to simultaneous formulation and device development, to commercial manufacturing, such a single supplier can help pharmaceutical companies minimize the need for complex and time-consuming technical transfer. In doing so, it can reduce the risk of costly delays and speed up project delivery.

PERFORMANCE BENEFITS ARISE FROM EXPERT PARTNERSHIPS

Another example of collaboration is the sharing of new, more targeted nozzle designs with soft mist nasal spray developers by nozzle manufacturers. These can create a narrower spray cone that addresses dosing problems posed by the wide-cone nozzles traditionally used in nasal devices, allowing more of the dose to reach the nasal cavity. Next-generation spray nozzles allow the fine-tuning of the spray cone angle, from 0° to 30°. Together with a significantly reduced spray velocity, this reduces the amount of formulation being deposited at the front of the nose. In doing so, it increases the dose reaching the upper turbinates and the olfactory regions of the nasal cavity. When used in a soft mist nasal spray, such a nozzle can evenly distribute a soft mist into the nasal cavity, resulting in uniform dosing, a longer residence time for the formulation in the nose, and potentially enhancing drug performance.[16]

The new nozzle formats used in soft mist nasal sprays are particularly beneficial for the delivery of sensitive formulations, such as many biologic products. They aerosolize the drug on delivery in a unique way, which limits the shear forces imposed on formulation particles, minimizing damage to the formulation itself and ensuring optimum effectiveness.[14] The customization of the spray cone of soft mist nasal sprays further simplifies development, as it can be easily adjusted to suit the unique needs of the biologic formulation without needing to invest the time to rework the whole device design.

SHARING INNOVATION UNLOCKS THE BENEFITS OF INHALED & NASAL BIOLOGICS

Inhaled and nasal administration offers an exciting alternative approach to both biologics development and the reformulation of existing treatments. New delivery technologies, such as the soft mist nasal spray, have made nasal a viable route for biopharma products. They can minimize development and regulatory time frames and optimize manufacturing efficiency. At the same time, they can help create a more convenient and easier-to-

use end product for HCPs and patients.

Knowledge sharing through partnerships between device specialists has played a key role in enabling the development of these technology platforms. With ongoing collaboration, the industry will be able to see further innovations that will transform biologics development and open up new routes of administration. As a result, drug developers will be able to launch new biopharmaceutical drug products or give their blockbuster biologic formulations a new lease of life and continue to address the self-administration needs of patients. ◆

BIOGRAPHY

Dr. Nicolas Buchmann is Chief Technology Officer at Resyca®. He has experience in the development of smart nebulizer and inhalation devices and has worked in this industry for most of his career. He has extensive knowledge in medical device development and managing complex development programs and portfolios for inhalation drug-device-combination products. Before joining Resyca, he held roles at Vectura (Chippenham, UK) as Program Manager and at Pari GmbH (Starnberg, Germany) as Technology Manager. He earned his PhD in Biomedical Engineering and is a certified senior project manager (IPMA).

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