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Transforming the Biologics Product Lifecycle with Inhalation Innovation

In recent years, the biopharmaceuticals landscape has witnessed a revolutionary shift with the emergence of new nasal inhalation technologies. Among these, soft mist nasal sprays have emerged as a promising avenue, particularly for the delivery of biologic drug products. Such nasal drug delivery innovations hold promise in transforming the way biologic drug products are administered and managed throughout their lifecycle.

In this article, Nicolas Buchmann, CTO, and Frank Verhoeven, Business Developer at Resyca (a joint venture between Bespak and Medspray), delve into the potential transformative impact of inhalation innovations on the biopharmaceutical product lifecycle.

A Dynamic and Growing Inhalation Market

The global market for inhalation drug delivery devices is experiencing rapid expansion, poised to reach a value of $20.7 billion by 2031, growing at a compound annual growth rate (CAGR) of 4.4%.[1] This growth trajectory is propelled by several key drivers, notably the escalating prevalence of chronic lung conditions worldwide and the need for more efficient and patient-friendly drug delivery methods.

Chronic respiratory ailments such as asthma, cystic fibrosis, pulmonary arterial hypertension (PAH) and chronic obstructive pulmonary disease (COPD) have increasingly been diagnosed globally. In 2019, 262 million individuals were living with asthma worldwide, with approximately 1,000 asthma-related fatalities occurring daily, many of which are preventable.[2] Additionally, PAH affects up to 70 million individuals globally, accounting for nearly 1% of the global population, a figure expected to rise as the population grows older and larger.[3] Cystic fibrosis, affecting 162,428 people globally, further underscores the demand for effective treatment modalities.[4]

Given the nature of these conditions, inhalation emerges as the preferred route for drug delivery, enabling targeted therapy directly to the affected sites within the respiratory system.

The burgeoning biologics market is exerting an unexpected influence on the inhalation landscape. Projected to be valued at approximately $854.86 billion by 2032, with a remarkable CAGR of 7.9% from 2023 to 2032,[5] the global biologics market is driving innovation in drug delivery methodologies.

Traditional approaches to drug delivery often present obstacles in achieving optimal therapeutic outcomes and patient compliance, particularly with biologic drugs. Given the sensitive nature of biopharmaceutical formulations, parenteral delivery routes are often required to bypass the gastrointestinal tract. However, this approach causes discomfort for patients and puts constraints on drug administration confined to clinical settings, creating inconveniences for patients and strain on healthcare provider (HCP) resources.

Innovations in inhalation delivery technologies, particularly in nasal inhalation such as soft mist nasal sprays, have opened avenues for novel drug delivery strategies. Nasal delivery now presents a viable alternative for administering a wide array of biologic formulations, offering improved patient experiences and expanding treatment accessibility beyond clinical settings.[6]

Large Molecule Innovation: Opportunities and Challenges for Developers

These developments in biopharmaceutical drug delivery present both opportunities and challenges for developers of large molecule drugs. As the biologics segment grows, competition within the biopharma industry will also intensify. Notably, major industry drugs, such as Humira, Keytruda, Revlimid and Eliquis, are set to lose their exclusivity in the coming years.[7] The resultant industry changes, partly fueled by patent expiries, are catalysing the expansion of the biosimilars market, projected to expand at a CAGR of 18.32% until 2029, reaching an estimated $82.27 billion within the next decade.[8]

In this fiercely competitive landscape, biologics manufacturers must strategise effectively to maximise the lifecycle value of their products. This includes exploring opportunities for reformulation to ensure continued relevance and market competitiveness. Soft mist nasal sprays and other innovative nasal inhalation devices have the potential to play a pivotal role in extending product lifecycles while enhancing patient outcomes.

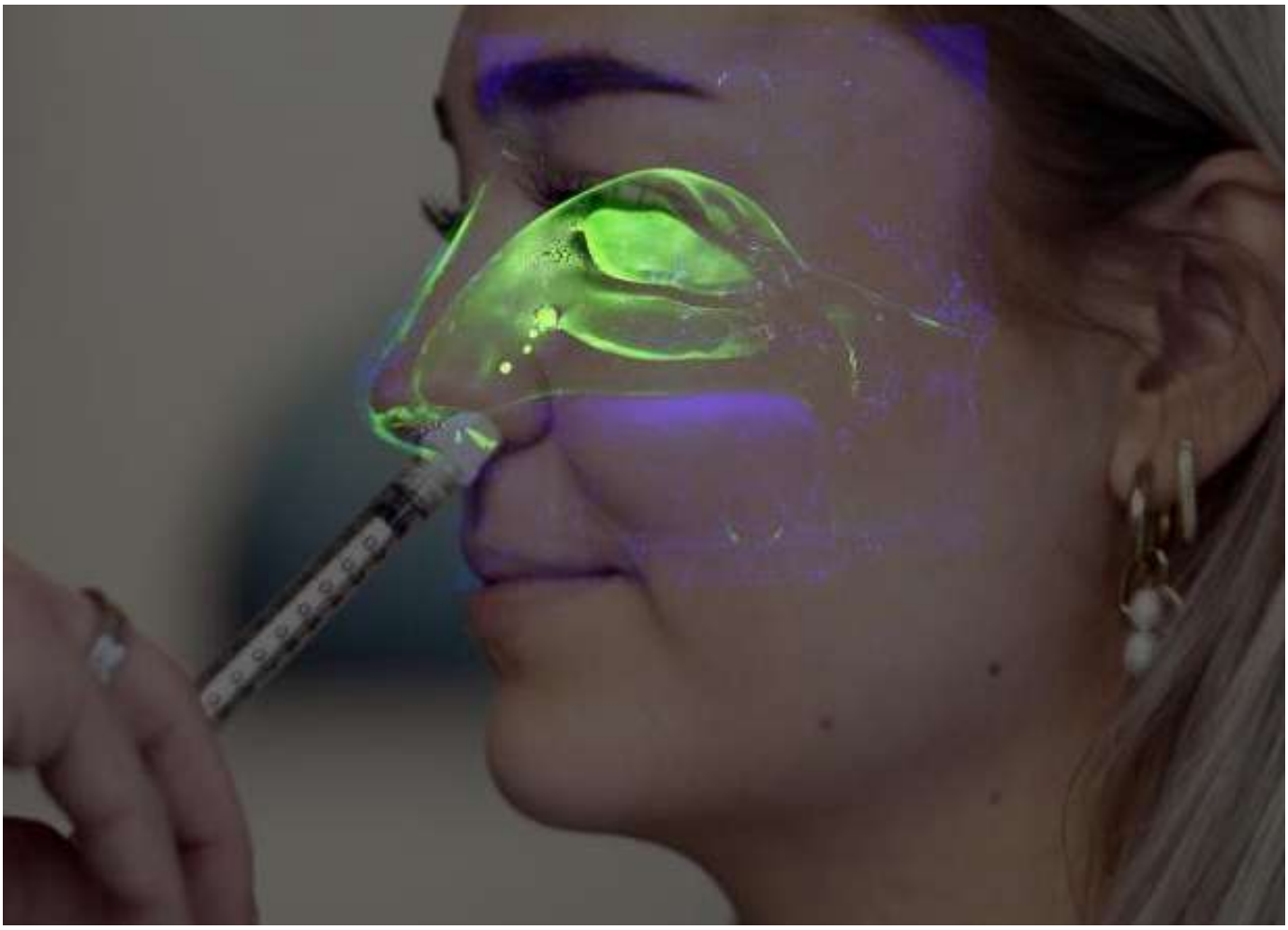
The nascent rise of the nasal route for biologics delivery is underpinned by compelling advantages demonstrated in recent studies. Nasal inhalation emerges as a promising avenue for systemic delivery of protein and peptide drugs, leveraging the nasal mucosa's extensive surface area (150 cm^2) and high vascularity, similar to the small intestinal mucosa. This route offers multiple benefits, including ease of administration, non-invasiveness, rapid onset of action, and circumvention of gastrointestinal degradation and hepatic first-pass effects. Notably, nasal delivery holds immense potential for enhancing the delivery of insulin to distal brain regions, marking a significant advancement in diabetes management.[9]

For vaccines, mucosal delivery offers superior and longer-lasting efficacy compared to traditional injection routes.[10] Mucosal vaccine delivery elicits robust protective immune responses at the sites of pathogen entry, strengthening the body's defences against infections. This approach, characterised by the induction of adaptive immunity at mucosal sites, can prevent the establishment of infections, particularly in the case of viruses such as influenza and coronaviruses.

These promising findings are translating to enhanced market projections, with the nasal vaccine segment expecting exponential growth, forecast to rise from $416.8 million in 2023 to $742.6 million by 2030.[11] This underscores the growing recognition of nasal delivery as a potent strategy for enhancing vaccine efficacy and combatting infectious diseases.

Reviving Product Lifecycles for Existing Biologics

To prolong the lifecycle of existing biologics, novel approaches need to be explored,



including the adoption of new indications and formulation enhancements aimed at promoting patient convenience.

Nasal delivery presents an opportunity for developers to rejuvenate their products, harnessing a fresh format for their intellectual property while enhancing patient adherence and comfort.

The regulatory advantages inherent in nasal biologics further amplify their appeal. The non-invasive nature of nasal delivery and its potential for targeted drug delivery with reduced side effects streamline the regulatory approval process, facilitating product lifecycle optimisation for developers.

Improving Delivery and Efficacy of Sensitive Biologics

However, the adoption of nasal delivery for biologic formulations poses some development challenges, such as the susceptibility of biologic formulations to damage from standard administration devices during spraying or nebulising. For example, a study by the University of Amsterdam has shown that lipid nanoparticles of the kind used in mRNA vaccines can be damaged by traditional nebulisers for oral inhalation.[12,13] Additionally, preservatives used in nasal delivery devices are often incompatible with biopharmaceutical formulations, complicating formulation development.

Further to these issues, achieving optimal drug efficacy requires meticulous consideration of dosing parameters and nasal cavity dynamics. Conventional nasal spray devices may exhibit limitations in dose uniformity and drug deposition, necessitating innovative solutions to overcome these obstacles. For instance, a traditional nasal spray often features a swirl nozzle with a spray cone angle of between 60 and 90°. This can result in most of the formulation being deposited on the walls of the nose, rather than penetrating further into the nasal cavity, with ramifications for dose uniformity.

The Role of Soft Mist Nasal Sprays in Overcoming Product Lifecycle Challenges

Soft mist nasal sprays represent a cutting-edge innovation in the biologics field, offering distinct advantages for both new product initiatives and lifecycle extension projects. The unique design features of these sprays streamline device customisation, significantly reducing development time and costs for biologic formulations.

Evolved from the soft mist inhaler (SMI) for oral delivery, soft mist nasal sprays deploy a liquid sprayer mechanism that generates a slow-moving aerosol cloud, facilitating efficient drug delivery to the posterior nasal cavity with minimal inspiratory effort from patients.

Advancements in soft mist nasal spray design have tailored these devices specifically for biologic formulations, with innovations such as more targeted nozzle designs. Narrow spray cone angles address dosing challenges inherent in traditional wide-cone nozzles, ensuring optimal drug deposition in the nasal cavity. Next-generation spray nozzles, enable customisable spray cone angles (from 0 to 30°), droplet sizes and plume velocities. 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 and enhancing drug distribution to critical nasal regions.[14]

These nozzle designs not only optimise drug delivery but also mitigate formulation damage, particularly crucial for sensitive biologic products. By minimising shear forces on formulation particles during aerosolisation, soft mist nasal sprays ensure the integrity and effectiveness of biologic formulations.

Regulatory Approval in Nasal Delivery: Streamlining Development

In addition to enhancing drug delivery performance, recent soft mist nasal spray innovations promise to streamline development and regulatory processes, making nasal delivery an attractive option for biologic product lifecycle extension. Emerging device platforms, including multi-use devices combined with disposable, pre-filled syringes, reduce the need for complex device customisation and high-volume manufacturing.

Moreover, customisable spray cone features simplify formulation-specific adjustments without necessitating extensive device redesign, further expediting development timelines and regulatory approvals.

These advancements not only make nasal delivery a viable option for new biologics but also present an opportunity for reformulating existing biopharmaceutical products to extend their lifecycle. By minimising development and regulatory hurdles while optimising manufacturing efficiency, soft mist nasal sprays pave the way for more convenient and user-friendly solutions for healthcare providers and patients alike.

Harnessing Nasal Innovation for Biologic Lifecycle Management

As the patents for numerous biologic products approach expiration, the demand for lifecycle extension solutions is growing. With increasing competition in the bio-similar market, drug developers are increasingly turning to innovative strategies to differentiate their products and meet evolving patient needs.

By leveraging nasal delivery, drug developers can breathe new life into blockbuster biologic formulations, ensuring sustained market relevance and improved patient outcomes.

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