PEER REVIEWED

INHALED mRNA:
The Race Has Begun

With targeted delivery and potential for improved patient adherence, inhaled mRNA therapies are emerging as the new frontier in respiratory and genetic medicine. A growing pipeline of candidates are laying the groundwork for a new class of precision biologics.

In short:

- **There are 29 inhaled mRNA drugs currently in development.**
- **44% of all mRNA candidates target infectious diseases.**
- **There are no candidates beyond Phase II as of April 2025.**
- **Cystic fibrosis and primary ciliary dyskinesia are the leading respiratory indications being considered for inhaled mRNA therapies.**
- **Nebulisers are used in the pre-clinical phase, while soft mist inhalers offer greater precision, portability and scale up continuity from Phase I trhough to commercialisation.**
- **Strategic partnerships between drug developers and inhalation device innovators are essential to move the field forward.**

INHALED mRNA:
A New Market for Drug Delivery

Messenger RNA (mRNA) vaccines have become a significant trend in the drug development world. These mighty molecules contain the 'instructions' needed for cells to make specific proteins that match with a pathogen's antigens. The immune system responds by dispatching antibodies and T-cells, an attack which can then be repeated if the patient is infected with the real virus.

This approach was tried and tested on a large scale during the COVID-19 pandemic, where novel Lipid Nanoparticle (LNP) technology helped vaccine developers overcome some of the challenges of transporting mRNA into cells smoothly. Thanks to this important advancement and the many benefits that mRNA offers, from powerful immune responses to rapid development timelines and flexible manufacturing, investment in the field has since surged.

There are now 386 different mRNA vaccines in development or pre-registration for various infectious diseases ranging from influenza to HIV/AIDs. Researchers are seeing a future for mRNA that extends beyond viral infections. Looking at the pipeline for all mRNA-based drugs in April 2025, 44% are indicated for infectious diseases, followed by 29% for oncology. Other therapy areas with mRNA activity include metabolic disorders (5%), respiratory (3%), and immunology (3%).

In this article, we explore the unique intersection of this drug development trend with another important trend in the industry, inhaled drug delivery.

The Benefits of Inhaled mRNA

As the development of mRNA-based drugs accelerates, inhaled delivery is emerging as the next frontier in the field. This is a particularly exciting trend in the respiratory therapy area, where inhaled mRNA therapeutics will deliver genetic instructions for fighting diseases like Cystic Fibrosis (CF) directly to the lung cells.

When it comes to vaccines, an inhalable formulation is believed to improve patient compliance amongst individuals with needle phobia. Inhaled vaccines can stimulate strong mucosal immune responses in the respiratory tract, where most vaccines enter the body. By inducing an immune response at the site of entry rather than the systemic response triggered by injected vaccines, inhalable formulations could help to reduce viral transmission more effectively than traditional ones.

There are currently 29 inhaled mRNA-based drugs under active development, with several being pursued in multiple indications. It is clearly early days in this field, with most candidates in the discovery stage and, as of April 2025, no companies having taken this technology further than Phase II (Figure 1).

Five clinical trials have been completed in this space while seven are currently ongoing, five of which are recruiting. The industry commenced an equal number of trials in 2023 and 2024, more than double that which started in 2022 (Figure 2).

Inhaled mRNA Pipeline Insights

The main therapeutic indications for inhaled mRNA (Figure 3) include CF and Primary Ciliary Dyskinesia (PCD) (Figure 4). CF is a rare inherited genetic condition which impairs the clearance of mucus in the airways, causing damage to the lungs, digestive system, and other organs. Beginning in childhood, it is a life-long and life-limiting condition with no cure. PCD is a similar rare genetic disease in that it also causes mucus build-up in the lungs, though the root cause of this effect is different. Both diseases are associated with recurrent respiratory infections and an increased risk of premature death.

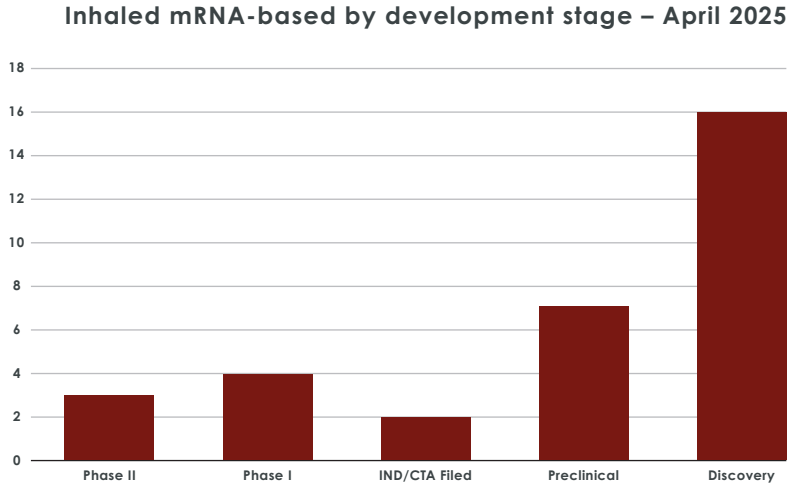

Figure 1

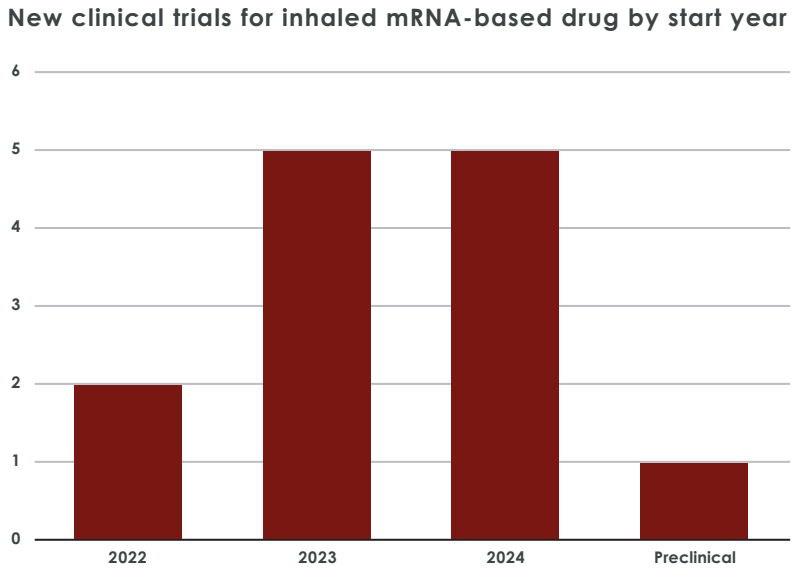

Figure 2

CF drugs are at the most advanced stage of the pipelines, Phase II. One therapy is a nebulised mRNA, designed to boost CFTR protein expression in the lung's secretory cells is currently in Phase II and has a 50% probability to progressing to Phase III. That's nearly double the bench market success rate for this stage, which stands at just 26%. Initial results are expected by June 2025, with full trial completion by year-end.

In early 2023, a biotech launched an inhaled mRNA programme shortly after receiving fast-track designation. This followed an earlier licensing deal with a leading mRNA developer. The candidate is a liquid aerosol aimed at correcting CFTR dysfunction.

A third molecule is being developed as an inhaled CFTR regulator and expects to complete a Phase I/II trial by the end of 2025. All three programmes share the same challenge: getting therapeutic particles through the thick mucus barrier in the lungs to reach epithelial cells – a key bottleneck in CF. Beyond CF, a fourth asset is targeting PCD with an inhaled mRNA therapy now in Phase I. It's not alone. In Europe, a biotech has three early stage inhaled assets for PCD and is positioning itself as a major player in respiratory gene delivery.

Who's Racing to Own the Inhaled mRNA Market?

In Europe, five different inhaled mRNA candidates aimed at respiratory diseases are in early stages. The lead programme is in Phase I and is targeting both asthma and Chronic Obstructive Pulmonary Disease (COPD). The therapy is delivered via the nasal route using a proprietary nanoparticle system designed to stabilise mRNA and enable efficient absorption in the respiratory tract. Recently, they completed its first-in-human trial in asthma, and recruitment is ongoing for a separate Phase I study in COPD. These two diseases represent large global markets with substantial unmet need and they offer developers the chance to position inhaled mRNA as a credible alternative to steroid-based or systemic biologics.

In the US, a biotech is developing a next-generation biodegradable polymer platform for mRNA delivery, an alternative to the LNPs commonly used in the field. The goal? Increased stability and tolerability in the respiratory tract.[1] The proprietary formulation is currently being used in several intranasal vaccine programmes, including COVID-19 boosters aimed at neutralising the virus in the upper airway before it can spread deeper. Respiratory Syncytial Virus (RSV) and influenza candidates are also in early-stage development.

This is not just a vaccine play, this can be applied in oncology. According to public data, there are at least three discovery-stage assets for non-small cell lung cancer, leveraging inhalation to drive immune response at the tumour site. A bold step in the evolution of mRNA beyond infectious disease.

In Asia, a dry powder formulation is being delivered through a proprietary inhaler

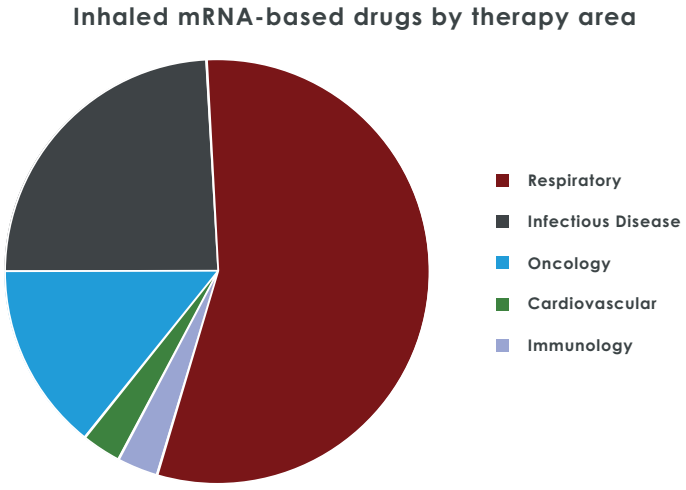

Figure 3

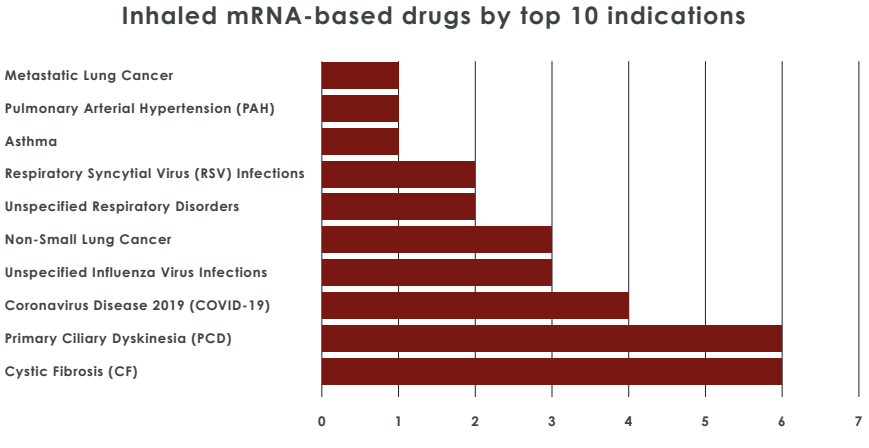

Figure 4

device. The lead programme is in a Phase I trial for advanced lung cancer and lung metastasis of solid tumours. The therapy is designed to train the immune system to recognise tumour antigens, enabling targeted destruction of cancer cells in the lung. Bypassing traditional injections by using a powder inhalation method, the formulation aims to achieve localised immune activation without systemic side effects. The trial is expected to run through to early 2027. If successful, this could mark one of the first clinical validations of dry-powder mRNA delivery in oncology – a major milestone for the field.

Future Outlook for Inhaled mRNA

While inhalable mRNA formulations are still emerging, they offer exciting therapeutic potential and are driving innovative developments in drug delivery. mRNA is inherently unstable, which makes maintaining its integrity during aerosolisation a key focus. Delivery requires the use of nebulisers and leads to Intellectual Property (IP) filings. Additionally, LNPs used to deliver mRNA may undergo changes such as aggregation or size increase, during aerosol delivery. Encouragingly, recent studies have shown that these effects can be mitigated through smart formulation strategies, such as incorporating polymers into the LNP structure. Zwitterionic polymers have shown promise in supporting efficient and stable aerosol performance.[2]

For inhaled mRNA formulations to advance further in the clinic and eventually reach the real-world patients that need them, collaboration will be required between the drug development community and inhaled platform experts such as Merxin Ltd. Merxin Ltd's Soft Mist Inhaler (SMI), MRX004, is the solution. By generating a slow-moving plume, MRX004 protects delicate molecules as they reach the deep lung.

Current inhaled mRNA delivery often relies on nebulisers for early clinical trials, which are bulky and non-portable devices that limit patient convenience. Compact, scalable alternatives like MRX004 will unlock new possibilities for inhalable mRNA, especially in rare and chronic respiratory diseases. Clinical trials can start with MRX004 and bypass the time-wasting stages of nebulisers. As the inhaled mRNA field grows, the integration of cutting-edge delivery platforms with pharmaceutical innovation will be critical to realising its full potential.

MRX004

MRX004 is a multidose Soft Mist Inhaler (SMI) designed for aqueous and ethanol-based formulations. MRX004 uses mechanical energy (no propellant or battery) to generate a fine, slow-moving aerosol for deep lung deposition. MRX004 is environmentally friendly and well-suited for novel molecule delivery, lifecycle management, or reformulation from nebulised products.

Get in touch: info@merxin.com, explore our work with biologics and accelerate your path to market. **www.mrx004.com**

MRX002+

MRX003

MRX004

MRX006

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