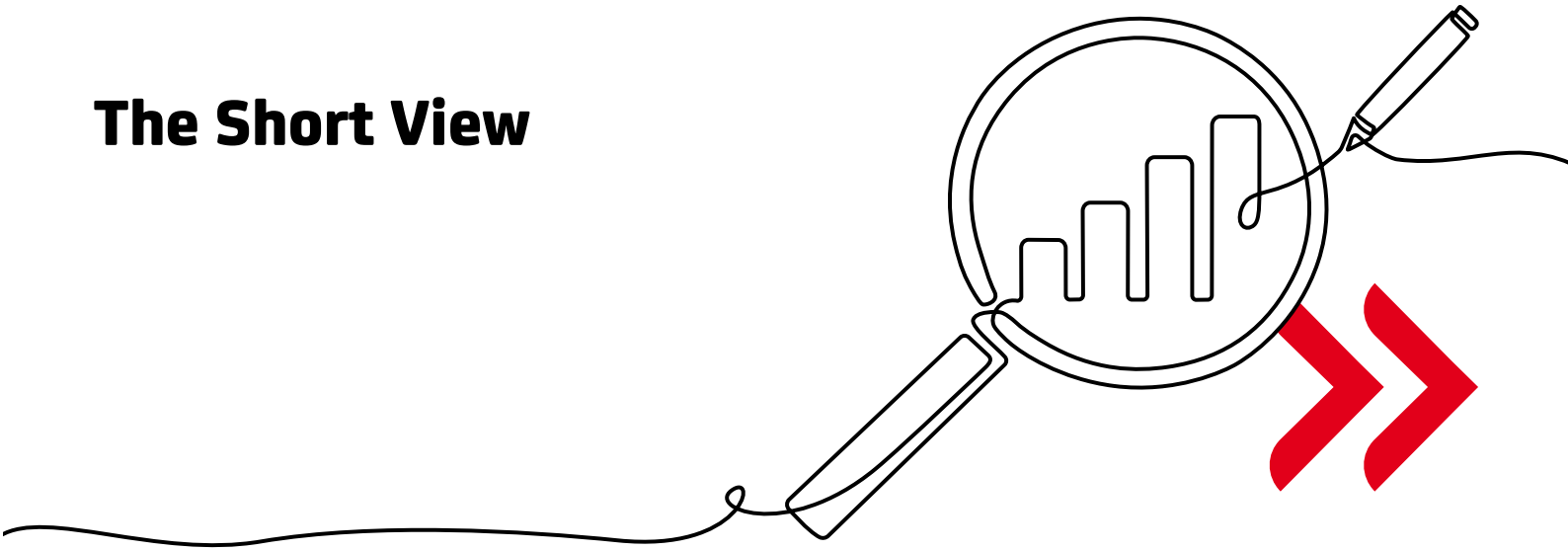
The Short View



The Short View offers insights on key macro and market stories and is designed to promote discussion and debate.

Behind Moderna: the opportunity of personalised medicine

3 September 2026

Moderna's Phase III success in developing a melanoma vaccine could mark a turning point for personalised medicine, showing how sequencing, AI and mRNA can enable individualised therapies at scale and create opportunities beyond drug developers.

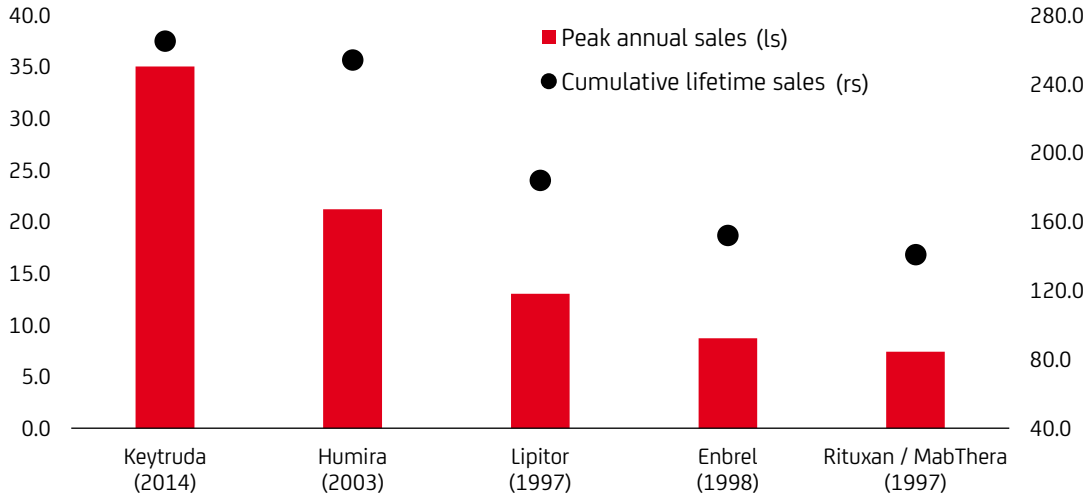
1. Moderna's Phase III results provide important clinical validation for individualised cancer therapy, showing that a patient-specific treatment can move from biological rationale to meaningful clinical benefit.
2. The approach is enabled by the convergence of sequencing, AI and mRNA technology. Sequencing identifies tumour mutations, AI selects the most promising immune targets, and mRNA turns those predictions into a patient-specific therapy.
3. The broader investment opportunity may lie in the life-sciences supply chain. As personalised medicine scales, every patient requires sequencing, specialised manufacturing inputs, purification, formulation and testing, creating opportunities that do not depend on predicting which therapeutic developer ultimately wins.

Why Moderna's Phase III results matter

It is not often that an S&P 500 stock rises 177% in a single session. This is what happened with Moderna. The company announced that its Phase III melanoma trial combining Merck's immunotherapy drug Keytruda with intismeran (mRNA-4157) met its primary and secondary endpoints at the first prespecified interim analysis. Detailed Phase III efficacy data have not been released yet, and overall survival data is still being tracked. So what are the implications of this announcement to justify such an extraordinary re-rating?

The significance of the melanoma vaccine could go well beyond positive Phase III results and Moderna itself. Understanding why requires starting with Keytruda, a cornerstone of modern cancer immunotherapy, and how it complements Moderna's approach.

THE WORLD'S BIGGEST PHARMACEUTICAL BLOCKBUSTERS
PEAK ANNUAL SALES AND CUMULATIVE LIFETIME SALES (USD BN)



Source: Company filings and annual reports; Evaluate Pharma consensus for Keytruda 2028E; The Investment Institute by UniCredit estimates.
Note: Peak annual sales are historical actuals, except Keytruda 2028E. Cumulative sales are shown through 2028E, based on reported sales and current run-rates.

Keytruda has helped redefine cancer immunotherapy and has become one of the greatest commercial successes in pharmaceutical history. Since its launch in 2014, the drug has generated roughly USD 180bn in global sales, including USD 31.7bn in 2025 alone. It has already overtaken Lipitor, the blockbuster cholesterol-lowering drug, in cumulative nominal sales, despite Lipitor having been launched in 1997. Keytruda, with cumulative sales projected to reach about USD 265bn by 2028, could become the highest-selling pharmaceutical product ever, overtaking Humira, the autoimmune-disease blockbuster launched 11 years earlier.

Keytruda's commercial success reflects the importance of the biological mechanism it targets. But it solves only one part of the problem.

Cancer cells often protect themselves from the immune system by exploiting an immune checkpoint called **PD-1**. PD-1 is a receptor on the surface of T-cells, while its "key", **PD-L1**, can be expressed by cancer cells. When T-cells encounter cancer cells and PD-L1 binds to PD-1, like a key fitting into a lock, it tells the T-cell to reduce or stop its attack. Keytruda blocks this mechanism, removing the brake and allowing the immune system to attack cancer cells. However, removing the brake does not completely solve the problem since the immune system must first know what to attack.

Cancer is particularly difficult because every tumour is different. As cancer cells accumulate mutations, they can produce abnormal proteins that healthy cells do not contain. Inside the cell, proteins are continuously broken into small fragments called **peptides**. Some of these fragments are then carried to the cell surface by molecules called **HLA**. HLA molecules act like small display platforms on the surface of cells. Their function is to show the immune system what is happening inside the cell, making internal proteins visible to T-cells that would otherwise have no way to inspect them. When a mutation creates an abnormal peptide that is presented by an HLA molecule and recognised by T-cells, it can act as a **neoantigen**, a tumour-specific target for an immune attack.

The difficulty is that a tumour can contain hundreds of different mutations, each potentially creating a different abnormal peptide. At the same time, every patient has a particular combination of HLA molecules, and each HLA type can present only certain peptides effectively. This creates many possible **mutation-peptide-HLA combinations**. Only some mutated peptides are produced, processed and presented on the tumour-cell surface. Hence, there are many possible mutation-peptide-HLA combinations, but only a small fraction can become useful immune targets.

This is where Moderna's intismeran, and AI, come in. For each patient, Moderna analyses the tumour mutations, using AI/ML models to make this enormous search problem computationally tractable. The models analyse each mutation together with the patient's HLA type and predict which mutated peptides are most likely to be produced by the tumour, bind strongly to HLA molecules, appear on the cancer-cell surface and trigger a T-cell response. The candidates are then ranked and the most promising, up to 34 in Moderna's vaccine, are selected, without having to experimentally test hundreds of possibilities for every patient. In practice, AI is used to identify, among many possible mutation-derived targets, the small number most likely to generate effective immune targets for that specific patient.

Moderna then creates an mRNA molecule, as with the COVID vaccines, encoding the selected neoantigens specific to that patient. Once injected, the mRNA is taken up by immune cells, especially dendritic cells, that read the mRNA, produce the encoded neoantigens and display them on their HLA molecules. This allows T-cells to learn what the tumour-specific targets look like.

The combination with Keytruda is therefore highly complementary. Intismeran tells the immune system what to attack, while Keytruda prevents the tumour from telling the immune system to stop attacking.

The investment perspective

This elegant mechanism would remain just that, as many promising ideas in medicine do, without clinical proof. Phase III is crucial because it provides evidence that the approach can translate from biological rationale into meaningful benefits for patients.

The clinical validation has been made possible by the convergence of three technologies that already existed independently. Together, they make an individualised treatment approach practical at scale in a way that none could achieve alone.

The parallel with AI is the convergence of technologies that already existed independently. Compute, algorithms and cloud infrastructure became transformative when combined. Individualised cancer vaccines may be following a similar path through the convergence of **sequencing**, **AI** and **mRNA technology**.

Next-generation sequencing identifies the mutations in that specific tumour. AI/computational biology makes the resulting search problem tractable, identifying which mutations are most likely to be therapeutically useful. mRNA manufacturing then rapidly converts those predictions into a physical, patient-specific drug.

From an investment perspective, the interesting question may therefore not be which personalised cancer vaccine ultimately wins, but which companies benefit as the entire field scales.

Moderna is unlikely to be the only company trying to exploit personalised cancer vaccines. If the Phase III results validate the approach, it should encourage more companies, more indications and more patient-specific programs.

The supply chain broadly follows the same architecture described above. At the front end, sequencing technology is needed to identify each patient's tumour mutations. The potentially more interesting economic opportunity, however, may be further downstream, because every individualised drug must be physically manufactured for every patient. This is particularly interesting because companies exposed to this part of the value chain can potentially benefit regardless of which therapeutic developer ultimately wins and whether production is kept in-house or outsourced. In either case, the industry still needs the specialised materials, equipment and processes required to manufacture, purify, formulate and test each therapy. This makes the life-sciences supply chain one of the clearest ways to gain exposure to the growth of individualised medicine without having to predict the eventual therapeutic winner.

Key terms

T-cell: An immune cell that can recognise and destroy abnormal or infected cells.

PD-1/PD-L1: PD-1 is a receptor protein found on T-cells, while PD-L1 is the partner protein found on normal cells and many cancer cells that binds to PD-1 to turn off immune responses. This immune checkpoint can reduce T-cell activity. Some tumours exploit it to escape immune attack.

Mutation: A change in DNA that can cause a cancer cell to produce an abnormal protein.

Peptide: A small fragment of a protein.

HLA (Human Leukocyte Antigen): Molecules on the cell surface that display peptides to T-cells so the immune system can check what is happening inside the cell.

Neoantigen: A tumour-specific target created by a cancer mutation and potentially recognised by T-cells.

mRNA (messenger RNA): A temporary set of genetic instructions that teaches cells which proteins to produce.

Dendritic cell: An immune cell specialised in presenting antigens to T-cells and helping activate an immune response.

Next-generation sequencing (NGS): A fast, high-throughput technology used to read DNA and identify the mutations present in a patient's tumour.

Personalised cancer vaccine: A vaccine designed around the specific mutations found in an individual patient's tumour.

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