INTRODUCING A NEW GENERATION OF INHIBITORS TO THE OLIGONUCLEOTIDE THERAPEUTICS MARKET

An interview with

SELECTA Biotech

DR VERONIKA NEMETHOVA (CO-FOUNDER OF SELECTA BIOTECH SE, HEAD OF THERAPEUTICS DIVISION)

Paving the way for a new generation of oligonucleotide therapeutics, Slovakia-based Selecta Biotech is working tirelessly to revolutionise the current standard in molecular diagnostics and therapy. Tackling side effects and adverse events resulting from drug promiscuity, the future-focused company is utilising its custom-built biotechnological ecosystem and industry-wide partnerships to deliver results that set in motion real societal change. Here we spoke to Dr Veronika Nemethova to find out more about Selecta Biotech's mission and how the company is achieving it, alongside its hopes and predictions for the future of biotechnology.

What is Selecta Biotech's core mission, and what are the two separate divisions it operates in?

Selecta Biotech holds proprietary technology and relevant know-how in the research and development of ultra-specific oligonucleotide-based therapeutics. Our mission is to improve patient health care through safe therapeutic solutions, implementing a new generation of inhibitors in clinical practice that achieve the desired therapeutic effect without side effects. We believe that eliminating drug promiscuity and inherent toxicity is the key to success in the development of highly effective and safe therapeutics for a broad range of currently intractable and devastating diseases affecting large patient groups.

Alongside the core therapeutics division, which represents the major agenda of the company, Selecta Biotech also operates a diagnostics division primarily focused on improving early detection of oncology markers. This division also provides consulting services to clients and offers strategic partnerships to biotech and pharma companies seeking to benefit from the remarkable sensitivity of detection and quantification of biomarkers in molecular diagnostics.

Can you tell us about your professional research background and what led to your interest in cancer genetics and clinically oriented research?

I have a degree in Molecular Biology and Genetics as well as Macromolecular Chemistry, and boast more than 15 years of professional experience in clinically orientated research. I gained extensive experience working as a specialist in molecular diagnostics and later became a leader in early-stage validation of therapeutic oligonucleotides with exclusive selectivity for leukaemia treatment. During my career, I have worked my way up to the position of Head of Therapeutics at Selecta Biotech. Under this title, I coordinate the R&D of a new generation of oligonucleotide therapeutics and manage their implementation into treatment strategies for several diseases.

In your opinion, what are the biggest obstacles companies face in the development stages of highly effective yet safe therapeutics tackling cancer?

New technologies supporting drug discovery methods and techniques are evolving at a significant rate. Several key players within the oligonucleotide therapeutics market run significant R&D investments to develop therapeutics predominantly for oncological, neurological, and other (mostly chronic) diseases. Although the growing incidence of cancer boosts the demand for novel approaches offering immense growth opportunities, toxicity stemming from drug promiscuity (responsible for many clinically relevant side effects or adverse events) and limited cell membrane penetration of oligonucleotide therapeutics challenge the market participants. Selecta offers its advanced technology addressing these major limitations to help companies upgrade their strategies with the aim of improving the safety profiles of oligonucleotide therapeutics in development.

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How does Selecta Biotech's highly advanced technology work to address drug promiscuity?

The standard design of oligonucleotides is relatively straightforward, as most modalities simply exploit the knowledge of the primary sequence of the molecular target. However, the promiscuity of oligonucleotides – in terms of their binding to homologous sequences – places severe limitations on this approach since off-target-related toxicity undeniably contributes to the poor toxicological profile of these drugs. Selecta Biotech developed an unconventional platform named ESiNAR-X®, which considers steric and thermodynamic aspects of the interactions between therapeutic oligonucleotides and their molecular targets as additional parameters during the structural design phase – significantly improving the drug's specificity and, hence, safety.

How does Selecta Biotech operate within the biotechnology sector?

We work very closely with more than 20 partners from both the academic and private sector, as well as with hospitals and non-profit organisations, supporting the activities and innovations aimed at improving the quality of health care and patients' very lives.

In cooperation with our regional partners and leading foreign institutions in the field of R&D, we have already established a functional biotechnological ecosystem with the primary aim of performing interdisciplinary biomedical research in the field of personalised medicine. We purposefully combine our expertise in nucleic acid chemistry, macromolecular chemistry, physical chemistry, structural biochemistry, molecular biology, genomics, and proteomics to achieve this.

What turnaround time can clients expect for a custom-made oligonucleotide-based inhibitor?

Our standard R&D pipeline involves rigorous bioinformatical analysis, structural design, lab-scale synthesis, and early-stage preclinical validation of a tailor-made inhibitor. Incorporating the extensive experience our professionals possess in the synthesis and functional evaluation of therapeutic oligonucleotides for various diagnoses, as well as our optimised working procedures, modern infrastructure, and strong scientific background, the development and pilot validation of a custom-made inhibitor typically takes four to six months.

Besides oncology diagnoses, what other diseases or infections can the revolutionary inhibitors be used to address?

Since our proprietary platform of oligonucleotide-based inhibitors is universally applicable, our vision is to spread its utility to other diagnoses as well. Besides oncology, preclinical validation of lead therapeutics is currently on-going for cardiovascular disease, kidney disease, and viral infections.

Can you tell us more about the highly successful inhibitor Selecta Biotech developed to fight SARS-CoV-2 and how its incredible results can help meet the global challenge of developing new and safe treatment modalities against other diseases of viral origin?

The persistent coronavirus pandemic and the high mortality rate associated with it demanded effective and safe therapeutic solutions. Accepting the challenge, we implemented our technology into developing a tailor-made oligonucleotide-based inhibitor targeting SARS-CoV-2, capable of spontaneously penetrating the cells, binding to viral RNA, and inducing its enzymatic degradation with a remarkable >98% efficacy after a single application. The demonstrated therapeutic potential of this inhibitor could translate into substantial benefits for patients with COVID-19 and is currently being reviewed by regulatory authorities for clinical trials.

Besides that, in the context of infectious diseases, our results provide implications for the research and development of analogous antivirals for other diseases of viral origin. The findings could help to meet the global challenge of developing new and safe treatment modalities.

What does the future hold for Selecta Biotech, and what evolutions do you expect to see in the biotechnology industry within Slovakia?

The Slovak biotechnological industry is relatively immature, with its future and Slovak innovations depending on larger strategic partnerships. Only after these are formed can a solid foundation pillar be created for autonomous applied research with original and accessible solutions. We can definitively build on unique technologies, which this segment already offers on a national scale. We know how to identify the gaps in the current knowledge and have the courage and determination to provide progress. We believe that when something is truly beneficial for society, we can even bend the universe for a good cause.

What about your personal future? Are there any scientific papers or major projects in the works?

From the company's point of view, we are currently investing all our energy in completing the preclinical validation of several promising therapeutic leads. At the same time, we are intensively communicating with the regulatory authorities and believe that we will successfully enter clinical trials soon to help those with unmet medical needs.

For more information or to view the full product portfolio, please visit **www.selectabiotech.com.**