



NEURO-HORIZON
PHARMA



JOINT NEWS RELEASE

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US-based Neuro-Horizon Pharma licenses promising compounds from NTU Singapore to combat multidrug-resistant tuberculosis

With multidrug-resistant tuberculosis (TB) causing outbreaks in both developing and developed nations, new treatments are urgently required to tackle this infectious disease.

A series of chemical-based compounds which could be potential drug candidates in the fight against TB have been developed in Singapore.

The compounds are developed by a joint team from **Nanyang Technological University, Singapore (NTU Singapore)** and the **Experimental Drug Development Centre (EDDC)**, a national drug discovery and development platform hosted by the **Agency for Science, Technology and Research (A*STAR)**.

Neuro-Horizon Pharma LLC (NHP), a US-based drug development company, has licensed the compounds for commercialisation from NTU's innovation and enterprise company, **NTUitive**, which had filed patent applications for the compounds.

The World Health Organisation¹ estimates that over 1.5 million people die from TB worldwide, making it the second leading infectious disease killer after COVID-19.

Caused by the bacterium *Mycobacterium tuberculosis*, TB is an infectious disease that has plagued humankind for more than 70,000 years², with an estimated 10 million new cases of tuberculosis annually.

¹ World Health Organization. (n.d.). Tuberculosis (TB). World Health Organization. Retrieved July 5, 2022, from <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>

² Barberis I, Bragazzi NL, Galluzzo L, Martini M. [The history of tuberculosis: from the first historical records to the isolation of Koch's bacillus](#). J Prev Med Hyg. 2017 Mar;58(1):E9-E12. PMID: 28515626; PMCID: PMC5432783.

Earlier in June, the Ministry of Health announced that 170 people had tested positive for TB in a large cluster³ in Singapore. TB is endemic in the developed city state and the prevalence of tuberculosis infection can be as high as 29% among those aged 70 to 79 years.

Founder and CEO of NHP Dr Vladimir Marshansky, said: “We are pleased to partner with NTU Singapore to develop compounds for treating pulmonary tuberculosis, which remains a public health crisis today.”

“Current regimens for treating tuberculosis are lengthy and suffer from toxicity issue while drug-resistant strains of the respiratory disease are becoming more prevalent, with only 1 in 3 people suffering from drug-resistant TB having access to treatment,” added Dr Marshansky.

This discovery was made possible through a transdisciplinary platform called **TOPNet** (Targeting Oxidative Phosphorylation Network) that is supported by the National Research Foundation Singapore ⁴(NRF Singapore).

TOPNET is led by **NTU Professor Dr Gerhard Grüber** in collaboration with EDDC and **Prof Thomas Dick** from the **Center for Discovery and Innovation Hackensack Meridian Health (CDI)** in the US.

Prof Grüber said that developing innovative solutions to tackle some of humanity’s greatest challenges, like the ever-evolving infectious diseases, is a key pillar of the NTU 2025 Strategic Plan.

“This partnership between NTU Singapore and NHP is a great example of how basic fundamental research at the University can yield great results years later, such as drug compounds that have a big impact on public health. When we started our research, it was imperative that we understood all the key processes needed for the survival of the TB bacterium. With that done, only was it then possible to identify key targets of the adenosine triphosphate (ATP) processes that could stop multidrug-resistant tuberculosis bacterium from proliferating and replicating, opening up the potential for new treatment options,” explained Prof Grüber.

These small molecule compounds were shown to inhibit a key enzyme used by the TB bacterium to produce ATP, an important molecule that is the primary source of energy for living cells.

³ Chew, E. (2022, June 25). Singapore Widens Tuberculosis Checks After Large Cluster Emerges. Bloomberg.com. Retrieved July 6, 2022, from <https://www.bloomberg.com/news/articles/2022-06-25/singapore-widens-tuberculosis-checks-after-large-cluster-emerges>

⁴ NRF Research Grant Number: NRF–CRP18–2017–01

At the molecular level, this ATP-producing enzyme is akin to a nano-sized Wankel⁵-like rotary motor that turns to convert energy from one type to another type. If the ATP-enzyme stops running, the ATP production process and the resulting energy supplied to the TB bacterium will be disrupted. This can be likened to how a car comes to a halt when its engine stops.

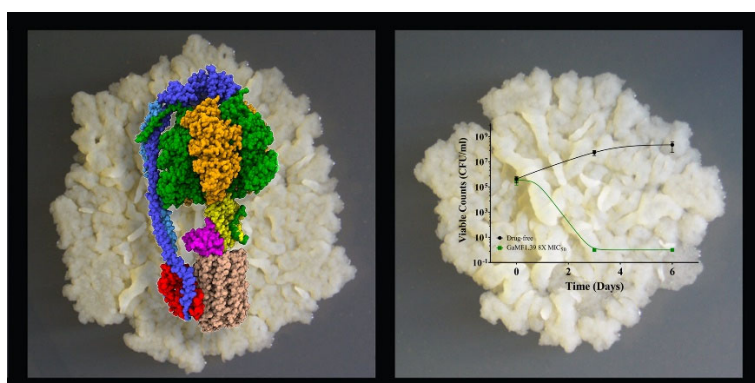
The path to the discovery and design of these small molecules was paved by earlier NTU studies on the metabolism of drug-resistant TB, done by **Prof Grüber**, **Assoc Prof Roderick Wayland Bates** from the School of Physical and Mathematical Sciences and **Assoc Prof Kevin Pethe**, Provost's Chair in Infectious Disease at the Lee Kong Chian School of Medicine.

The researchers then combined their expertise in structural biology, mycobacterial physiology, bioenergetics, and drug discovery, with EDDC's expertise and experience in drug design and medicinal chemistry, to successfully develop the lead series of small molecule inhibitors.

Professor Damian O'Connell, Chief Executive Officer of EDDC, said, "As Singapore's national drug discovery and development platform, EDDC works with key players in the local ecosystem to translate R&D into medicines that address unmet needs, and drive better health outcomes for society. EDDC is proud to partner with NTU in the development of these small molecule inhibitors, and we look forward to NHP progressing these molecules as drug candidates for tuberculosis patients."

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Note to Editors:



The above figure shows two forms of mycobacterial colony formation. The mycobacterial F-ATP synthase (left) is the target of the new chemical compound, which is shown to be potent in killing the bacterium (right).

⁵ https://en.wikipedia.org/wiki/Wankel_engine

Media contact:

Lester Kok
Senior Assistant Director
Corporate Communications Office
Nanyang Technological University, Singapore
Email: lesterkok@ntu.edu.sg

Vladimir Marshansky MD, PhD.
Founder and CEO
Neuro-Horizon Pharma LLC
Email: vlad@neuro-horizonpharma.com

About Nanyang Technological University, Singapore

A research-intensive public university, Nanyang Technological University, Singapore (NTU Singapore) has 33,000 undergraduate and postgraduate students in the Engineering, Business, Science, Medicine, Humanities, Arts, & Social Sciences, and Graduate colleges.

NTU is also home to world-renowned autonomous institutes – the National Institute of Education, S Rajaratnam School of International Studies, Earth Observatory of Singapore, and Singapore Centre for Environmental Life Sciences Engineering – and various leading research centres such as the Nanyang Environment & Water Research Institute (NEWRI) and Energy Research Institute @ NTU (ERI@N).

Under the NTU Smart Campus vision, the University harnesses the power of digital technology and tech-enabled solutions to support better learning and living experiences, the discovery of new knowledge, and the sustainability of resources.

Ranked amongst the world's top universities, the University's main campus is also frequently listed among the world's most beautiful. Known for its sustainability, over 95% of its building projects are certified Green Mark Platinum. Apart from its main campus, NTU also has a medical campus in Novena, Singapore's healthcare district.

For more information, visit www.ntu.edu.sg

About Neuro-Horizon Pharma

Neuro-Horizon Pharma LLC (NHP) is a US-based drug development company with a platform founded on extensive expertise in the area of molecular and cell biology of ATP-driven rotary nano-motors and small GTPases and their use as therapeutic targets for innovative drug design and development.

The primary driving effort of NHP is to exploit fundamental novel insights in the function of rotary nano-motors, including the V-ATPase in humans and the F-ATP synthase in pathogenic bacteria. Leveraging our experience in this field, our main interest is to

develop innovative small molecule drugs and peptides specifically targeting cellular pathways that depend on these nano-motors and small GTPases for the treatment of neurodegenerative disorders and infectious diseases.

Recently licensed inhibitors will be used by NHP to develop innovative small molecule drugs targeting F-ATP synthase nano-motor of *Mycobacterium tuberculosis* to treat multidrug-resistant tuberculosis (TB) worldwide.

About the Experimental Drug Development Centre (EDDC)

The Experimental Drug Development Centre (EDDC) is Singapore's national platform for drug discovery and development, formed from the integration of the Experimental Therapeutics Centre (ETC), Drug, Discovery and Development (D3), and Experimental Biotherapeutics Centre (EBC) in 2019. EDDC aims to develop therapeutics and diagnostics that save and improve the lives of patients in Singapore, Asia and around the world. Hosted by the Agency for Science, Technology and Research (A*STAR), EDDC works collaboratively with public sector and industry partners to translate the great science arising from Singapore's biomedical and clinical sciences R&D into innovative healthcare solutions.