

The logo for NOVAREMED features a stylized graphic of a person with arms raised, resembling a bird or a person in a state of joy or triumph, positioned above the company name. The text "NOVAREMED" is written in a bold, blue, sans-serif font. The background of the entire page is a detailed, artistic rendering of a neural network, with neurons depicted as glowing blue spheres with intricate, branching dendrites and axons, set against a dark blue, starry background.

**NOVAREMED**

# **NOVEL MEDICATION FOR NEUROPATHIC PAIN**

# NRD.E1 – a treatment for diabetic related neuropathic pain

## Novaremed's Dr Eli Kaplan shares research on NRD.E1 and explains how it can help to treat diabetic related neuropathic pain

Founded in 2008, Novaremed is an Israeli pharmaceutical company developing a pipeline of compounds for treatment of various diseases. At the top of the list is NRD.E1, the proposed treatment for neuropathic pain: A first in class, efficacious and safe remedy which has a unique mechanism of action.

The company is headed by Dr. Eli Kaplan, and supported by a staff with vast professional expertise.

There are 2 types of pain: Chronic and acute. Chronic pain can also be divided into 2 types: Nociceptive and Neuropathic, depending on the body organ affected. Nociceptive Pain comes from damage to the body tissues, to muscles, joints and bones, whereas Neuropathic Pain is a continuous pain resulting from damage to the nervous system. The specific cause of Neuropathic Pain is often difficult to classify and treat, such as back pain, peripheral neuropathy associated with diabetes, shingles etc.

### Global health problem

Neuropathic Pain, is a significant global health issue and a growing medical challenge as a consequence of aging population, rising incidences of diabetes and shingles, the treatment for which presents a significant unmet need. In the US, an estimated 100 million people having experienced at least one chronic pain episode in the last 12 months. This results in an annual cost of around \$600 billion in medical treatment and lost productivity.

Pain affects more people than cancer, diabetes and heart disease combined.

Numbers show that in 2008 there were between 9 and 16 million sufferers in the US and Western Europe, expected to increase to between 16 and 22 million by 2018, totalling an expected market size of between 7 and 10 billion US dollars.

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“Novaremed’s discovery is a medical breakthrough that, if proved to be effective, has the potential to bring relief to a large population suffering from a problem that has not yet been adequately addressed.”

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“Moderate-to-severe pain has been and continues to be dominated by opioids, which are increasingly being reformulated to offer abuse-resistance, whereas mild pain is effectively treated with non-steroidal anti-inflammatory drugs (NSAID). However, significant unmet needs remain, as chronic pain subtypes – and particularly neuropathic pain – do not respond well to existing therapies:

“The drugs that are available today in the market have not been developed specifically for neuropathic pain and their effect on them has been discovered by chance,” says Kaplan, “but because they work on the central nervous system, they have so many side effects that many patients avoid them and prefer to suffer the pain”.

### Neuropathic pain

Neuropathic pain is caused by damage to the nervous system. 15% of people with diabetes develop neuropathic pain over the years due to poor blood supply, which causes nerves to continue to transmit pain to the brain via an intracellular enzyme.

Once this enzyme was found, the pathway to developing the drug in question was paved: the molecule Kaplan discovered – NRD.E1 – inhibits the enzyme, thus preventing the feeling of pain from reaching the brain.

In June 2016, the Company completed successfully the Phase IIa study. The main objectives were to assess the safety and tolerability of NRD.E1 as well as finding the effective dose. The study was conducted in Israel at 10 sites (both medical and health care centres). 88 diabetic patients with chronic neuropathic pain were randomly recruited into four treatment groups: low dose (10 mg / day), medium dose (40 mg / day), high dose (150 mg / day) and placebo treatment.

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At the end of 3 weeks of treatment, NRD.E1 moderate-dose (40 mg/day) showed clear preference over the other groups:

- It reduced the mean daily pain score by 29.7% vs. placebo (2.6%) which was the study's primary end point. ( $p=0.034$ );
- The highest impact of pain reduction was noted in the sub-group of strong pain (NPS of 7-9 at screening): An improvement of 38.5% vs. worsening of 5.03% in the placebo group. ( $p=0.0048$ );
- NRD.E1 is well tolerated: The numbers of adverse events in the 40 mg/day group was less than in the placebo and in the high dose group.

As all secondary study endpoints showed the same trend of improvement as the primary end point indicating positive totality of the data – we concluded that



the dose of 40 mg/day is the best choice for further development of NRD.E1 as a drug candidate for the treatment of Diabetes Related Neuropathic Pain.

Currently – Novaremed is planning its Phase IIb study in which the effect of NRD.E1 will be tested on 3 treatment groups, (2 doses of NRD.E1 vs. Placebo), app. 100 Diabetic patients with related neuropathic pain per group.

Novaremed's discovery is a medical breakthrough that, if proved to be effective, has the potential to bring relief to a large population suffering from a problem that has not yet been adequately addressed.

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# Fighting against antimicrobial resistance

## Antimicrobial resistance is a global problem that requires commitment to tackle it, shares EU Health Commissioner Vytenis Andriukaitis in a speech

Antimicrobial resistance (AMR) is a global health threat that continues to grow throughout the EU and worldwide. The European Commission has recently launched a new Action Plan to tackle the growing threat as part of the One Health approach that addresses resistance in both humans and animals. The new Action Plan will also aim to boost research and further incentivise innovation between Member States, as well as public and private sectors across Europe and beyond.

Here, EU Commissioner for Health and Food Safety, Vytenis Andriukaitis, highlights in a speech in Washington DC, the Commission's commitment to tackling AMR.

“My principal role as European Commissioner with responsibility for health and food safety is to support the 28 European Union countries towards achieving common objectives. But many of these, particularly in the field of health, are not confined within the borders of the European Union.

It is clear that this is not only a European issue. Bacteria do not respect national borders or walls and this is why AMR is a truly global health problem.

### The burden of AMR

The social and economic burden of AMR is already unacceptably high with an annual human death-toll estimated to be in excess of 700,000 people.

By 2050, antibiotic resistant bacteria are projected to kill 10 million people a year.

Furthermore the long-term economic damage of AMR could be worse than the 2008 financial crisis.

In the European Union alone, it is estimated that AMR annually costs €1.5 billion in additional healthcare expenses and productivity losses.

The case for urgent action on a global scale is plain for all to see.

Last year I attended the United Nations General Assembly in New York, where a number of countries, including the United States – made the commitment to implement activities of the WHO Global Action Plan on AMR.

Since the adoption of this Global AMR Action Plan and the United Nations Declaration on AMR, many countries have made significant progress in tackling AMR – and these achievements should be recognised and applauded.

This has been the case for the USA and also the EU.

In the EU, we take pride in the fact that the EU banned the use of antibiotics for growth promotion in animal production as long ago as 2006. I am a firm believer in this policy and would like to see its further adoption beyond the EU.

An external evaluation of the Action Plan that we have launched back in 2011 highlighted considerable achievements – in areas such as harmonised surveillance in food producing animals. However, it also concluded that greater efforts were needed to tackle AMR and in a more concerted manner.

This explains my firm commitment to stepping up current efforts. At the end of this month, I will present a new European Union One Health Action Plan. It will focus on 3 strategic pillars:

- Making the EU a best-practice region;
- Boosting research and innovation; and

## Editorial

- Shaping the global agenda.

I hope that this Plan will serve as the principal vehicle for the EU to contribute towards implementation of current global commitments – particularly those under the WHO Global Action Plan.

### International action

Let me expand a little bit on international action under the third pillar that is ‘shaping the global agenda’.

I see the US as a key strategic partner in addressing AMR. In addition to cooperating within international organisations – such as the World Health Organization (WHO), the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization (FAO), and international forums such as the G7 and G20 – I want to reinforce bilateral relations between the US and the EU.

Indeed, the US and the EU share many interests on AMR and there is already good collaboration at technical level within the Transatlantic Partnership on Antimicrobial Resistance (TATFAR).

A key guiding principal underpinning our EU actions to fight AMR continues to be “one health approach” – bringing together the health and veterinary sectors in a unified and coherent effort to tackle AMR. As diseases can spread between humans and animals, these 2 sectors are undoubtedly interconnected.

Let me stress that I am under no illusion as to the magnitude of the task ahead.

I recognise that there is still a mountain to climb if we are to successfully defeat AMR.

To this end, more needs to be done to address AMR across all relevant sectors with a one-health approach applied at national, regional and international level.

Finally, I want to stress that citizens have an important role to play in this multi-lateral effort.

Let me tell you about a little experiment my trainees have done on the occasion of the European Antibiotic Awareness Day.

My trainees went to 3 pharmacies around the building where our offices in Brussels are and asked a simple question: how many packs of Antibiotics do you sell a day?

What they learnt is the following: on average these 3 pharmacies sell 41 packages a day.

If we imagine that these trends are common, there are 5000 pharmacies in Belgium... 5000 times 41 is 205 000 packs a day!

I am not claiming it is a real study, though I am sure I could ask to put it on my twitter with a claim: ‘last study shows 41 packs of antibiotics are sold in Brussels per day’.

I reassure you I won’t do this, as a medical doctor I know that doing real study takes a bit more than visiting 3 pharmacies...

Many people out there really need these drugs, therefore we should not stigmatise anyone.

But what we are interested in – is what all the pharmacists said. They said that they sell too much and way too often the prescriptions are inadequate. They also added that people tend to get angry if they don’t get antibiotics prescriptions and often is the question of knowledge, education... and awareness. People do not know that antibiotics do not kill viruses, or that they are ineffective against colds. This little experiment is just a snapshot illustration, in its relative capacity of course.

That’s why citizens matter. We need to change the perception of how antibiotics are used.”

This is an edited version of a speech, which can be found [here](#).

**Vytenis Andriukaitis**

**Commissioner for Health and Food Safety**

**European Commission**

[www.ec.europa.eu/commission/commissioners/2014-2019/andriukaitis\\_en](http://www.ec.europa.eu/commission/commissioners/2014-2019/andriukaitis_en)

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