Novaremed is developing NRD.E1, an innovative therapy for Diabetic Neuropathic Pain

PS90

Results from a proof of concept study

Eva Tiecke[1], Maurizio Rainisio[2], Elon Eisenberg[3], Eli Kaplan[1], Michal Silverberg[4], Liat Hochman[4], Sara Mangialaio[1]

1 Novaremed AG, Basel, Switzerland; 2 AbaNovus srl, Sanremo, Italy; 3 Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel; 4 Novaremed Ltd, Petah Tiqwa, Israel.

Background

Diabetic Neuropathic Pain (DNP) is chronic pain caused by damage to the nerves caused by diabetes. More than 15 million patients experience a DNP that requires treatment and substantially impairs their quality of life[1].

Existing treatments for DNP have strong limitations:

- First line therapy (pregabalin, gabapentin, duloxetine and TCA) control the disease in not more than 30% of the patients[2] either because of lack of efficacy or lack of tolerability.
- Treatment with opioids is associated with major safety concerns (abuse, physical dependence, respiratory and CNS depression).

Novaremed is currently developing NRD.E1, a small orally available molecule that has shown efficacy in a human Proof of Concept study, as well as in multiple preclinical models for both acute and chronic pain.

NRD135S.E1 (NRD.E1)

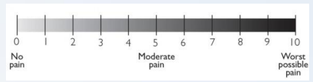
- New Chemical Entity, small orally available molecule
- Mechanism of action different to that of approved pain therapies
- Efficacious in several pre-clinical models for acute or chronic pain
- Very good safety profile in 3 week toxicology studies (rats and dogs)

NRD.E1 was assessed in a Proof of Concept study in patients with Diabetic Neuropathic Pain.

Methods

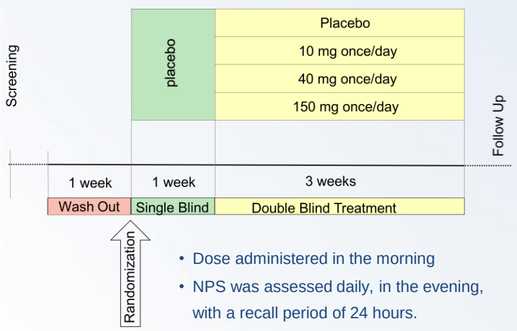
Patient population: moderate and severe DNP at screening (i.e. patients who reported pain intensity of 4-9 on Numerical Pain Scale (NPS; single 11-point numeric scale also known as NRS)

Figure 1. ***Numerical scale used for rating pain***



Study design: randomized, double-blind, placebo-controlled dose-finding trial; 3 week duration

Figure 2. ***Study Design***



- Dose administered in the morning
- NPS was assessed daily, in the evening, with a recall period of 24 hours.

Endpoints

1. Change from baseline to week 3 in weekly average of daily pain intensity measured by NPS.
2. Responders rate on weekly average of daily NPS (30% and 50% reduction from baseline to Week 3)

N.B: two baselines were used: Single Blind Placebo Run-in week (endpoint 1 with this endpoint was the primary endpoint) and Wash-out week (analysis used by all competitors in the past)

Analysis sets

a) Modified Intent-To-Treat set (mITT) i.e. all patients who received at least one dose of study drug in double blind and had at least one NPS assessment (primary analysis).

b) patients with confirmed moderate/severe DNP, i.e. patients who had an NPS at Screening either ≥ 5 or (≥ 4 and receiving pain medications) AND NPS at Washout ≥ 5

Results

88 patients were enrolled into the study in 10 centers in Israel

Figure 3. ***Patient Disposition***

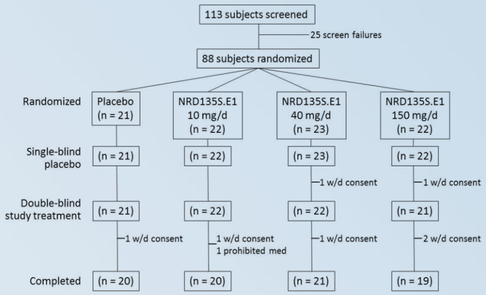
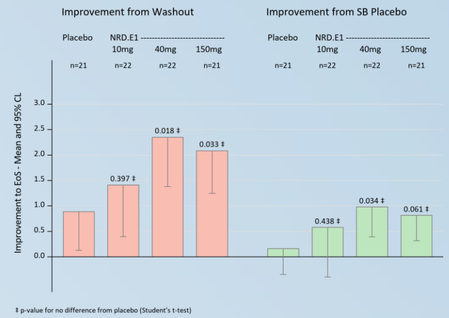


Figure 4. ***Change from SB Placebo and Washout Week to EoS in Weekly Average NPS*** ***(mITT Set)***



‡ p-value for no difference from placebo (Student's t-test)

Figure 6. ***Change from SB Placebo and Washout Week to EoS in Weekly Average NPS*** ***(Confirmed Moderate/Severe Pain)***

‡ p-value for no difference from placebo (Student's t-test)

Figure 5. ***Responder Rate (%) and Number Needed to Treat (NNT) in Change to W3 in Weekly Average NPS*** ***(mITT Set)***

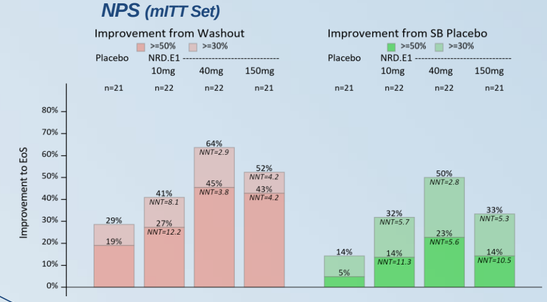
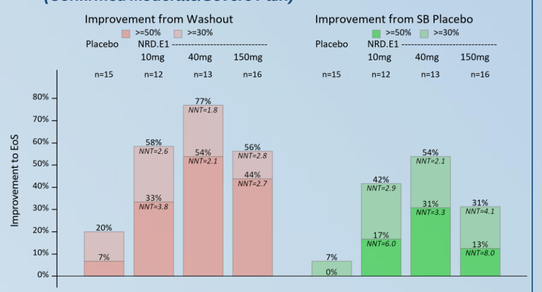
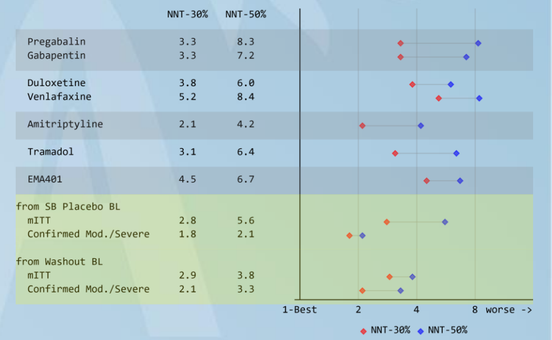


Figure 7. ***Responder Rate (%) and Number Needed to Treat (NNT) in Change to W3 in Weekly Average NPS*** ***(Confirmed Moderate/Severe Pain)***



Number Needed to Treat (NNT) is a common way to communicate the effectiveness of a treatment. It is the number of patients that need to be treated to obtain one more success than with placebo. It is strictly bound to the success rate, being computed as the inverse of the difference in success rate between active and placebo.

Figure 6. ***NNT for NRD.E1 vs Compounds currently available to treat DNP[3,4,5]***



Conclusions

- NRD.E1 was efficacious and well tolerated:
  - Clinically relevant reduction in DNP after 3 weeks of treatment.
  - Well tolerated over 3 weeks at all tested doses up to 150 mg/day.
- NRD.E1 is anticipated to be an innovative therapy for diabetic neuropathic pain.
- NRD. E1 will be further evaluated in a large scale Phase 2b trial of 12 week duration.

Safety Summary

No deaths and no serious adverse events during DB treatment

No severe AEs

No dose-relation

4 premature discontinuations due to AE

- All these AEs resolved and only in one subject they were considered drug-related by the investigator

Laboratory tests, vital signs, body temperature, ECG variables and physical examination: no safety signal identified

Table 1: ***Drug Related Adverse Events (DRAEs) during Double Blind Treatment Period***

	Placebo	NRD.E1		
		10mg	40mg	150mg
	N=21	N=22	N=22	N=21
Pts with at least one AE	7	12	11	9
Pts with at least one DRAE	1	2	1	3
Headache	1			3
Asthenia	1			
Apathy	1			
Blood LDH Increase			1	
Blood TG Increase		1		
Dizziness				1
Eructation				1
Nausea				1
Nervousness	1			
Ventricular Extrasystoles		1		
Vomiting				1

References

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3. Pop-Busui R et al. *Diabetes Care*. 2017; 40: 136–154
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5. Rice ASC et al. *Lancet 2014*; 383: 1637-47

Disclosures

Sara Mangialaio (corresponding author) , Maurizio Rainisio, Eli Kaplan, Liat Hochman and Michal Silverberg and Eva Tiecke are employees or consultants of Novaremed. Elon Eisenberg discloses advisory board activity for Novaremed.

Source of Financial Support for the Project

Since its inception in 2008, Novaremed AG has been financially supported by angel investors and non-dilutive grant funding. To date, Novaremed has raised CHF18.4 M from these sources.

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