

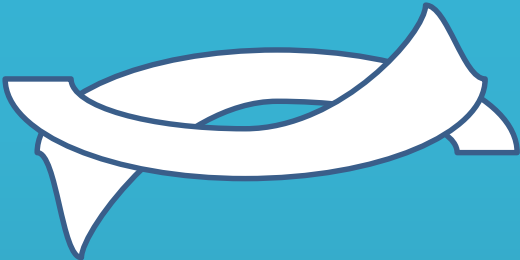
ATED THERAPEUTICS

*Taking the best of what
was accomplished as
the core for moving
forward*

A New Therapy for Neurological Disorders

**Addressing ADNP:
*A Protein Essential for
Normal Neural Development***

September 2022



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Statements made about ATED Therapeutics, other than statements of historical fact, reflect Management's current beliefs and assumptions founded on the data and information currently available to us. Statements of the company's progress, results, timing of pre-clinical and clinical trials and projections for product pipelines are examples of forward-looking statements. By definition, such undertakings involve risks, uncertainties and assumptions, and are subject to a number of such factors that could cause actual results to differ substantially from statements made, including but not limited to: risks associated with the success of clinical trials; research and development programs; regulatory approval processes for clinical trials; competitive technologies and products; patents, inception and/or continuation of corporate and other strategic partnerships and the need for additional funding or financing.

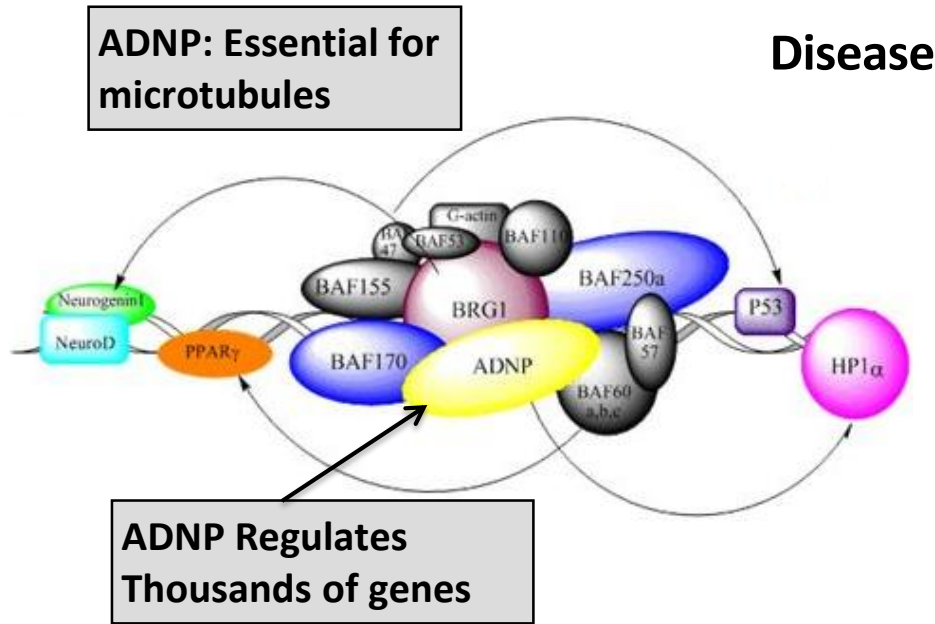
Although forward-looking statements contained in this presentation are based upon what management of ATED Therapeutics believes are reasonable assumptions, there can be no assurance that forward-looking statements will prove to be accurate, as actual results and future events could differ materially from those anticipated in such statements.

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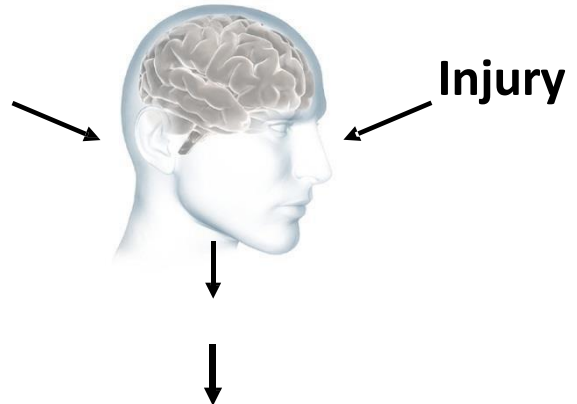
This document is not an offer for the sale of securities of ATED Therapeutics or for investment in ATED Therapeutics. By providing this document to a recipient, ATED Therapeutics is not assuming an obligation to engage in discussions or negotiations for a potential investment. This presentation is not intended to serve as legal, business or tax advice.

Our Discovery: Activity-Dependent Neuroprotective Protein (ADNP)

- Discovery of brain protective molecules: essential for brain formation and function



Disease



Activity-Dependent Neuroprotective Protein (ADNP)



No ADNP = No Brain



Normal Embryo



ADNP Knockout has disrupted brain formation: Dies in utero

ADNP Mutations/ADNP Deficiency:

ADNP Syndrome, ASD, Schizophrenia, Mild Cognitive Impairment, ALS, Alzheimer's disease

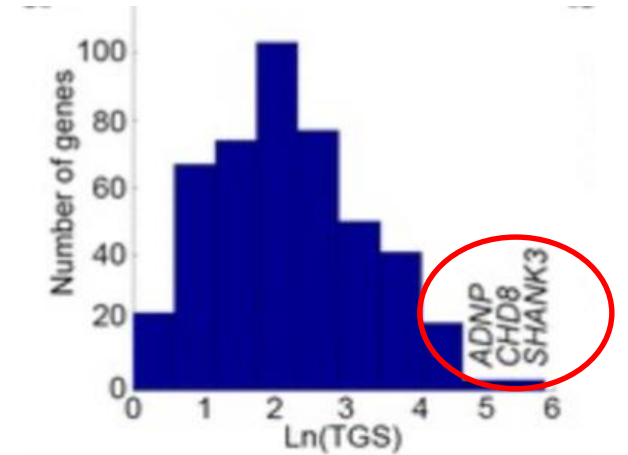
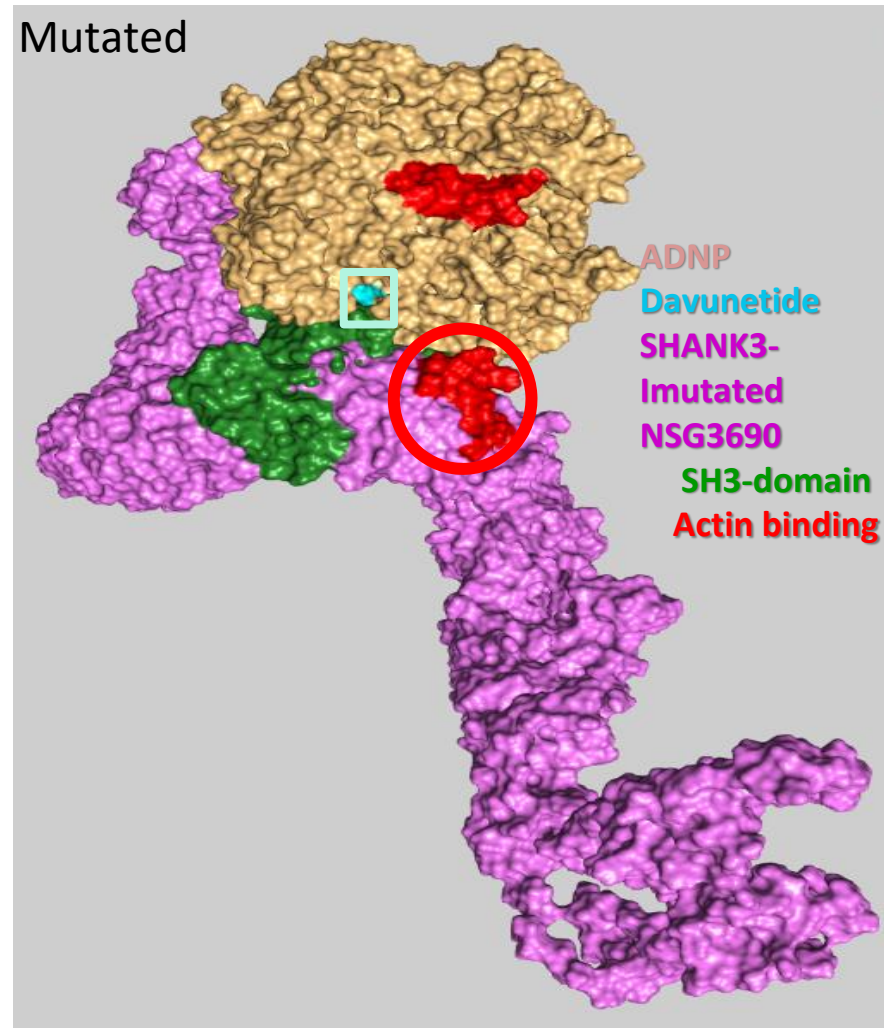
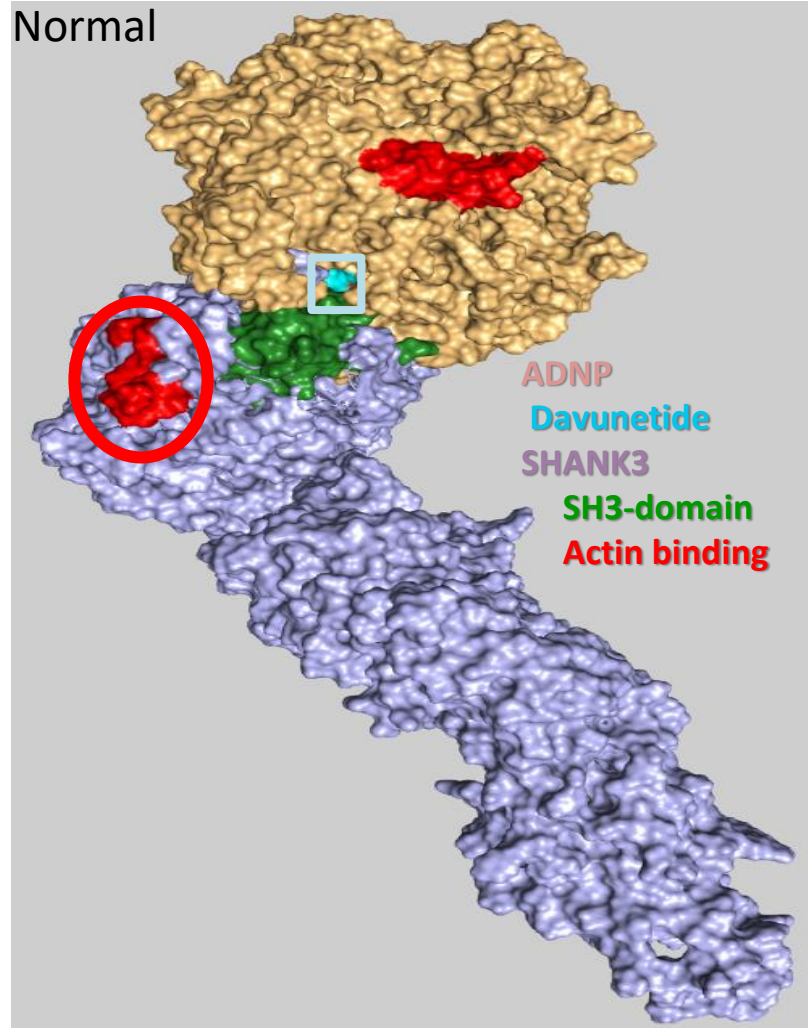
Our ADNP platform

- NAP (*Davunetide* – previously CP201 and AL-108)
- SKIP (A shorter version of NAPVSIPQ, containing a protecting fragment)
- ADNP Syndrome (Autism Spectrum Disorder – ASD)
 - Schizophrenia, ALS, Parkinson's disease, and Alzheimer's disease



ADNP: A Precise Mechanism of Action

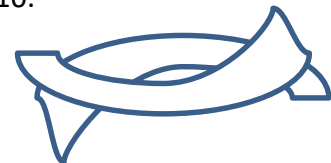
In the SH3 Domain, it Binds and Regulates with SHANK3 through its Davunetide Structure



Long genes like ADNP and SHANK3 are most associated with Autism Spectrum Disorders (ASD)
Mol Autism. 2016 Oct 21;7:44.

[SH3- and actin-binding domains connect ADNP and SHANK3, revealing a fundamental shared mechanism underlying autism.](#)

Ivashko-Pachima Y, Ganaiem M, Ben-Horin-Hazak I, Lobyntseva A, Bellaiche N, Fischer I, Levy G, Sragovich S, Karmon G, Giladi E, Shazman S, Barak B, **Gozes I**.
Mol Psychiatry. 2022 May 10.



Fundamental Mechanism Underlying Autism

SUMMARY: ADNP and SHANK3

Two key autism proteins interact directly with SH3 Domain binding and indirectly through actin binding. Poor or no interaction can cause Autism - or schizophrenia.

Davunetide is a segment of ADNP and repairs mutated SHANK3* in mice:

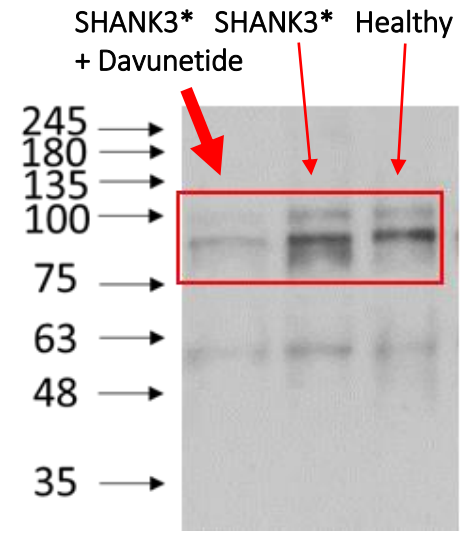
- Deficient protein interaction – repaired
- Anxiety – repaired
- Repetitive behavior – repaired
- Aberrant social behavior - repaired

[Reference](#)
[SH3- and actin-binding domains connect ADNP and SHANK3, revealing a fundamental shared mechanism underlying autism.](#)

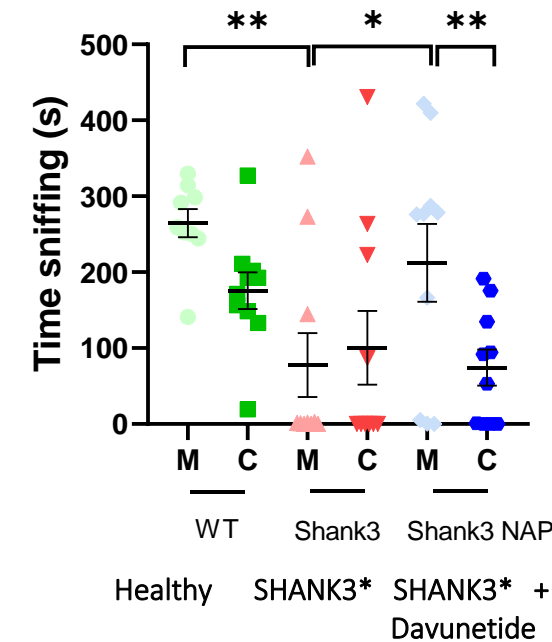
Ivashko-Pachima Y, Ganaïem M, Ben-Horin-Hazak I, Lobyntseva A, Bellaïche N, Fischer I, Levy G, Sragovich S, Karmon G, Giladi E, Shazman S, Barak B, Gozes I. Mol Psychiatry. 2022 May 10

Note:
Other autism proteins/genes also interact with ADNP

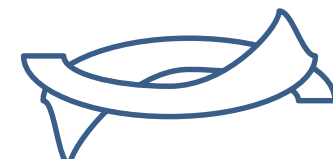
Actin Binding
Mutated Shank3* (mouse brain) shows abnormal interaction with actin - corrected by Davunetide treatment.



Abnormal protein (actin) binding is corrected by Davunetide



Behavioral Repair
Mutated Shank3* mice are "autistic" - do not differentiate between an empty cup (C) or a mouse (M), which is corrected by Davunetide treatment.





Brain Repair Mechanism: Davunetide

ADNP (activity-dependent neuroprotective protein) is an essential protein for brain formation and function.

- NAP is the smallest active site of ADNP
- Protects against ADNP deficiency while inhibiting nerve cell death.

Davunetide is ATED's name for the protein fragment NAP that can address its deficiencies. It

- Is protected by our exclusive patent portfolio.
- Fortifies brain microtubules (MT)
- Has been shown to protect against MT disruption leading to tau pathology in Autism, ALS, Alzheimer's disease (AD) and other dementias (animal and human studies).

Validated in Clinical Trials > 300 Individuals

Davunetide has been shown to be safe and non-toxic in Phase 1-2a & a pivotal Phase 2/3 clinical trials with little to no side effects.

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*Lead Compound -
Davunetide*

ADNP: Precise Mechanism of Action

It Binds and Regulates Microtubules through its Davunetide Structure



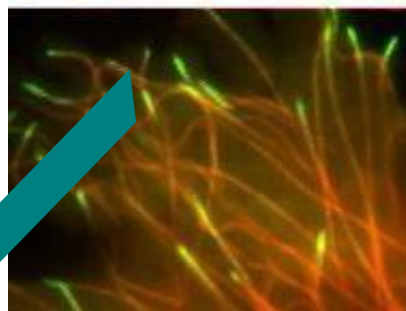
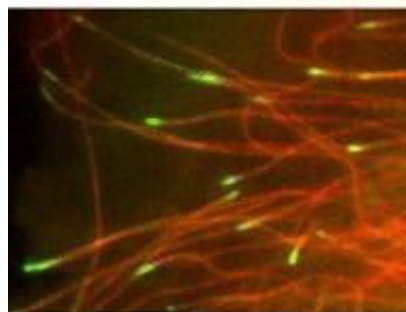
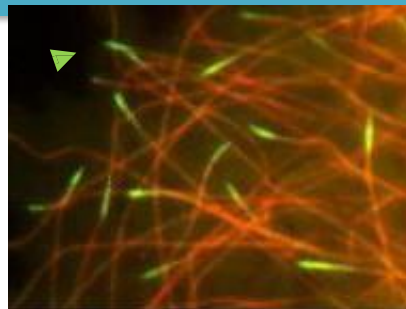
Key Point

Davunetide provides an Amplifier Effect on SxIP Containing Proteins: THE Deficiency in Brain Diseases

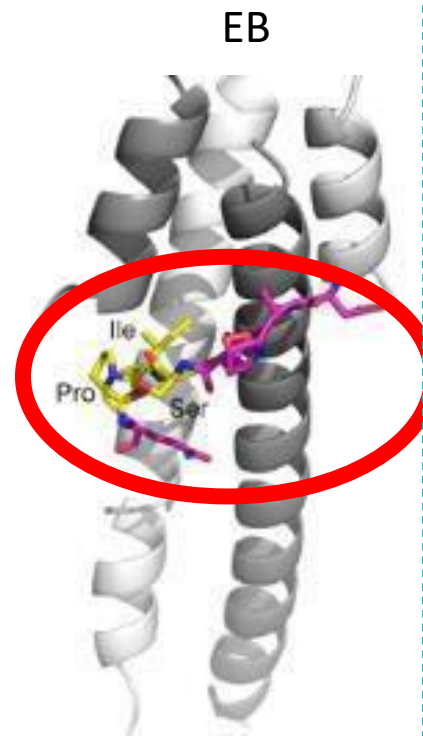


Microtubules:

Microtubules give cellular structure, stability, and transport rails: the end binding proteins (**EB 1 & 3**) are essential for transport & synapse formation



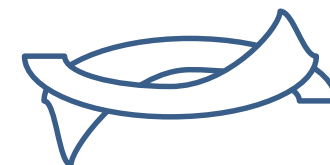
Green: EB Comet
—leading the
microtubule track



Davunetide - **key**
Docked on **EB** - **lock**

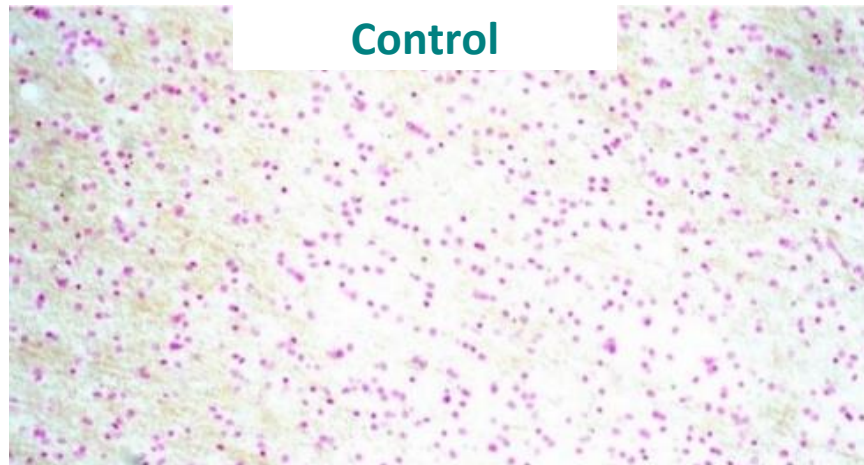
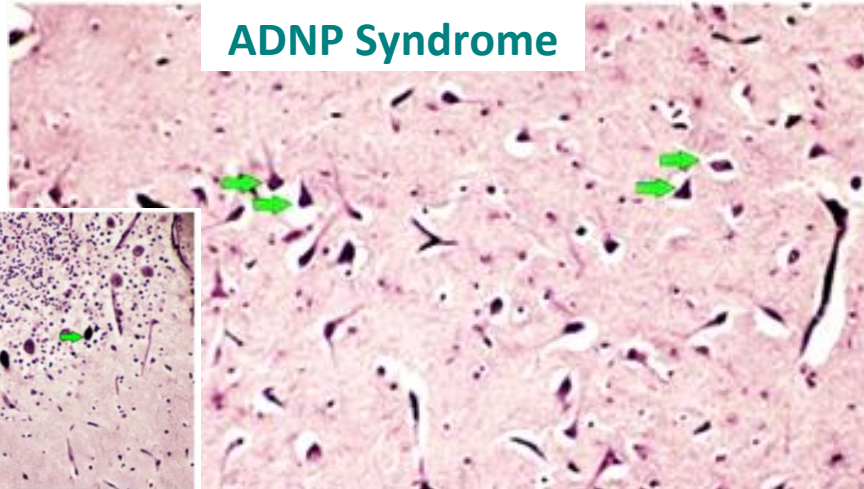
The microtubule end-binding (EB) motif (**SxIP**) is found in davunetide - NAP = NAPV**SIP**Q (and in ADNP). Davunetide enhances microtubule dynamics and the associated protein – enables Tau microtubule-interaction

Mol Psychiatry. 2014;19(10):1115-24
Mol Psychiatry. 2016;21(10):1467-76.
Sci Rep. 2015;5:16300.
Mol Psychiatry. 2017;22(9):1335-1344



ADNP Mutation in Humans –Tauopathy: Connecting Neurodevelopment and Neurodegeneration

ADNP Syndrome Brain Tauopathy Black: Tau Toxic Deposits



Impaired Neurodevelopment/Degeneration

- > Destabilization and breakdown of microtubules
- > Tau hyperphosphorylation **and Tau aggregation – toxic deposits - tauopathy**
- > Progressive loss of function
- > Leads to cell death

Neuroprotection

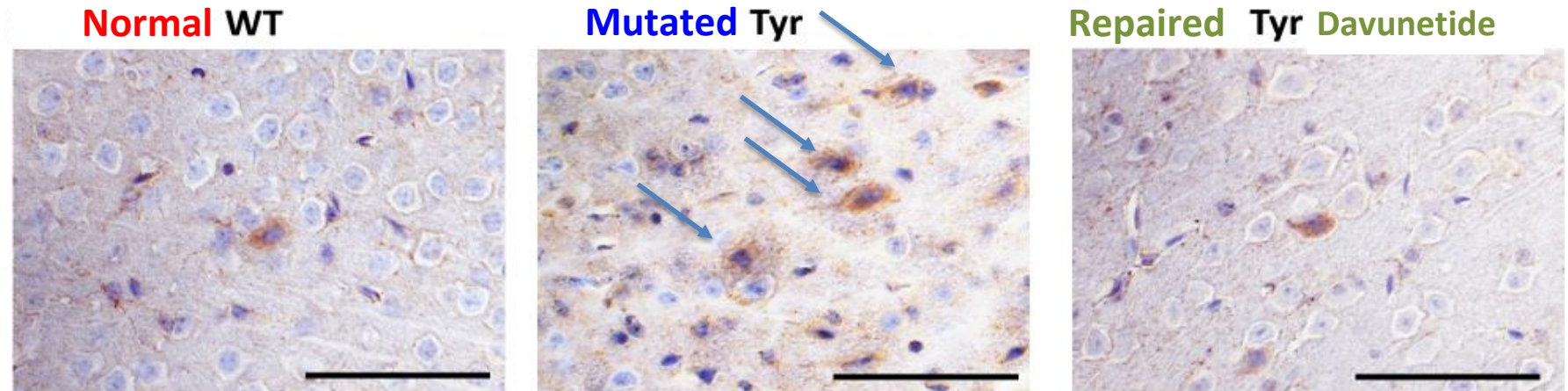
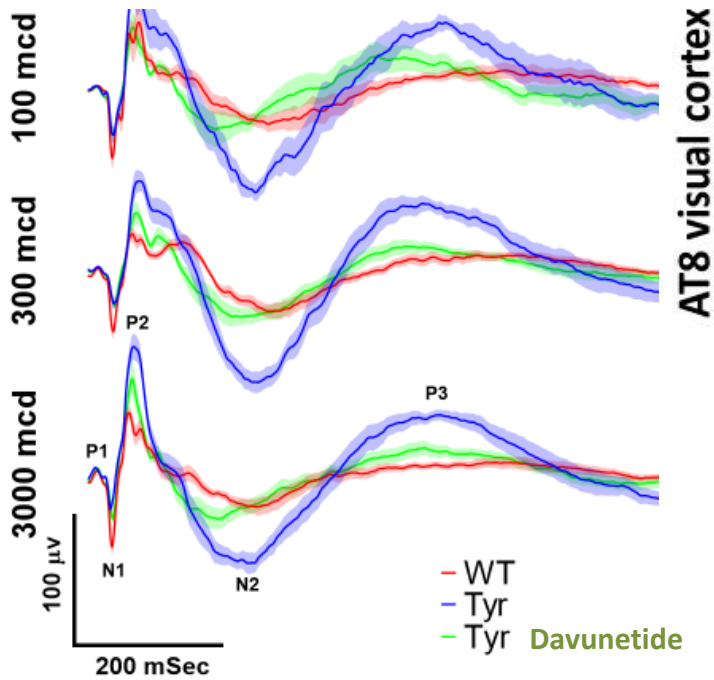
- > Davunetide crosses the human blood brain barrier and the cell barrier
- > Enhances through microtubule end binding protein (EB) association – Tau-microtubule binding
- > Reduces Tau hyperphosphorylation
- > **Repairs** microtubules-protects against Tauopathy
- > Restores neuronal structure and function

Tauopathy in the Young Autistic Brain: Novel Biomarker and Therapeutic Target. I Grigg, Y Ivashko-Pachima, TA Hait, V Korenková, O Touloumi, R Lagoudaki, A Van Dijk, Z Marusic, M Anicic, J Vukovic, RF Kooy, N Grigoriadis, I Gozes *Transl Psychiatry.* 2020 Jul 13;10(1):228.



ADNP Mutation: Davunetide Repairs – Tauopathy in Mice & Visual Evoked Potential Impairments (VEP)

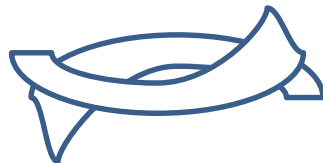
Visual Evoked Potential Impairments (VEP) - Davunetide Repairs



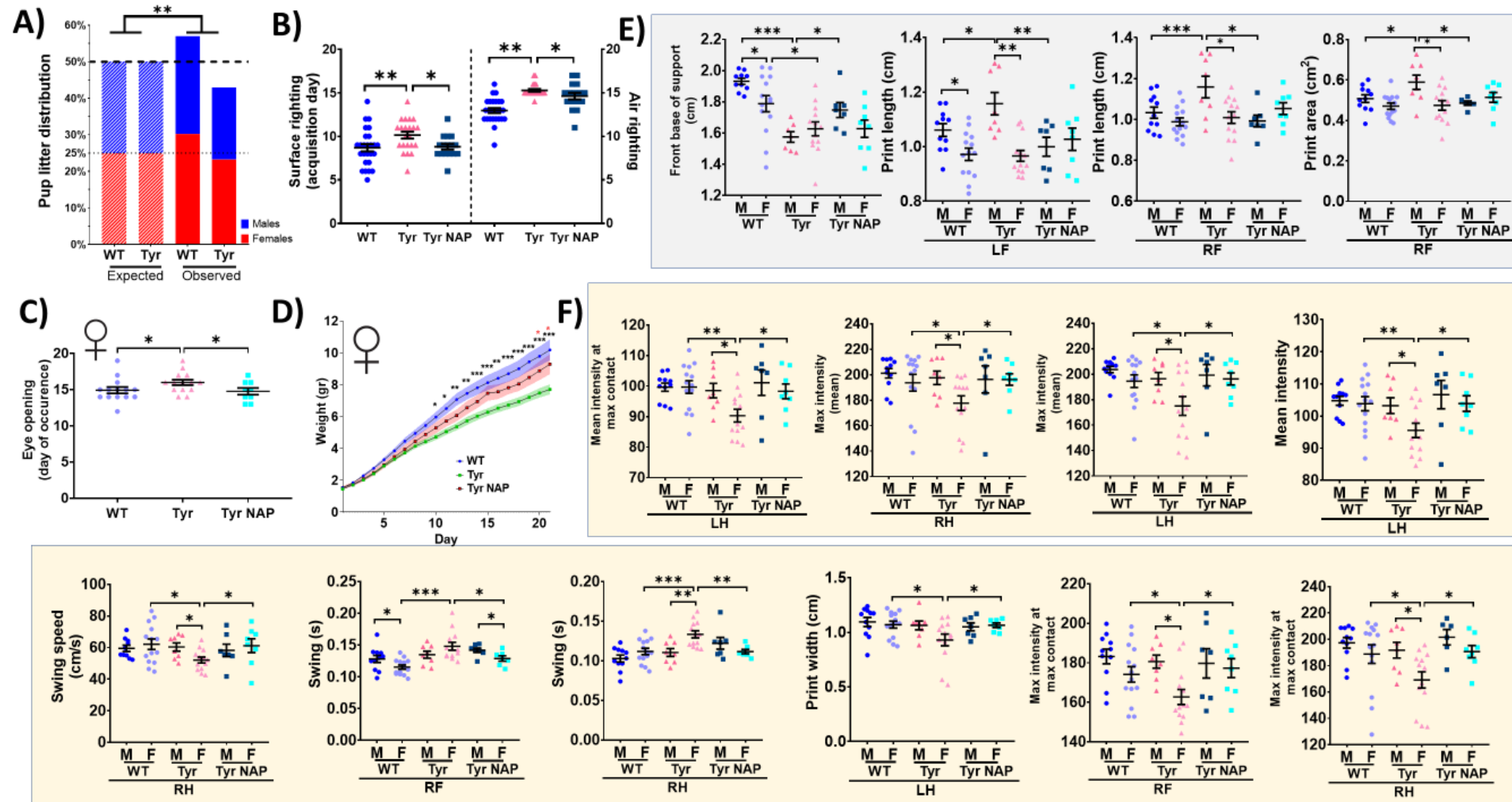
ADNP Mutation – Brain Pathology in Mice– Davunetide Repairs

[Novel ADNP Syndrome Mice Reveal Dramatic Sex-Specific Peripheral Gene Expression With Brain Synaptic and Tau Pathologies.](#)
Karmon G, Sragovich S, Hacoheh-Kleiman G, Ben-Horin-Hazak I, Kasperek P, Schuster B, Sedlacek R, Pasmanik-Chor M, Theotokis P, Touloumi O, Zoidou S, Huang L, Wu PY, Shi R, Kapitansky O, Lobyntseva A, Giladi E, Shapira G, Shomron N, Bereswill S, Heimesaat MM, Grigoriadis N, McKinney RA, Rubinstein M, **Gozes I.** *Biol Psychiatry.* 2022 Jul 1;92(1):81-95.

EDITORIAL: [Sex and the Brain: Novel ADNP Syndrome Mice Are Protected by NAP.](#) Amal H. *Biol Psychiatry.* 2022 Jul 1;92(1):8-9.



Pup Mortality, Developmental Delays and Gait Deficits: Corrected by Davunetide



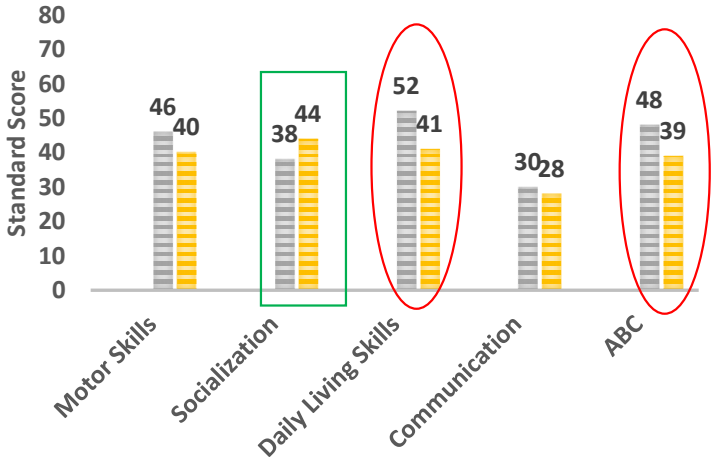
[Novel ADNP Syndrome Mice Reveal Dramatic Sex-Specific Peripheral Gene Expression With Brain Synaptic and Tau Pathologies.](#) Karmon G, Sragovich S, Hacoheh-Kleiman G, Ben-Horin-Hazak I, Kasperek P, Schuster B, Sedlacek R, Pasmanik-Chor M, Theotokis P, Touloumi O, Zidou S, Huang L, Wu PY, Shi R, Kapitansky O, Lobyntseva A, Giladi E, Shapira G, Shomron N, Bereswill S, Heimesaat MM, Grigoriadis N, McKinney RA, Rubinstein M, **Gozes I.** *Biol Psychiatry.* 2022 Jul 1;92(1):81-95.

EDITORIAL: [Sex and the Brain: Novel ADNP Syndrome Mice Are Protected by NAP.](#) Amal H. *Biol Psychiatry.* 2022 Jul 1;92(1):8-9.

ADNP Mutation – in Humans: Delayed Development Potential Neurodegenerative Processes: Natural History

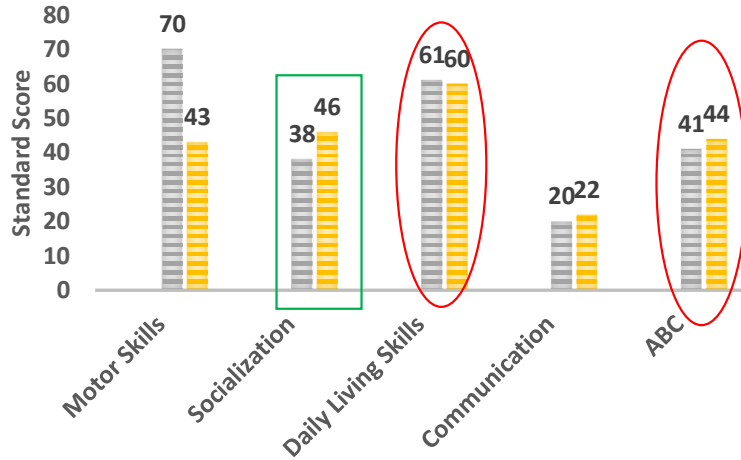
SUBJECT A

■ 6.7 Years ■ 8.4 Years



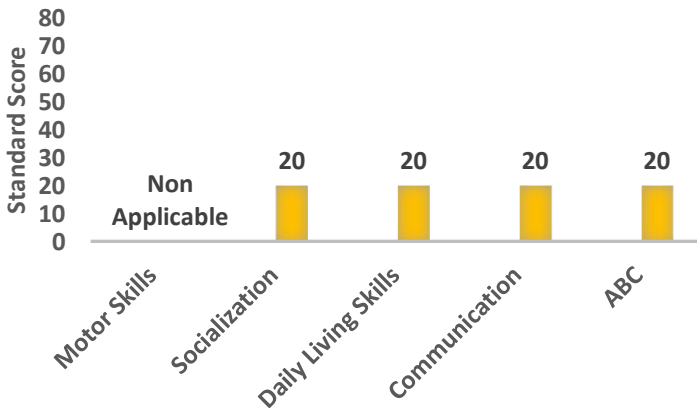
SUBJECT B

■ 6.6 Years ■ 8.5 Years



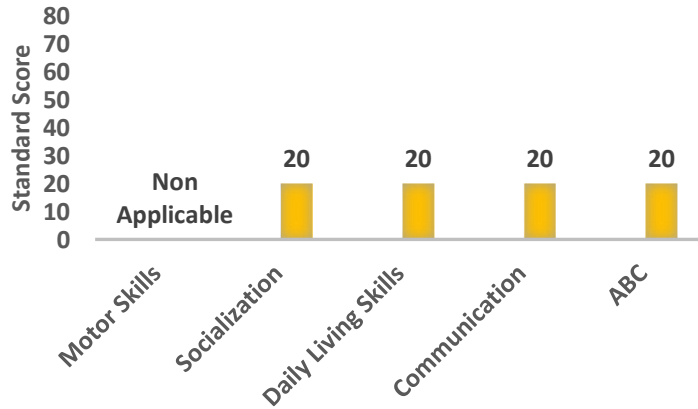
SUBJECT C

■ 27 Years

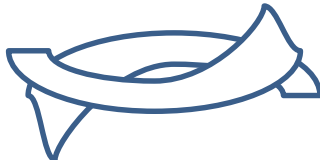


SUBJECT D

■ 27 Years



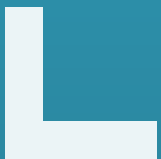
[Vineland Adaptive Behavior Scale in a Cohort of Four ADNP Syndrome Patients Implicates Age-Dependent Developmental Delays with Increased Impact of Activities of Daily Living.](#) Levine J, Hakim F, Kooy RF, **Gozes I. J** Mol Neurosci. 2022 Aug;72(8):1531-1546.





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*Taking the best of what
was accomplished as
the core for moving
forward*



Davunetide in the Clinic



Protects the brain
by simple nasal
spray

**An Approach Based on Strong, Continuously
Progressing Science**



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Clinical Plan: Summary

ADNP Syndrome Trial

Helsmoortel Van Der Aa Syndrome Trial

- Initiates as Pivotal Phase II/III – compound safety previously demonstrated in over 300 adults
- Multi-center study with age-based cohort group design
- Pediatric patients with established ADNP syndrome
- Includes preparatory diagnostics for ADNP Syndrome and ASD
- Administration is intranasal
- Trial expected to be double blind, placebo-controlled



Development Milestones

- Meeting with FDA for ADNP Syndrome – Q42022/Q1 2023
- Initial of ADNP Trial – 1H2023
- Completion of ADNP trial – 2H2024
- Review with/approval by FDA – 2H2025
- Supportive preclinical work for diagnostic and next addressable conditions – 36 months with annual reporting.

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*Initial
Milestones*



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Patent Portfolio

Selected:

7,960,334

8,618,043

7,452,867

8,143,221

8,377,875

8,586,548

9,518,994

2521919

10,118,943

Including:

- *Use of ADNP fragments polypeptides for treating mental diseases*
- *Novel formulation of neuroprotective peptides*
- *Method for diagnosing and monitoring schizophrenia and tauopathies*
- Novel compounds and methods for inhibiting cell death
- Novel therapeutics based on microtubule dynamics
- NAP alpha-aminobutyric acid analog with neuroprotective activity
- And applications, PCTs

Proven Technology with Great Potential: Autism Syndromes & Other Neurological Disorders

- **Davunetide is an ADNP protein fragment – a sequence of NAPVSIPQ**
- **Pipeline patent protected**
- **Pipeline: diagnostic tools for patient stratification**

Novel Disease Target

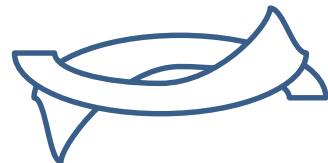
- ADNP (Activity-Dependent Neuroprotective Protein) is essential for brain formation. Mutations cause the autistic **ADNP Syndrome and present interactions with other autistic conditions**

Proven Safety and Efficacy

- Drug candidate protects against ADNP abnormalities in multiple cellular and animal models and in clinical trials (ALS, Schizophrenia, and Alzheimer's disease)*

Promising Advancements

- GMP Ready - batch available for Fill and Finish and Clinical Trials
- **Orphan Drug & Pediatric Rare Disease (PRD) designations**
- Multiple future markets in other Autistic Syndromes



The ADNP/Davunetide Connection: Synapse Protein Deficiencies



Billions of Synapses = nerve cell connections & brain plasticity

Mutations in synaptic proteins cause Autism, Schizophrenia and in a somatic form potentially Alzheimer’s disease

Autism Syndromes:
For example - the ADNP Syndrome

Autism Spectrum Disorder (ASD)/ Intellectual Disabilities	Schizophrenia	ALS
<p>1 in 44 children have an ASD diagnosis. 0.17% of these children have ADNP syndrome (3,000 est. U.S.)</p> <p>ADNP (interacting with many autism genes) is one of the leading autism spectrum genes with ADNP de novo mutations driving the ADNP syndrome</p> <p>Davunetide, the ADNP-derived compound, protects mouse models of ADNP deficiency/mutation as well as related Autistic Syndromes (for example, Shank3 mutation).</p>	<p>1.1% of the U.S. population (3.3M) suffers from schizophrenia</p> <p>ADNP is dysregulated in the schizophrenia brain and blood</p> <p>Davunetide, the ADNP-derived compound, protects in animal models and in clinical trials</p>	<p>~ 30,000 people WW have ALS. No effective current disease modifying therapies.</p> <p>Davunetide, the ADNP- derived compound, protects in animal models.</p>

Prevalent degenerations
For example – Parkinson’s disease & Alzheimer’s disease

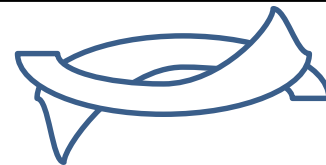


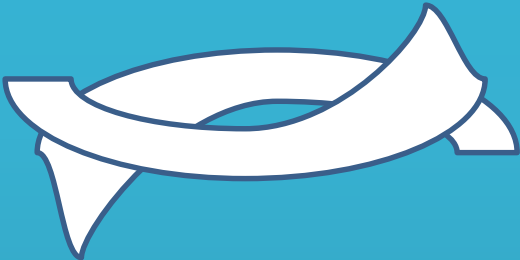
Competitive Landscape: Autism Spectrum Disorder

Drug Name	MOA	Company Name	Developmental Stage	Route of Administration	Intent to treat	Notes
Davunetide	Microtubule repair	ATED	Phase 2/3	Intranasal	ADNP Syndrome	
Ketamine	NMDA antagonist	Mount Sinai Hospital	Phase 2A	Intravenous (single dose)	ADNP Syndrome	Open label trial
Autism Spectrum Disorder (ASD)						
Aripiprazole (Abilify)	D2 receptor agonist	Otsuka	Phase 4	Oral	Irritability	
Risperidone	5-HT2A/D2 receptor agonist	J&J	Phase 4	Oral	Irritability	
CM-AT	Powdered Chymotrypsin	Curemark	Phase 3	Oral	Irritability	No data since 2011
AB-2004	Positively affect gut-brain axis	Axial (https://www.axialtx.com/asd)	Phase 2	Oral	Irritability	Gut directed; side effects unknown.
GWP42003-P	Cannabinoid	Jazz	Phase 2	Oral	Core Symptoms	

Source: Clinicaltrials.gov

Comparison of Davunetide with other compounds and indications is available upon request





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Management Team



JEFF R. SWARZ

CEO



M.M. Dillon & Company Managing Director (2011-). Prior served as a Senior Managing Director at Caris & Company. Brings 22 years of experience in product development and marketing, equity analysis, capital raising, and investment analysis for companies in various segments of the healthcare industry. Prior to joining Caris, was a Managing Director at FBR and Life Sciences Group where he was responsible for corporate finance, mergers and acquisitions and private financing. Before that, he was a partner at EGS Healthcare Capital Partners, a healthcare private equity fund investing in biotechnology, specialty pharmaceuticals, and medical device companies. As an equity analyst in biotechnology research at Credit Suisse First Boston and Goldman Sachs, he was rated among Wall Street's top ten analysts in biotechnology by Institutional Investor Magazine for ten years. Mr. Swarz was a National Institutes of Health Research Fellow in Neurovirology, completed a Postdoctoral Fellowship from Johns Hopkins School of Medicine's Department of Neurology and earned a Ph.D. in Neuroscience from the University of Rochester.

JOSEPH CHIARELLI

CFO



Managing Director MM Dillon (2017-), prior, Chief Executive of SANUWAVE Health. Prior to SANNUWAVE, responsible for financial advisory, business development, and a healthcare hedge fund at Auriga Capital Management. Chairman of Clarent Hospital Management Corp. Prior work included Wall Street Access and Oppenheimer & Company where he was the head of the healthcare research teams. J.P. Morgan & Co. (JPM) (now JPMorgan Chase) where he was responsible for three healthcare sectors of the equity markets as the Senior Investment Research Analyst and an Institutional Investor All Star for both equity and high yield research. Prior to his work in healthcare, he served JPM as the Chief Financial Officer of two large independent subsidiaries, J.P. Morgan Bank (Delaware) and Morgan Securities Services Corporation and was a manager with Coopers & Lybrand (now PriceWaterhouseCoopers). He is a Colonel in the USAF (ret).

ILLANA GOZES

CSO

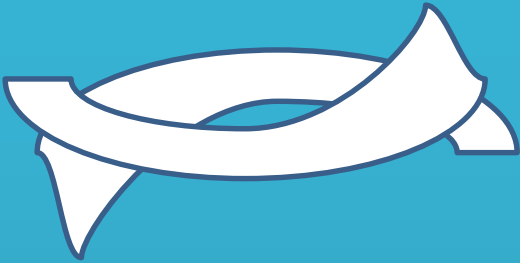


Discoverer of ADNP and inventor of NAP and pipeline products. Professor Emerita of Clinical Biochemistry, Head, Elton Laboratory for Molecular Neuroendocrinology, Faculty of Medicine, Tel Aviv University. (1990-) Formerly, Lily and Avraham Gildor Chair for the Investigation of Growth Factors. Former Director, the Adams Super Center for Brain Studies. Formerly, Associate Professor, Weizmann Institute of Science. Serves as Editor-in-Chief of the Journal of Molecular Neuroscience (Springer-Nature), Secretary of the European Society for Neurochemistry, member of the Israel Council for Higher Education. Former President, Israel Society for Neuroscience, Former Director/CSO, Allon Therapeutics and Coranis Neurosciences. Distinguished fellowships MIT, Salk Institute, Charite Hospital. Author of >350 papers and recipient of multiple prizes, including, Humboldt, Teva, Landau, Fogarty-Scholar-in-Residence (NIH) Champion of Hope, Humboldt and US National Academy of Sciences Catalyst Awards. Ph.D. in Neurobiology, Weizmann Institute of Science.

IDENTIFIED

CMO

Accomplished physician executive with ~24 years of Industry experience in small and large companies, both public and private, including C-level positions, such as CMO and CEO, over the past 10 years. In these roles, he has interacted closely with a broad range of investors and scientific experts. His background includes comprehensive research, development, and commercialization experience for small molecules, biologics/vaccines, and devices, across multiple therapeutic areas, including neuroscience. He was the Global Clinical Leader at a major pharmaceutical company playing a key role in multiple regulatory approvals. He was educated at Yale (BS), Univ. of Wisconsin (MD), Univ. of Washington (MPH), and Yale (MBA). laying a key role in multiple regulatory approvals. He was educated at Yale (BS), Univ. of Wisconsin (MD), Univ. of Washington (MPH), and Yale (MBA).



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Thank You



For further information

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Illana Gozes, Chief Scientific Officer
igozes@tauex.tau.ac.il

Professor Gozes - Champion of Hope – Science International 2016: *Please Join Us in Our Journey*



25 years to the
discovery of
ADNP



Parent Meeting 2019



Moving forward!