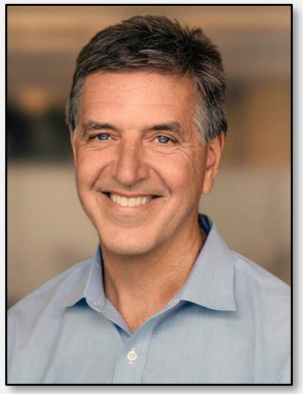
SCOPE 01/15/2025

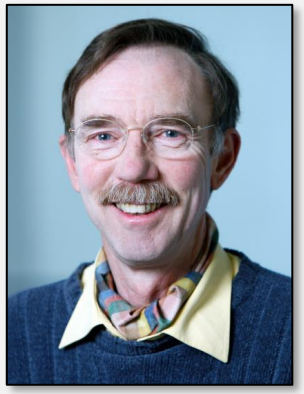
The valley of death: Hurdles that are often interconnected

Wings for Life Accelerated Translational Program Workshop

April 21, 2024



Stephen M Strittmatter



Martin E Schwab

Aileen J Anderson

Angela Ruban

Hassan Al-Ali

Armin Curt

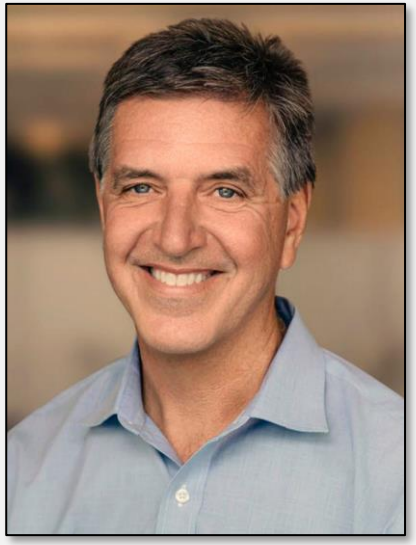
Adrien Cohen

Successful Translational Journeys

In-Progress Translation

Novel Funding Mechanisms

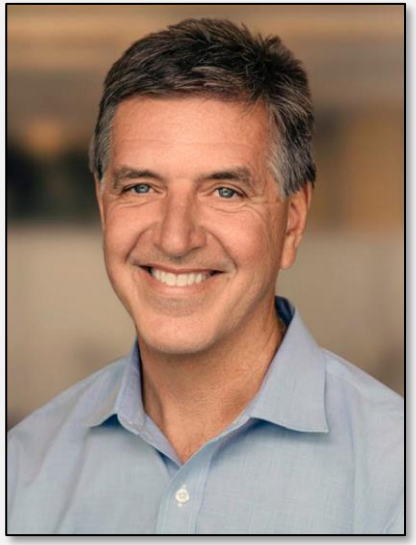
Successful Translational Journeys



Stephen M Strittmatter

- **Session title:** NgR-Fc (Axer-204): Safety, tolerability and efficacy of Axer-204, a Nogo Trap biologic in subjects with chronic spinal cord injury.
- **Affiliation:** Yale University School of Medicine, USA.
- **Compound:** Nogo Receptor decoy (**AXER-204**) one-year post-injury, with first ascending doses then 6 intrathecal boluses at a fixed dose over 104 days.
- **Overview:**
  - RESET clinical trial.
  - Multicenter, randomized, double-blind, placebo-controlled.
  - phase I/II (NCT03989440).
  - Tested in 52 chronic SCI.
  - Completed in 2023.
- **Funding:** Wings for Life, NINDS, etc.

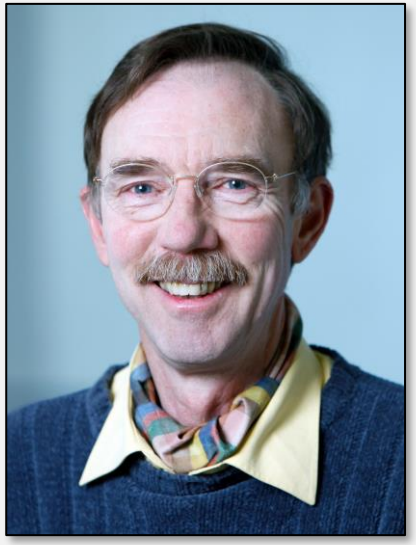
Successful Translational Journeys



Stephen M Strittmatter

- **Target Product Profile (TPP):** Needed as early as possible.
- **Preclinical studies:** Essentials in the creation of the TPP.
- **Production**: Complex and nearly impossible in academia.
- **Preclinical toxicology**: Translating doses across species is challenging.
- **Regulatory process:** A slow endeavor.
- **Clinical trial designs:** Years in the making.
- **Central IRBs:** An indispensable help.

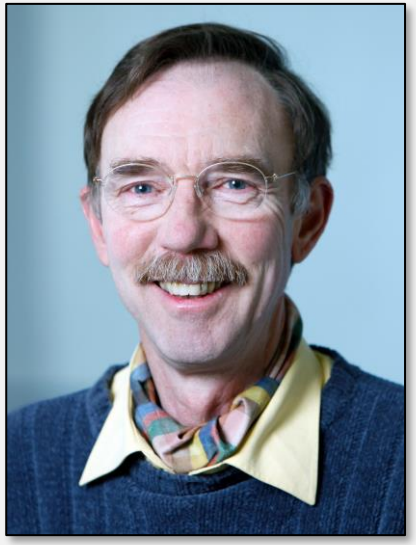
Successful Translational Journeys



Martin E Schwab

- **Session title:** NISCI: Antibodies against Nogo-A to enhance regeneration and functional recovery after acute spinal cord injury, a multicenter European clinical proof of concept trial.
- **Affiliation:** ETH Zurich, Switzerland.
- **Compound:** Nogo Antibody (**NG-101**) 4 to 28 days post-injury, 6 intrathecal bolus injections over 4 weeks.
- **Overview:**
  - NISCI clinical trial.
  - Multicenter, randomized, double-blind, placebo-controlled.
  - phase II (NCT03935321).
  - Tested in 129 acute SCI.
  - Completed in 2023.
- **Funding:** Wings for Life, Horizon 2020, Swiss Paraplegic Research, etc.

Successful Translational Journeys



Martin E Schwab

- **Preclinical drug development:** Challenges in stability, yield and immunological properties.
- **Patents:** Costly and time-consuming.
- **Preclinical toxicology:** Impossible in academia and require external help.
- **Investigational Medicinal Product Dossier**: Essential but complex documentation.
- **Clinical trial application:** TPP, IMPD, investigator's brochure & trial protocol.
- **Clinical trial design**: Investigator-initiated trial.
- **Funding:** 10 million euros.

Successful Translational Journeys

Aileen J Anderson

- **Session title:** HuCNS-SC: A Phase I/II Study of the Safety and Preliminary Efficacy of Intramedullary Spinal Cord Transplantation of Human CNS Stem Cells.
- **Affiliation:** University of California, Irvine, USA.
- **Compound:** Human Central Nervous System Stem Cells (HuCNS-SC), 4–24 months post-injury.
- **Overview:**
  - StemCells, Inc. clinical trial.
  - Multicenter, single-blind, randomized, parallel-arm.
  - phase II (NCT02163876).
  - Tested in 12 chronic SCI.
  - Completed in 2016.
- **Funding:** NIH, California Institute for Regenerative Medicine (CIRM), etc.

Successful Translational Journeys

Aileen J Anderson

- **Complexity and Regulatory Scrutiny**: Cell therapies involve additional complexity and risks.
- **Challenges in Cell Therapy:** Donor and batch variations impact the final product.
- **Intrinsic and Extrinsic Factors:** Need to understand of the “niche” environment.
- **Funding:** Transitioned from NIH grants to larger translational grants.
- **Scaling Up Production:** Need for surrogate assays.
- **Quality Control and Costs:** Need of an early TPP. Costs are huge even in an academic setting.
- **Company Creation Timing:** Delaying the creation preserved the integrity and direction of the therapy's development.

Successful Translational Journeys

Q&A

Question 1: Why are you able to conduct an investigator-initiated clinical trial at a lower cost, and why don't more people go this route?

Question 2: Is there a comparable funding program in the US?

Question 3: Since we have participants from other fields like MS, are we doing something wrong? Are we simply not skilled enough?

In-Progress Translation

Angela
Ruban

- **Session title:** European Innovation Council – Accelerator Fund.
- **Affiliation:** Tel Aviv University, Israel.
- **Compound:** New anti-glutamatergic drug licensed to NeuroHagana.
- **Status:** Phase 1 trial in 2025.
- **Importance of Early Characterization:** Lack of funds or interest might lead to missing important steps (stability, solubility, mode of action, etc.) and will end up costing more later.
- **Regulatory & Funding Strategies:** Innovation Task Force Briefing are free.
- **Company's Development Path:** EIC supports preclinical and trial phases up to € 50 million.

In-Progress Translation

Hassan Al-Ali

- **Session title:** NIH Blueprint Neurotherapeutics Network (BNN) – small molecules and biologics.
- **Affiliation:** Miami Project, USA.
- **Compound:** Kinase inhibitor drug.
- **Importance of Early Development Decisions:** TPP guides research and minimize costly missteps
- **IP:** Balancing academia and entrepreneurship is hard and requires an honest assessment of the personal priorities.
- **Multidisciplinary Team and Expert Engagement:** FDA consultants and business development experts.

In-Progress Translation

Q&A

Question 1: What is the best approach for taking an investigational product forward—forming your own company or getting a bigger company interested?

Question 2: Should researchers focus on forming their own companies to make money from their products, or should they stay in academia and collaborate with industry?

Question 3: When is the right timing to spin something out?

Novel Funding Mechanisms

Armin
Curt

- **Session title:** Wings for life Accelerated Translational Program.
- **Affiliation:** University of Zurich, Switzerland.
- **Flexibility & Network:** Lack of application deadlines and strong support network.
- **Collaboration & Founding:** Promotes co-funding strategies.
- **Executive oversight committee:** Provides regular and detailed guidance.
- **How to apply:** Need of a comprehensive plan, solid team, and clear clinical goals.
- **Values:** Interdisciplinary approaches, thorough trial designs, and inclusive protocols.

Novel Funding Mechanisms

Adrien Cohen

- **Session title:** SCI venture capital for early-stage SCI-innovation.
- **Affiliation:** London, United Kingdom.
- **What it supports:** Early-stage SCI companies and reinvests all proceeds.
- **Who is behind it:** Supported by five foundations.
- **Aim:** Attracting VC investment by reducing risks and leveraging foundation networks.
- **Selected companies:** Augmental, Sania Therapeutics and Axonis Therapeutics.

Novel Funding Mechanisms

Q&A

Question 1: The "Valley of Death" seems to be especially challenging for SCI. For example, startups often must adapt their models to fit generic drug development frameworks and teach CROs how to conduct specific experiments. Do you think simply providing more money may solve these issues?

Question 2 (Adrien): What is the typical investment size for a program, and how does it compare to other life science venture capitals?

Conclusions

The lessons learned fall into some common themes:

- **Early Identification and Development:** Step where most of the IP is created.
- **Regulatory Engagement:** Understand the requirements, often focused primarily on safety.
- **Collaboration and Expertise:** To complement what is not available in an academic environment.
- **Intellectual Property Protection:** Key to facilitating commercialization.
- **Funding:** Previous steps which should be considered as groundwork.
- **Timing of Company Formation:** If funds are available, delaying the creation of a company might make the product more appealing for pharma.
- **Balancing Academic and Entrepreneurial Roles:** Possible, but only after a proper introspection of personal preferences and skills.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