



# Investor Meet Company and ProActive Investor Events

## Harnessing The Power of Sulforaphane

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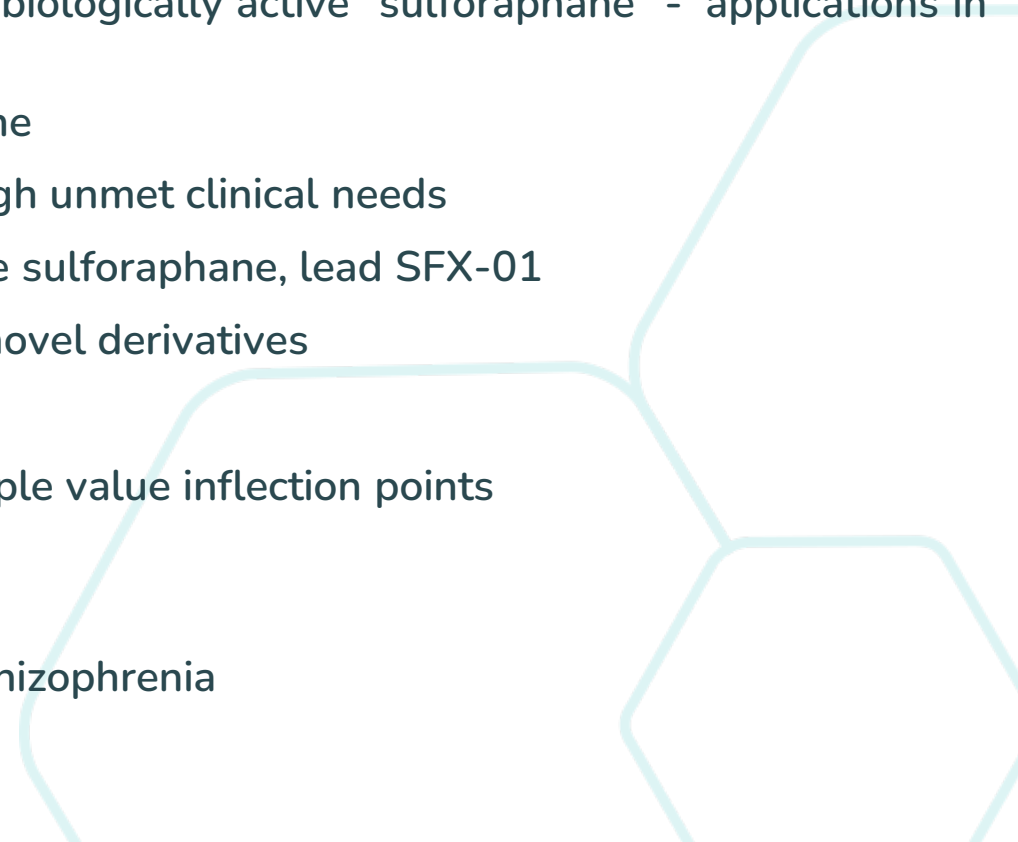
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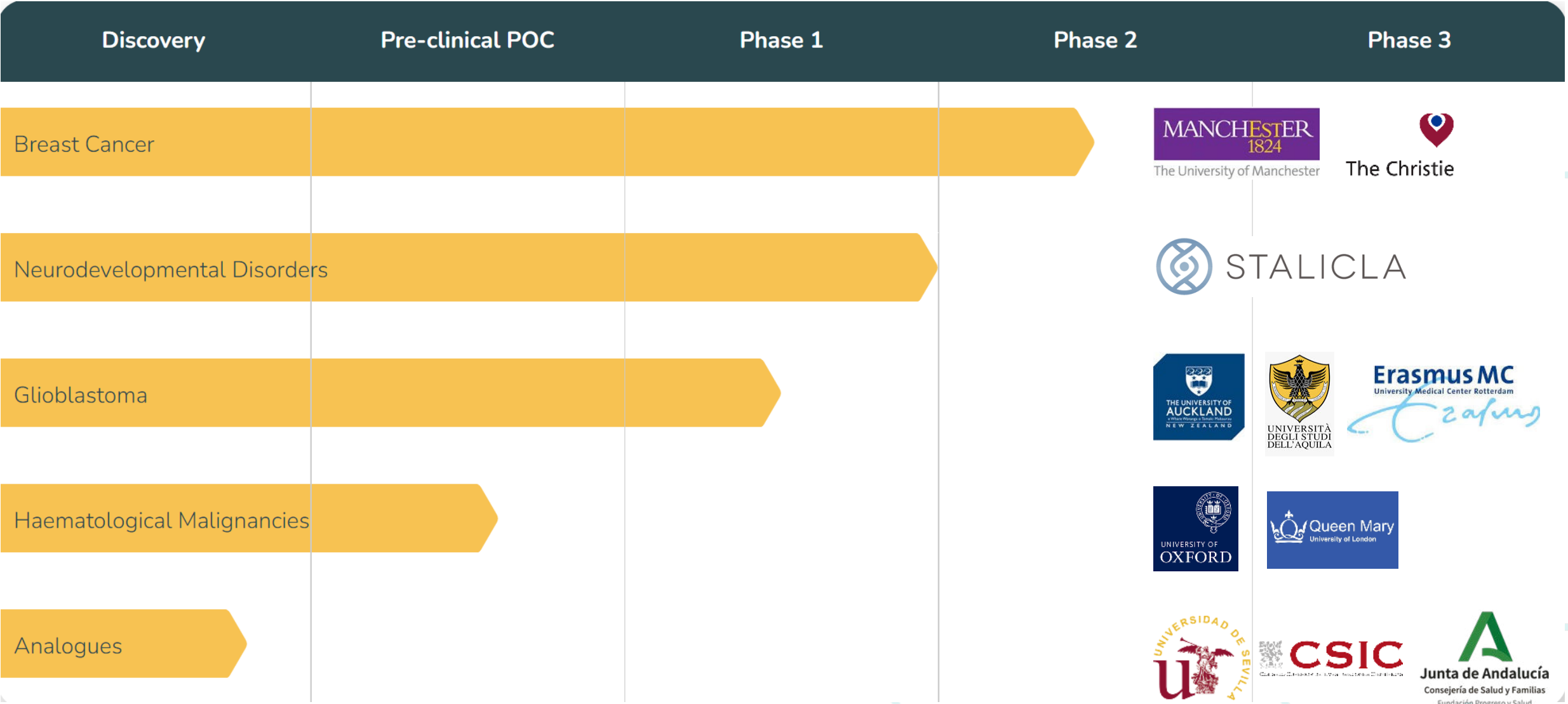
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# Evgen - A Clinical Stage Drug Development Company

Focus on breast cancer, glioma and other cancers. SFX-01 has three molecular targets; STAT 3, Nrf2 and SHP2

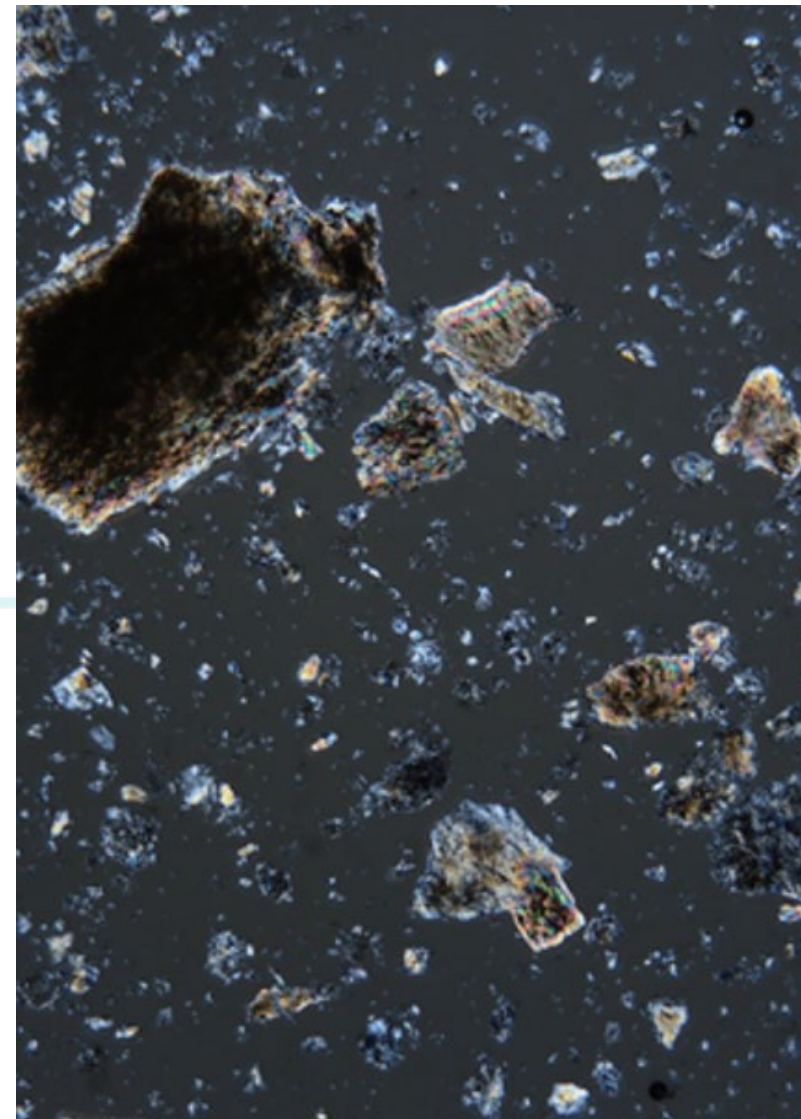
- Developing a new class of pharmaceuticals - based on highly biologically active “sulforaphane” - applications in multiple therapeutic areas based on a network of targets
  - Strong third party pre-clinical and clinical data on sulforaphane
  - Four target diseases in cancer and inflammation, each with high unmet clinical needs
  - Unique platform technology – Sulforadex<sup>®</sup>, stabilises unstable sulforaphane, lead SFX-01
  - Strong, granted IP covering composition, manufacturing and novel derivatives
  - Highly experienced board and management
  - Business model: establish proof of concept and partner. Multiple value inflection points
  - Two out-license collaborations:
    - Juvenescence – nutraceutical
    - STALICLA SA – neurodevelopmental disorders and schizophrenia
  - Strong cash position as at 30 September 2022
  - Cash runway beyond Q4 2024
- 

# Our Pipeline



# Highlights, 2022

Regulatory	UK Regulatory Authority MHRA approval for PK/PD Healthy Volunteer Study
Manufacturing	Scale-up of the active ingredient in SFX-01 to GMP standards and commercial scale achieved with a number of process improvements
New EC Tabs	New formulation of SFX-01 manufactured to GMP in enteric coated tablet form enabling scale-up to supply late-stage clinical trials and commercial use
mBC	Positive progress in our pre-clinical collaboration with the University of Manchester, Manchester Breast Biology Centre and The Christie Hospital.  Encouraging <i>in vitro</i> data in cells that are CDK4/6i resistant
Academic collaboration on radio-sensitisation	Prof Francesco Marampon, University La Sapienza, Rome, evaluating SFX-01 plus radiation <i>in vitro</i>
Academic collaboration on colorectal cancer	Dr Grace Chen, University of Michigan, potential anti-tumour effects of SFX-01 in models of colorectal cancer



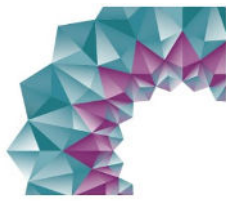
# Q3/4 2022 to Q1 2023

Transformative Transaction	Out-licensing deal for SFX-01 in neurodevelopmental disorders and schizophrenia with STALICLA SA  Milestones of \$160.5m, double digit royalty
Netherlands Regulatory Authority (MEB)	Positive scientific advice regarding the SFX-01 programme in glioblastoma (GBM)
GBM clinical study	Following extensive consultation with world experts, initial SFX-01 GBM study to be conducted as an investigator sponsored study (ISS) led by Prof Marjolein Geurts at the Erasmus University, Rotterdam
Academic collaboration: SFX-01 radio-sensitisation	Evidence of enhancement of the effect of radiotherapy by SFX-01 <i>in vitro</i> even in cells that had developed resistance to radiation from Prof Marampon's Lab at La Sapienza, Rome
Phase 1/1b Healthy Volunteer clinical study	To evaluate PK and PD effects of new SFX-01 formulation. Started on schedule, all cohorts dosed, top line data received showing appropriate release, total levels in line with levels in pre-clinical experiments



# Pre-clinical data in rhabdomyosarcoma

## Abstract



SFX-01 in the treatment of rhabdomyosarcoma: preclinical results in cellular models

**Background:** Rhabdomyosarcoma (RMS) is the most frequent soft tissue sarcoma in childhood. This study evaluated the efficacy of SFX-01 (Evgen Pharma plc, UK), a complex of synthetic d,l-sulforaphane stabilized in alpha-cyclodextrin, in two RMS *in vitro* models, alveolar (ARMS) and embryonal (ERMS), as single agent and in combination with ionizing radiation (IR).

**Methods:** Cell cycle and apoptosis were analysed by flow cytometry, whilst the modulation of specific genes was measured by Real Time PCR and Western blotting assays. Irradiation was carried out exposing RMS cells to a single dose of 4 Gy and the radiosensitivity was assessed by clonogenic and modified high density survival assays. DNA damage repair (DDR)-related markers were studied by Western blotting and Protein Simple WES technology. The effects of SFX-01 on cancer stem cells were assessed by evaluating rhabdosphere formation in ultra-low attachment plates.

**Results:** SFX-01 (10  $\mu$ M) treatment reduced the growth of RH30 (ARMS) and RD (ERMS) cells by inducing G2 cell cycle arrest with the concomitant Cyclin B1 up-regulation and triggering early-apoptosis. Interestingly, the specific knocking down of Cyclin D1 expression by RNA interference seems to enhance the cytostatic/cytotoxic effects induced by SFX-01 on RMS cells. We also found both p62 and LC3 II over-expression after SFX-01 exposure, this suggesting a block of late-stage autophagy. SFX-01 drug synergized with IR by strongly enhancing the effects of both single-agent treatments by showing a drastic reduction of clonogenic ability, block of DDR (persistent activation of  $\gamma$ -H2AX) and increased G2/M cell cycle arrest. Finally, pre-treatment with SFX-01, alone and in combination with IR, significantly affected the ability to form rhabdospheres in both the parental and the clinically relevant radioresistant RMS cells.

**Conclusions:** For the first time, we described the antitumor activity of SFX-01 in preclinical models of RMS tumours. SFX-01 and IR have strong cytotoxic effects and drastically inhibit the formation of cancer stem cell-derived tumorspheres, this indicating that the combined treatment might have therapeutic benefits, mainly in the clinical managements of patients with aggressive RMS disease.

### Authors

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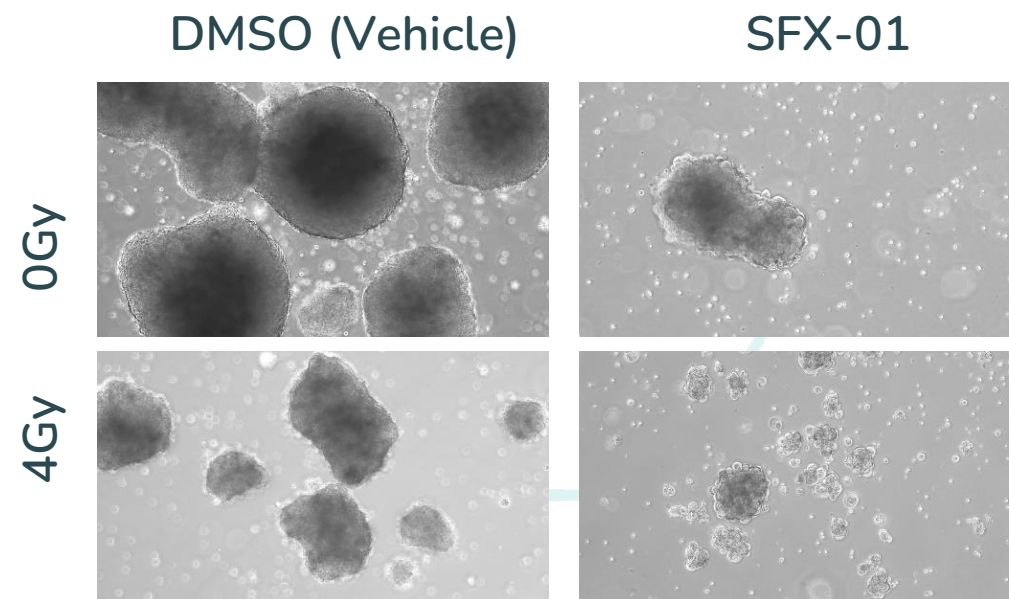
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# SFX-01 in Rhabdomyosarcoma cells and rhabdospheres

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- SFX-01 reduced rhabdomyosarcoma tumour cell growth
- SFX-01 produced a reduction in cell growth that was synergistic with radiation
- SFX-01 reduced tumour cell growth and rhabdosphere formation in radioresistant cells



RH30 radioresistant cells/rhabdospheres

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# SFX-01 Pharmacokinetic and Pharmacodynamic Phase 1b study

## *Top line pharmacokinetic data received*

- Sulforaphane was released by the new enteric coated tablet beyond the acid environment of the stomach based on the time course seen, as predicted
- Levels of sulforaphane and its active metabolites in blood increased predictably with increasing dose
- Total levels of sulforaphane and active metabolites in blood are in the range previously seen to be effective in pre-clinical experiments and clinical studies in a range of target diseases including breast cancer and glioblastoma
- No serious adverse events observed
- Pharmacodynamic analysis now underway, via highly sophisticated experiments on a longer time scale, focused on how the drug modulates disease-relevant molecular targets and will be reported in due course
- The study is on schedule for full reporting in the second quarter of 2023





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**Dr Huw Jones**  
CEO

Over 30 years' experience of leadership in public and private R&D-based companies within the biotechnology and pharmaceutical sector: Chronos Therapeutics, CV Therapeutics, Elan Corp and SB (GSK)



**Richard Moulson**  
CFO

Qualified chartered accountant with over 20 years experience working as a CFO for UK quoted and venture capital-owned companies including: Intercytex Group Plc, ReNeuron Group plc and Cobra Therapeutics Ltd



**Barry Clare**  
Chairman

Former main Board member of Boots Company plc and Chairman UHSM Foundation Trust



**Dr Sue Foden**  
NED

NED and Chair of the Remuneration Committee at BTG and Vectura Plc. Has previously Chaired Bergenbio



**Dr Alan Barge**  
NED

Former CMO of ASLAN Pharmaceuticals and former VP and Head of Oncology and infection at AZ



**Susan Clement-Davies**  
NED

Over 25 years of capital markets and investment banking experience and former Managing Director of Citigroup and Salomon Smith Barney and recently Torrey



**Dr Helen Kuhlman**  
CBO

Over 20 years' experience in government funding and equity investment together with scientific and business roles in public and private R&D-based biotechnology companies



**Dr Glen Clack**  
CMO

Over 25 years' experience in oncology drug development with a specialism in translational medicine