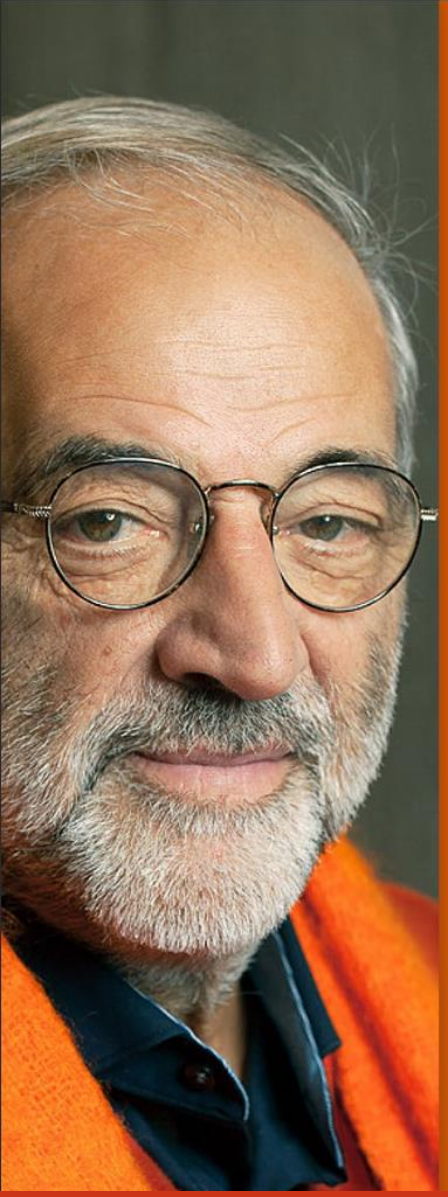


# Yehezkel Ben-Ari, **a founder serving innovation**

## *Academic and private expertise*

- 4 decades of academic research on brain development and disorders
- Founded & Directed the internationally renowned French neuroscience institute (INMED)
- Amongst the 5 most quoted French neuroscientists (>60000 citations)
- Grand prix of the French Medical research institution (INSERM)
- Grand prix of the EU and US epilepsy foundations
- Grand prix of a the Gagna Van Haeck (the Belgian FNRS)
- Founder and CEO of 3 startups dedicated to treat autism and brain tumors

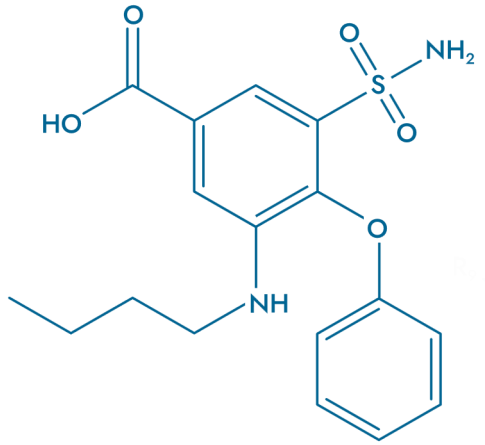
IBEN

W

in

blog

portal




# NKCC1 INHIBITORS TO TREAT AUTISM

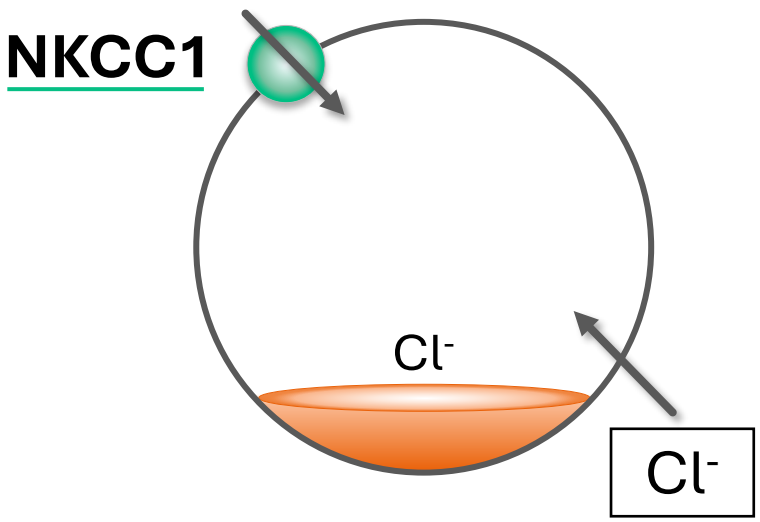
NEUROCHLORE

PAR YEHEZKEL BEN-ARI

# NKCC1 INHIBITORS TO TREAT AUTISM & EPILEPSIES

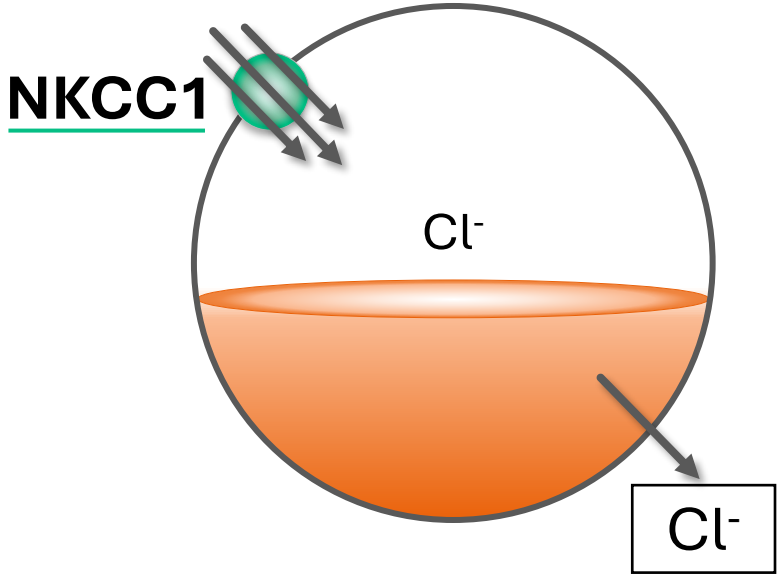
**Control**

*GABA Inhibitor*



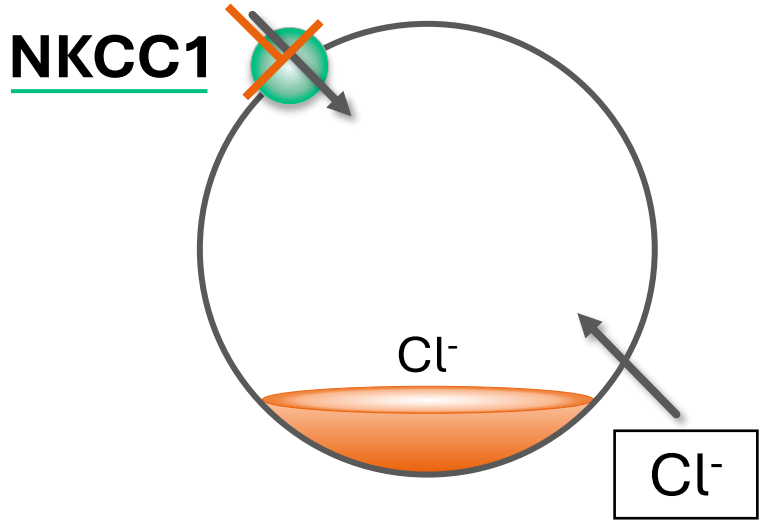

**Pathology**

*GABA Excitatory*

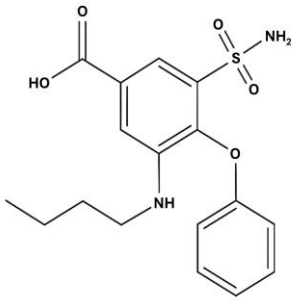



**NKCC1 Inhibition**

*GABA Inhibitor*




**Bumetanide**

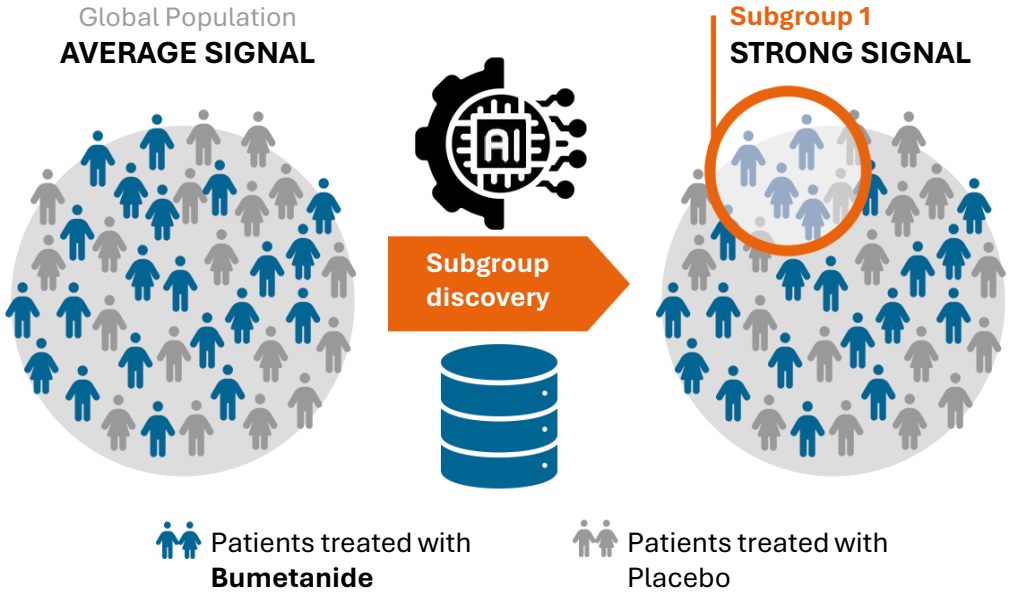


# 30 TO 40% OF CHILDREN WITH AUTISM RESPOND TO BUMETANIDE

- Bumetanide **attenuates autism severity** in our 2 trials (symptoms improvement: visual and social interactions …)
- Bumetanide ameliorates visual interactions, identification of emotive figures and functional MRI alterations *(Hadjikhani et al 2018)*
- **Validated in 7 other phase 2 trials** (>1030 children) performed in many different countries *(Xiao et al 2024)*

But… our Phase III trial failed like all phase 3 of all Neurodevelopmental disorders

→ **Too heterogeneity in disorders**




Using **MACHINE LEARNING**, we **identify 30% to 40% responder subgroups**

Relying on SRS, CARS, DSM subscales


D. RAVEL
Drug Developer

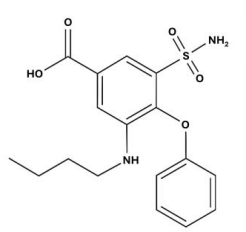
H. RABIEI
M. BEGNIS

AI Experts - Analysis team

# PROGRAM AND FINANCIAL PERSPECTIVES - AUTISM

**OUT-LICENSING**

**NOVEL INHIBITORS**



**Bumetanide**

Autism
**Incidence > 2%**

Treat the **core symptoms**

**Minimal** side effects

**Non-toxic, liquid** formula

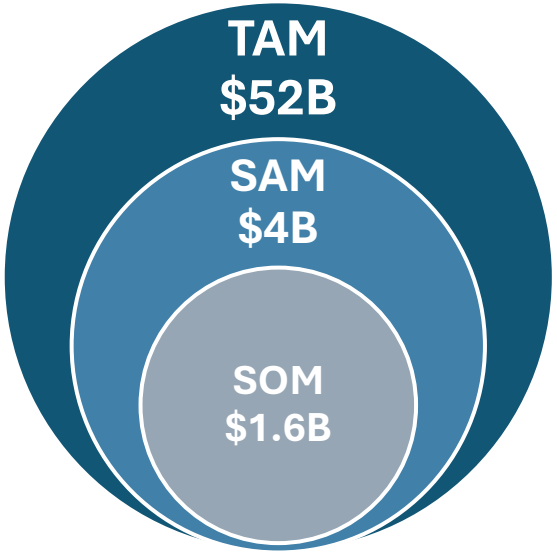
**Low cost** of production

**Exclusive license**

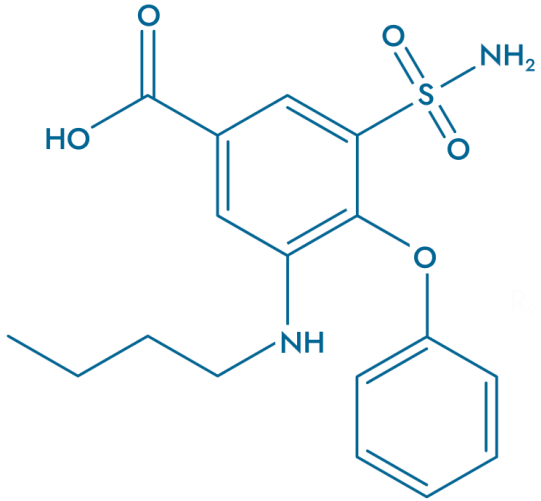
Catalyze | THE INNOVATION CONSULTANTS

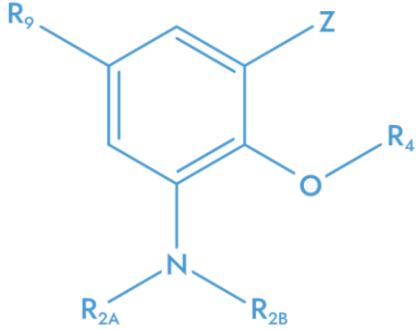
## $52B world market by 2031

**PATENT PROTECTION:**
"Treating clinically identified subpopulations of children & adolescents with Autism with inclusion parameters restricted to the children having 2 sub-parameters of criteria identified by machine learning"




Where:
- TAM = world-wide market for ASD treatments
- SAM = Initial focus on **US** and **European** markets
- SOM = 30 - 40% predicted penetration




# NKCC1 & MICROTUBULE INHIBITORS TO TREAT BRAIN TUMORS

B&A ONCOMEDICAL

PAR YEHEZKEL BEN-ARI

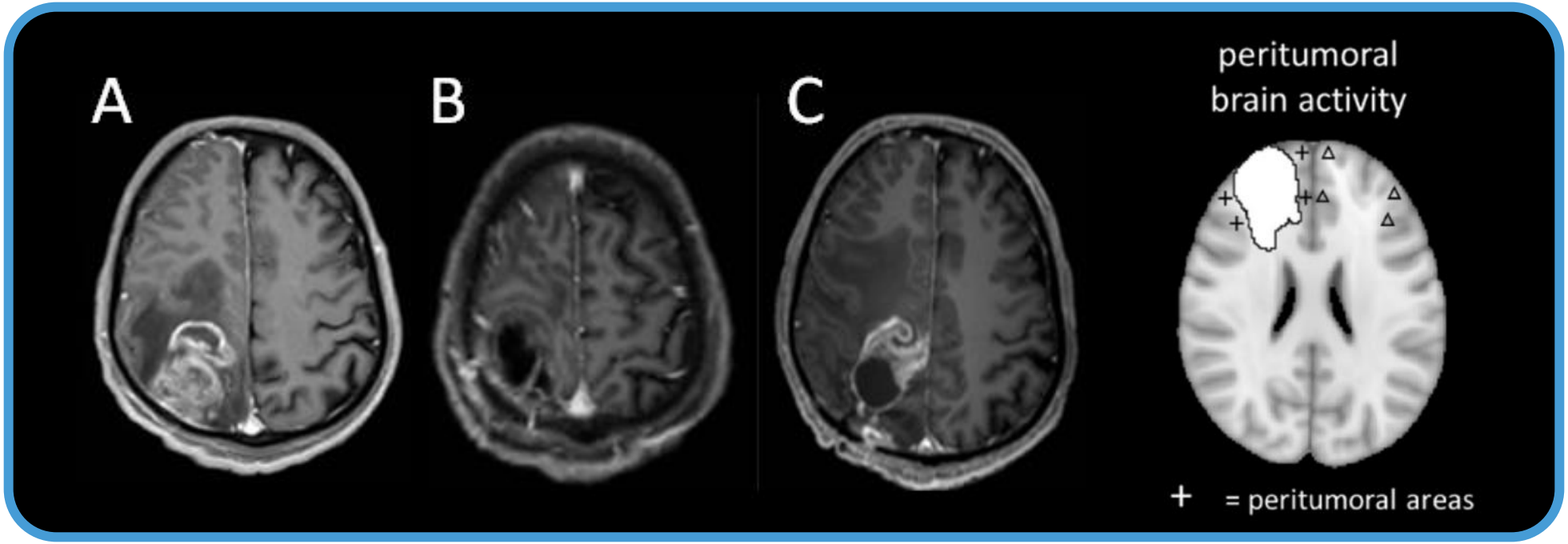
NEUROCHLORE

PAR YEHEZKEL BEN-ARI

# WHY ARE WE FAILING TO TREAT BRAIN TUMORS?

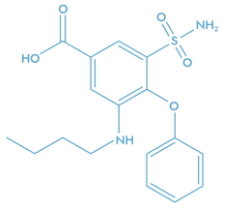
- The **neuronal environment** establishes **synapses** with the tumor, generating **hyperactivity & enhancing metastasis.**

- Therefore, a **dual strategy** is needed, one drug to **block environmental hyperactivity** and another drug to **kill tumor cells.**



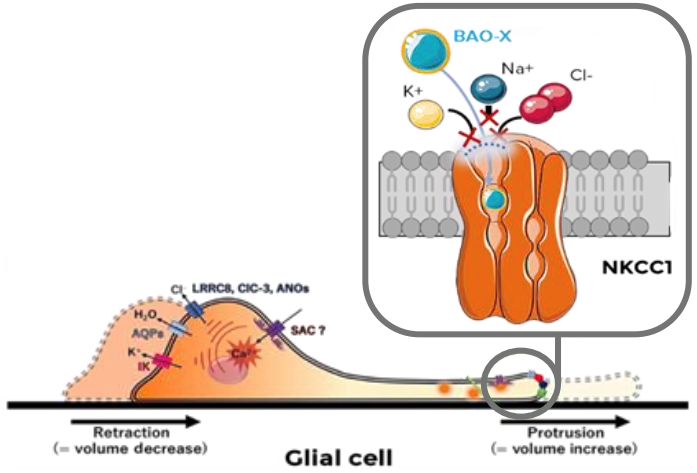

*Venkataramani et al Cell 2022 and many other studies published by the most prestigious journals*

# COMBO OF 2 ANTICANCER GENERIC DRUGS



## Bumetanide (BUM)

→ Blocks hyperactivity
Prevents metastasis

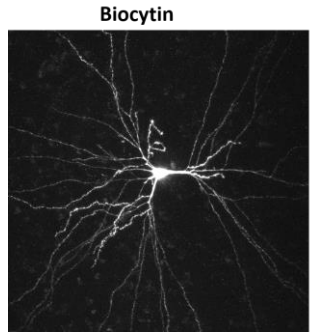


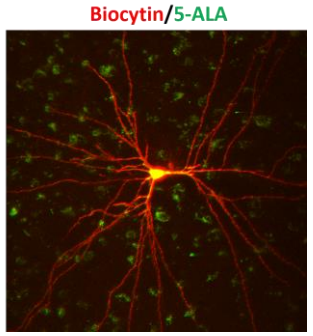

*BAO-X blocks chloride uptake by inhibiting NKCC1*
*Low chloride concentration:*

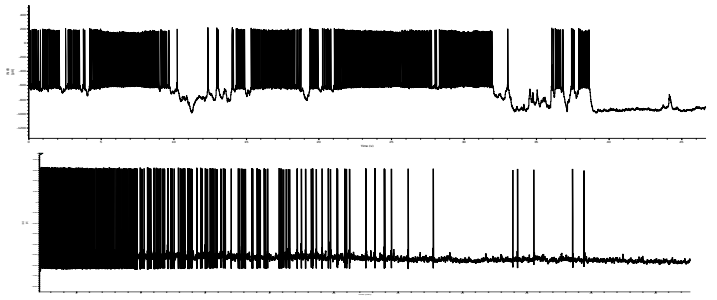
- *Prevents volume changes*
  - *Prevents migration*
  - *Prevents proliferation*
- *Promotes apoptosis*

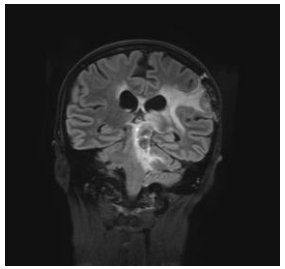
## BUM & MBZ ACT IN SYNERGY

**BUM Blocks all activity (25nM)**
**+**
**MBZ Kills glioma cells**

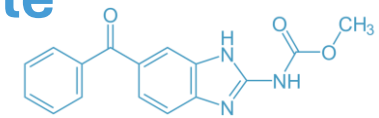


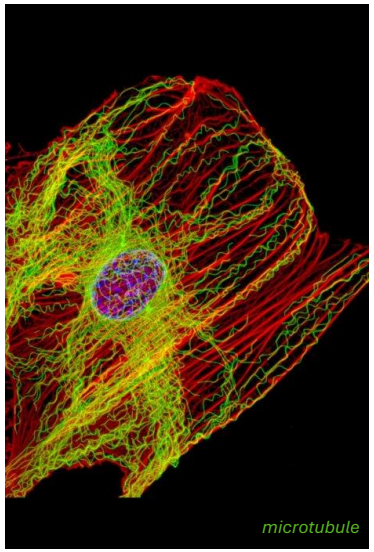





## Mebendazole (MBZ)



Destroys microtubule ←
Kills 95% of cells



# PROGRAM AND FINANCIAL PERSPECTIVES – BRAIN TUMORS

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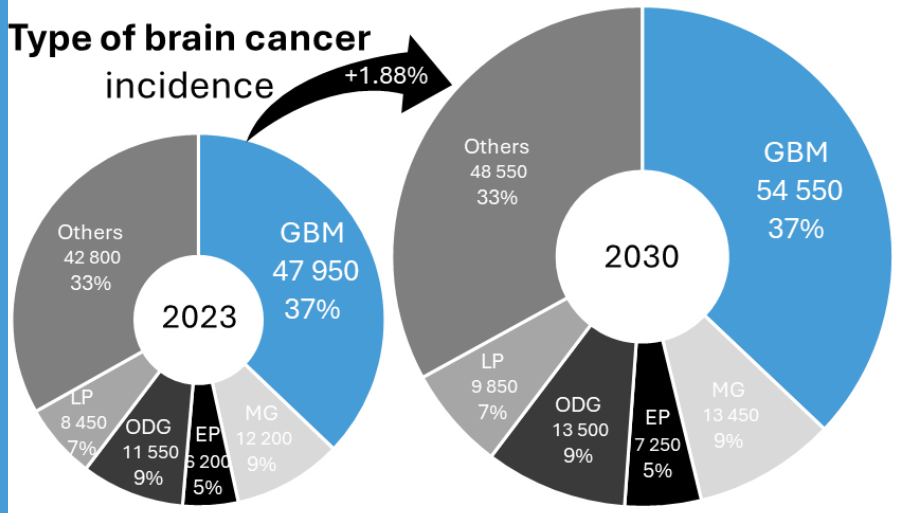
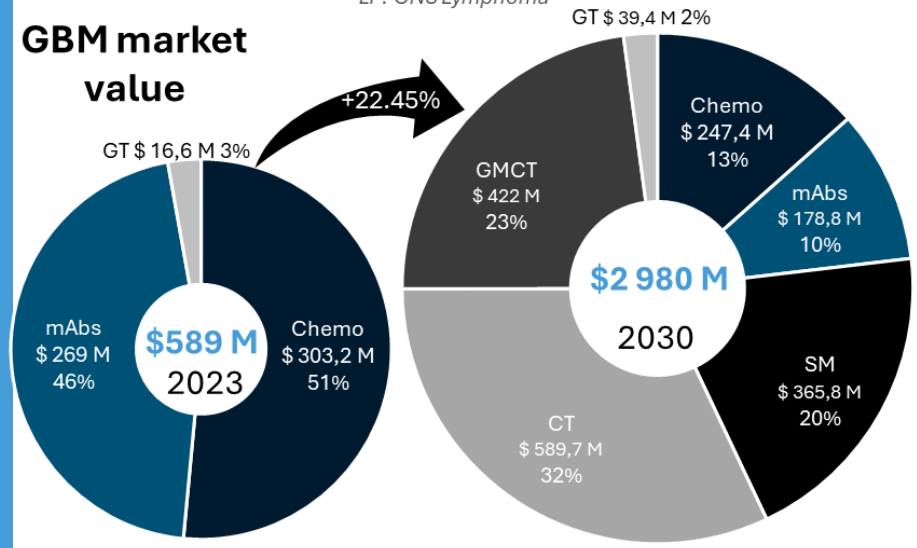
**Out-licensing**

**Type of brain cancer incidence**

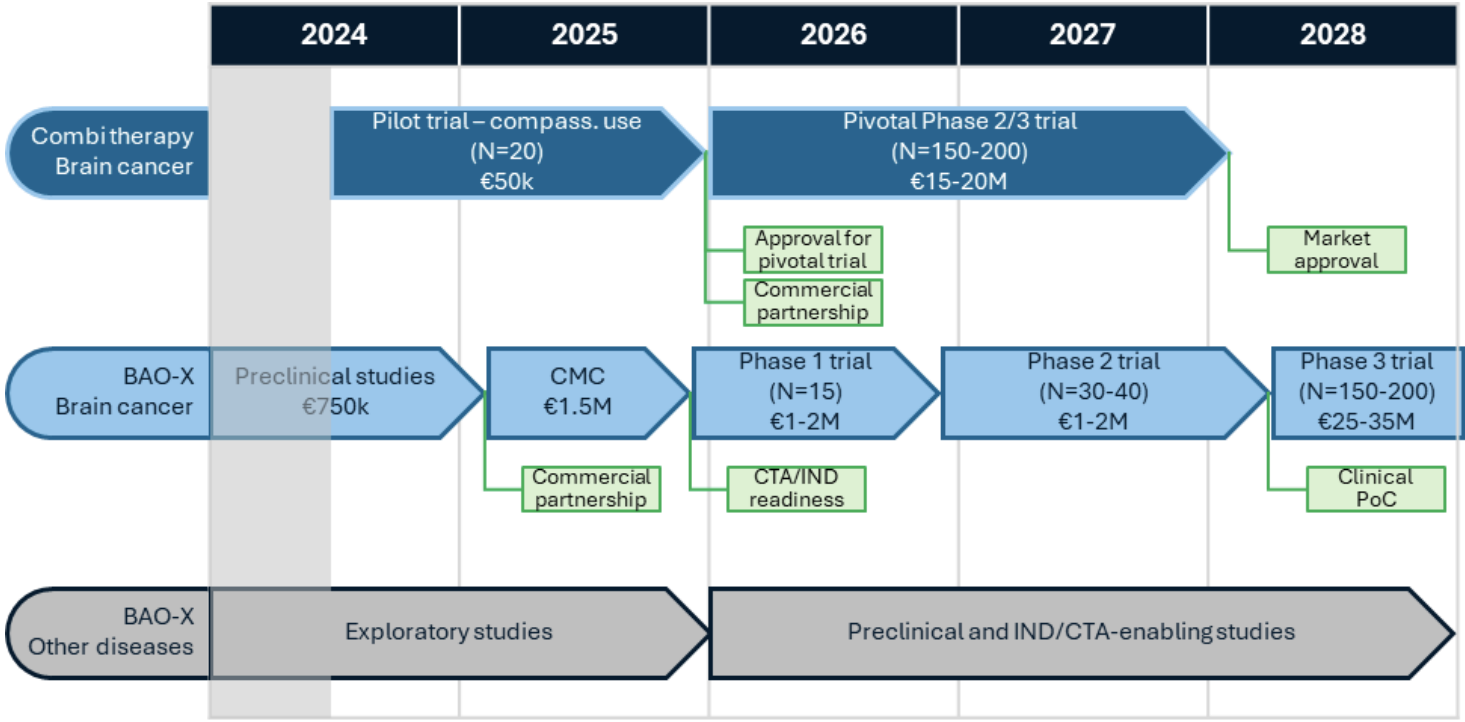



*GBM: Glioblastoma; MG: Meningioma; EP: Ependymoma; ODG: Oligodendroglioma; LP: CNS Lymphoma*

**GBM market value**



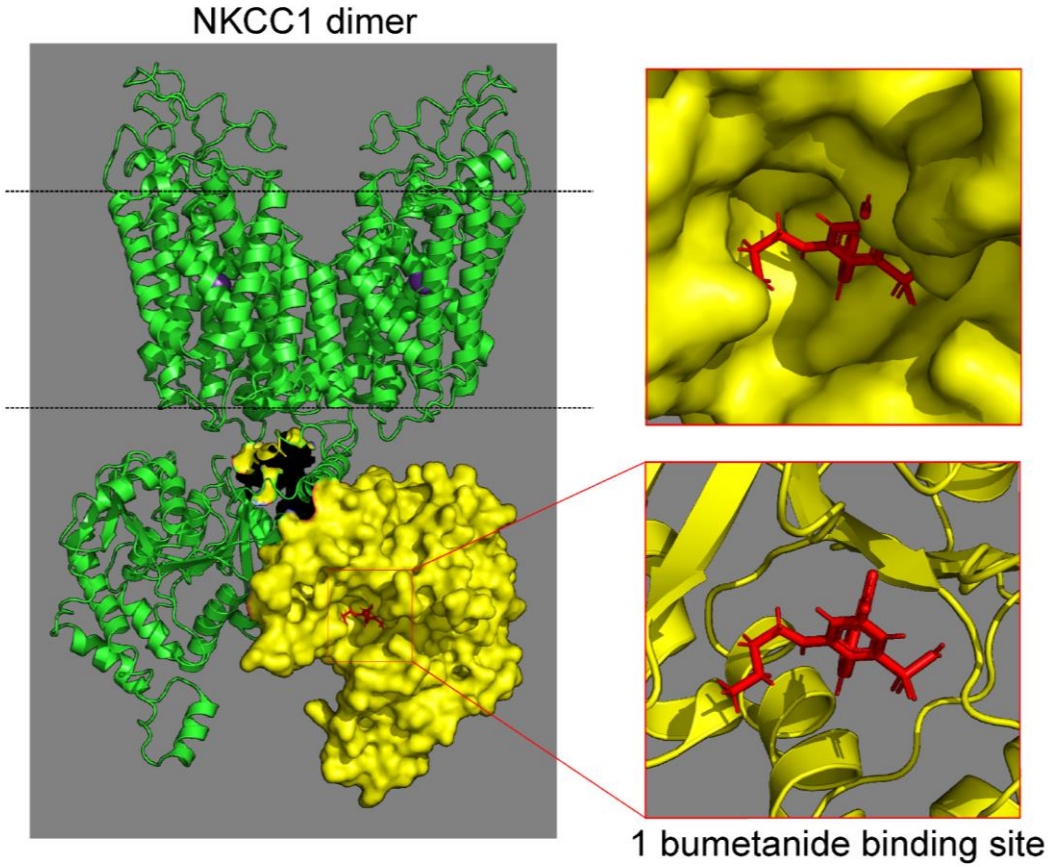

*mAbs: monoclonal antibodies; SM: small molecules; CT: cell therapies; GMCT: gene-modified cell therapies; GT: gene therapies*

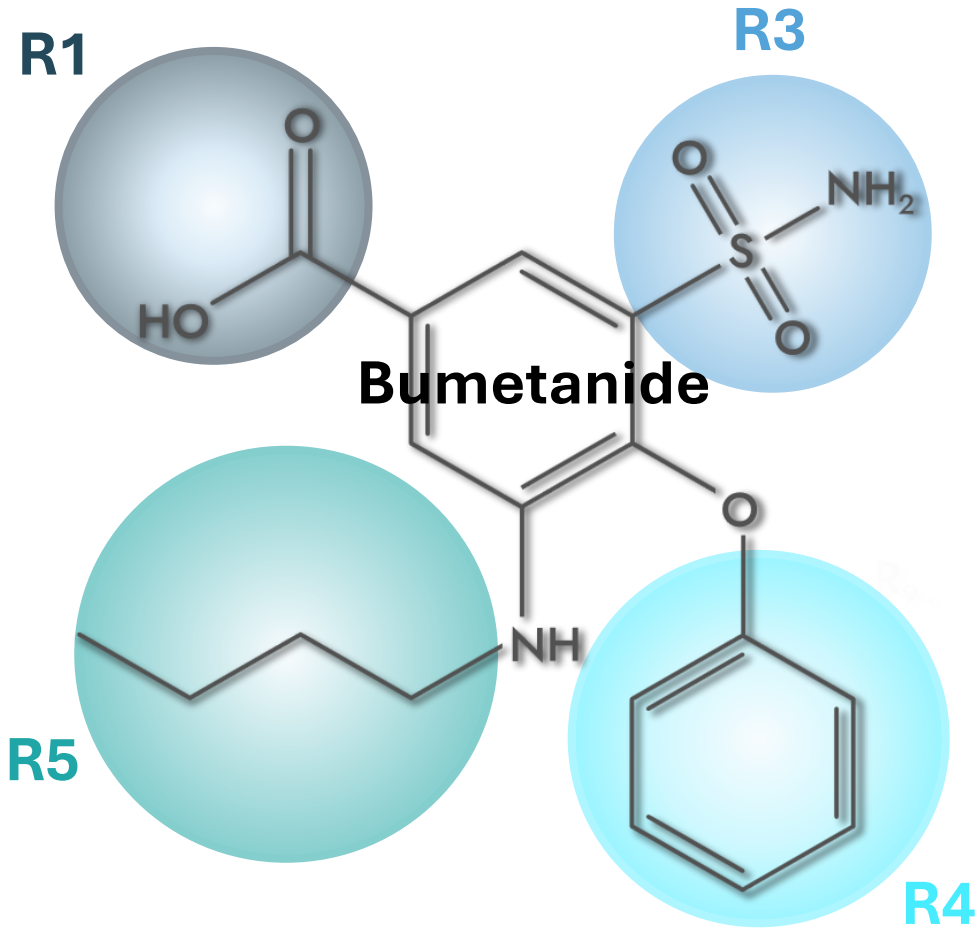



**PCT - PATENT COMBO PROTECTION:**

"Treating brain tumours and epilepsies with a combo of **NKCC1 inhibitors** & **Mebendazole family** of anthelminthic drugs " 2023

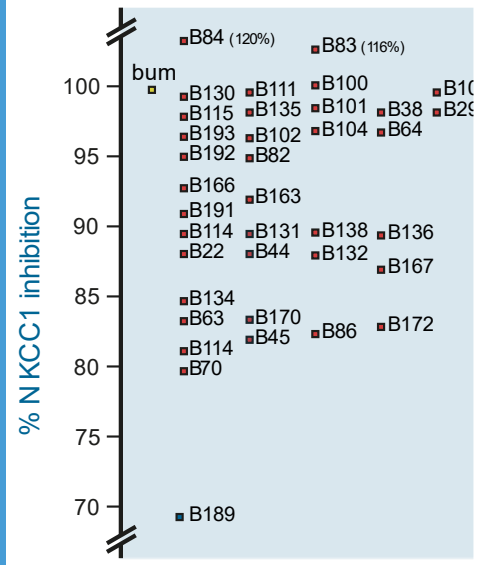
# DEVELOPING NOVEL PROPRIETARY NKCC1 INHIBITORS




**2nd generation NKCC1 inhibitors**

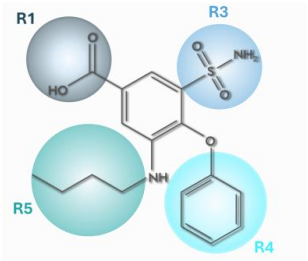
# 2ND GENERATION : 120 NOVEL NKCC1 PROPRIETARY INHIBITORS



E. DELPIRE
Vanderbilt University

P. GEORGE - Chemist

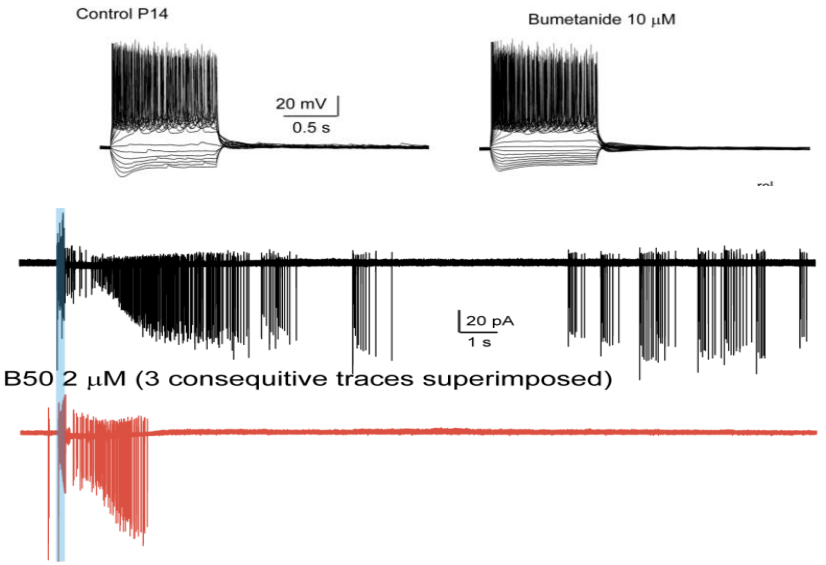
edelris




**Blocking effect NKCC1 120% >** BUM

PK ADME BBB etc. determined

- **Block activity** in fresh **tumors**
- **Enhance cell death**
- **No effect** on **intrinsic currents**




↪ **NKCC1 inhibitors** have been suggested to **ameliorate** literally **hundreds of disorders**

- **Glioblastoma**, cancers (pancreas, lungs)
- **Autism**, epilepsies
- Alzheimer *(Taubes et al 2022)*

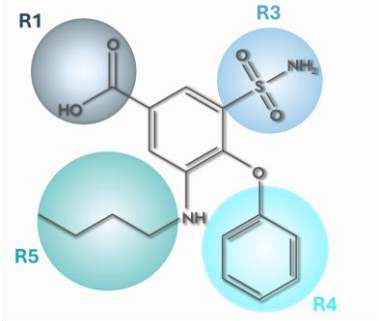
... And many others...

**PATENT 120 NKCC1 NOVEL INHIBITORS**
to treat brain disorders...
Need **8M€** to reach **Pre IND to phase 1 for our best 5 molecules**

❖ **2 short term strategies to treat**

**Autism and Brain tumors**

❖ **1 long strategy using Novel Proprietary Molecules**




*Let's treat patients with novel conceptual approaches*
*Genuine discoveries are always made in sideways not highways*

**MORE INFO**

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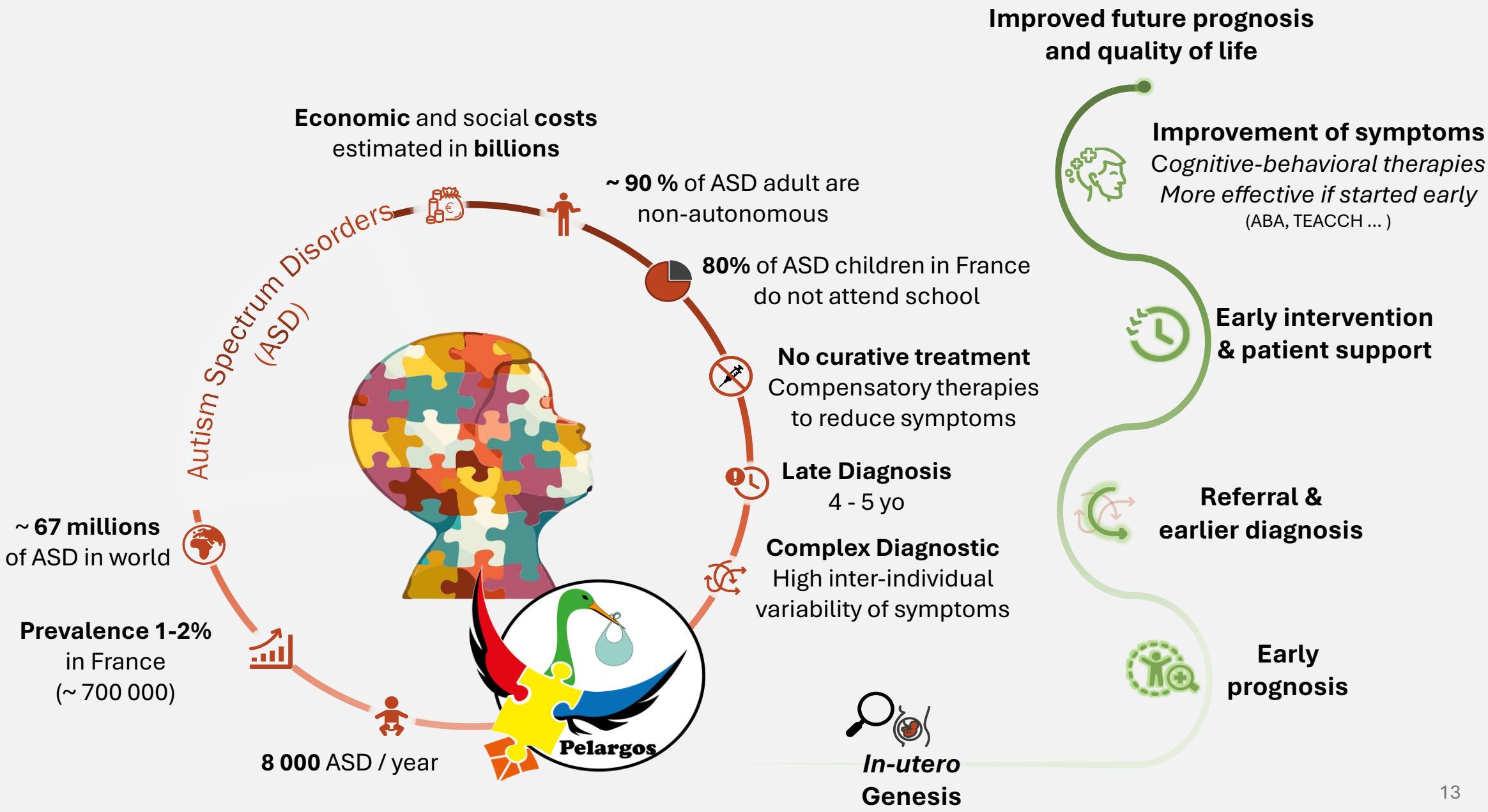
PAR YEHEZKEL BEN-ARI

# AI TO PREDICT AUTISM SPECTRUM DISORDERS FROM BIRTH

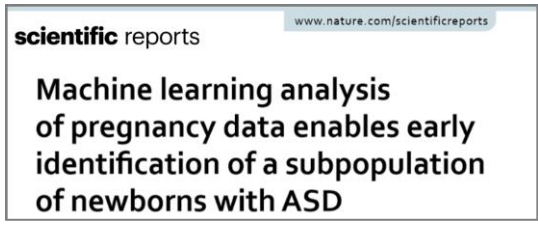
B&A BIOMEDICAL

PAR YEHEZKEL BEN-ARI

# ASD Challenges & Pelargos Solution

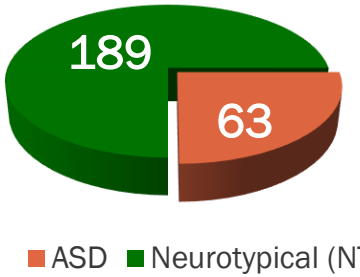


# PRELIMINARY PHASE DONE



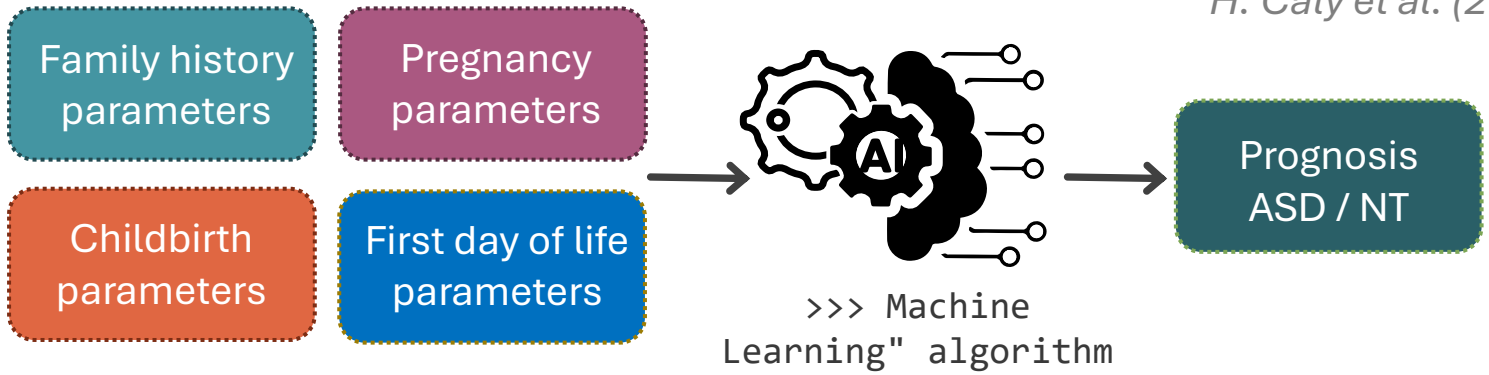

*H. Caly et al. (2021)*

## Subjects (N=252)



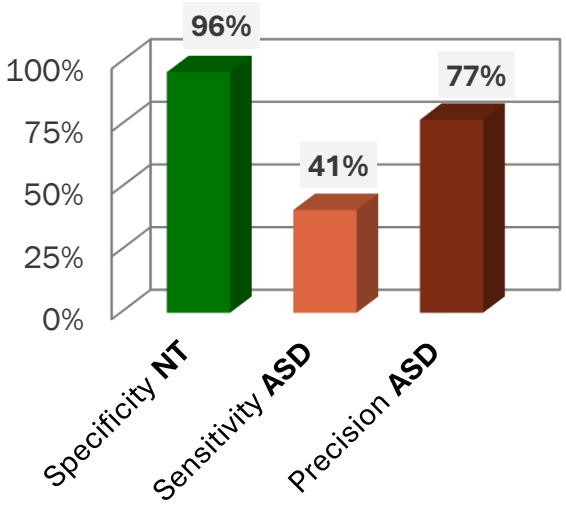

- Born in 2012-2013 in Limoges
- Diagnosed with ASD 2-5 years later

## Analysis process

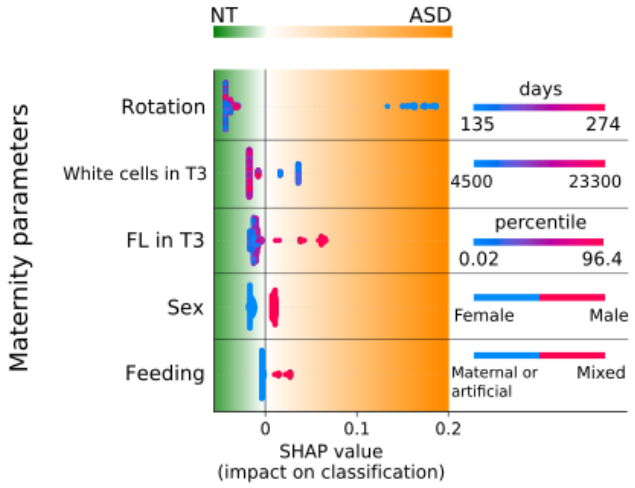



## Results

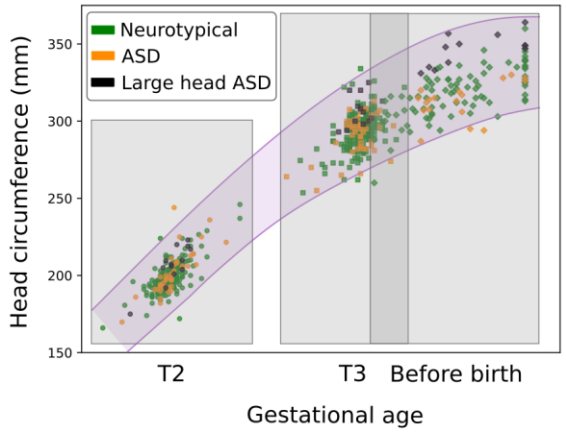
### Cross-validation scores



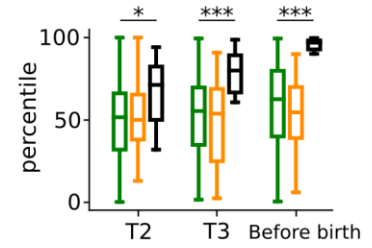

### **Interpretation** of classification




### Statistical analysis of parameters of interest




40% of ASD individuals have a significantly larger head circumference from T2 onwards.



# ❖ Innovation and technological agility in healthcare and biology.

## ❖ Data analysis solutions that transform the prediction, detection, and modelling of biological events into powerful and accessible tools.

**Predict** disorders development risk

**Predict** life duration of Parkinson batteries

**Identifying** Responders population

**Determine** brain tumors type relying on brain MRI

B&A BIOMEDICAL

AI-POWERED MEDICINE & BIOLOGY

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# INSTITUTE FOR INNOVATION

## Inauguration fall 2026

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