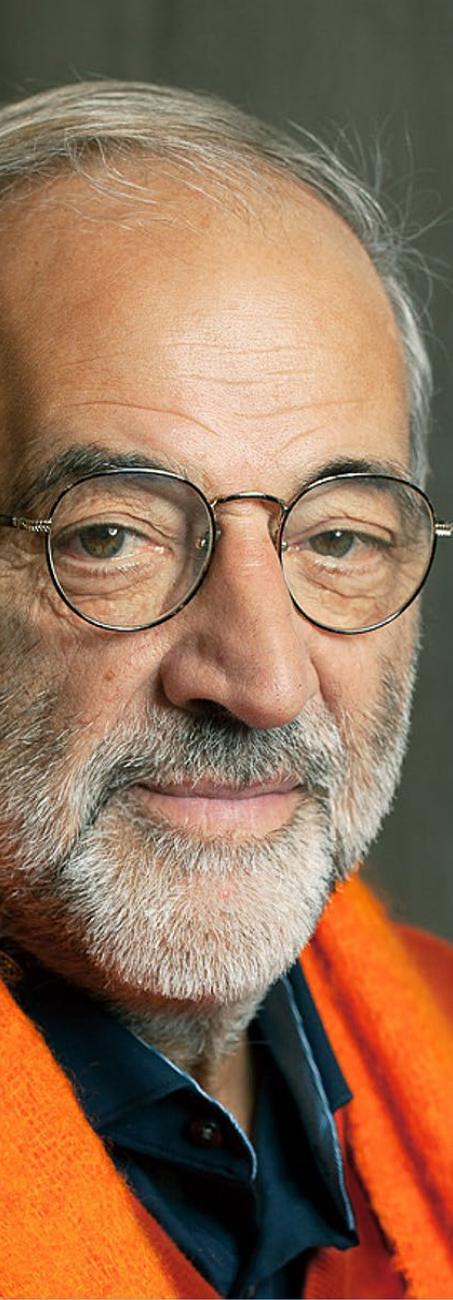


# NKCC1 & MICROTUBULE INHIBITORS TO TREAT BRAIN TUMORS AND EPILEPSIES





## Yehezkel Ben-Ari, a founder serving innovation

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### 5 DECADES OF ACADEMIC & PRIVATE RESEARCH

- > 4 decades academic research on brain development and disorders
- > founder & 1<sup>st</sup> director of INMED a large public neuroscience institute
- > More than 520 publications, amongst the most quoted 5 French neuroscientists
- > Awards include the highest French biomedical research of the National Institute (INSERM), the European and US epilepsy foundations, the Belgian Gagna Van Haeck & Doct. Hon. Causa of Liege University
- > 15 years private Founder & CEO of Neurochlore & BA-oncomedical - dedicated to treat autism and brain tumors



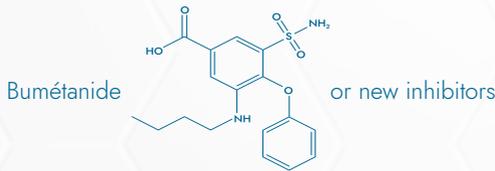
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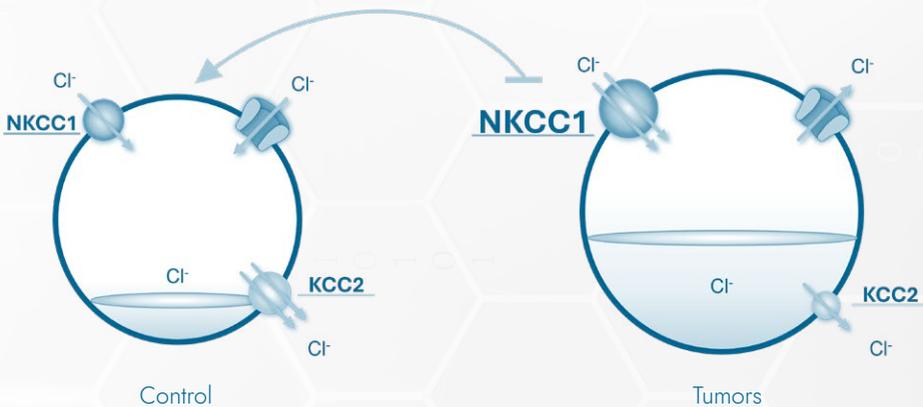


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# THE NKCC1 CO-TRANSPORTER IS INSTRUMENTAL IN BRAIN TUMORS



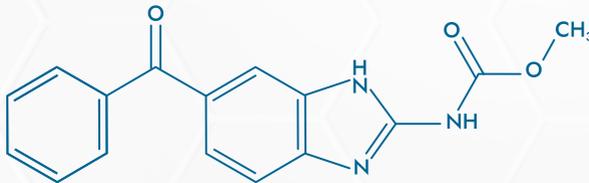
*NKCC1 inhibition*



- NKCC1 controls  $(Cl^-)_i$  levels & cell volume & its activity is increased in brain tumors
- NKCC1 is present on the leading edge of the metastatic protrusion
- Bumetanide attenuates the severity of tumors in animal models, human cell lines and brain tumoroids
- Adding Bumetanide to Temozolomide increases its anti-cancer activity
- The activity of NKCC1 correlates with the grade severity of Glioblastoma in patients

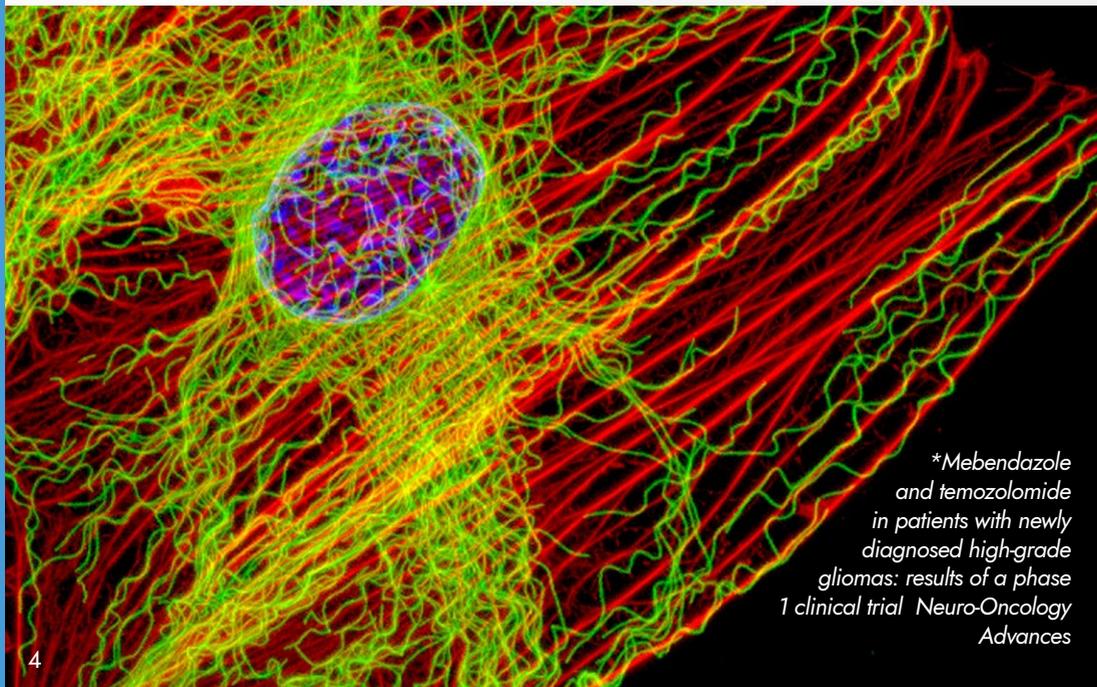
# MICROTUBULE INHIBITORS ARE INSTRUMENTAL IN BRAIN TUMORS

➤ In experimental conditions, anthelmintic drugs like Mebendazole augment apoptosis and attenuate tumors



Mebendazole

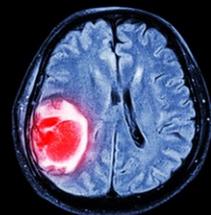
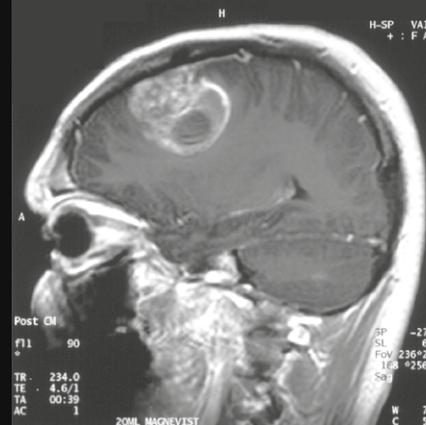
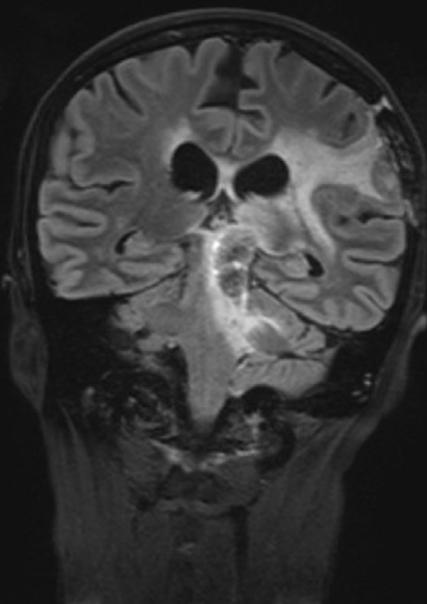
➤ Mebendazole administered with Temozolomide demonstrated a 21-month survival time at 2 years (*Kaplan-Meier analysis*) & long terms safety, acceptable toxicity (*Gallia et al 2021*)\*



\*Mebendazole and temozolomide in patients with newly diagnosed high-grade gliomas: results of a phase 1 clinical trial Neuro-Oncology Advances

# COMPLEMENTARY ACTIONS OF MEBENDAZOLE & BUMETANIDE TO TREAT BRAIN TUMORS

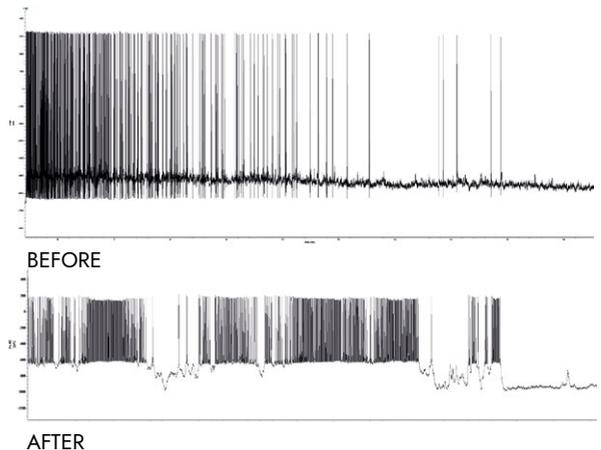
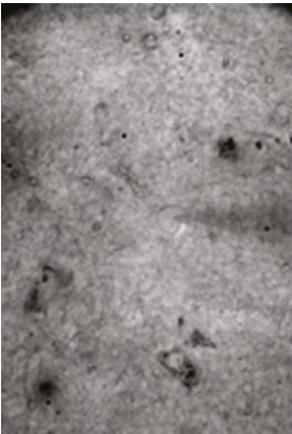
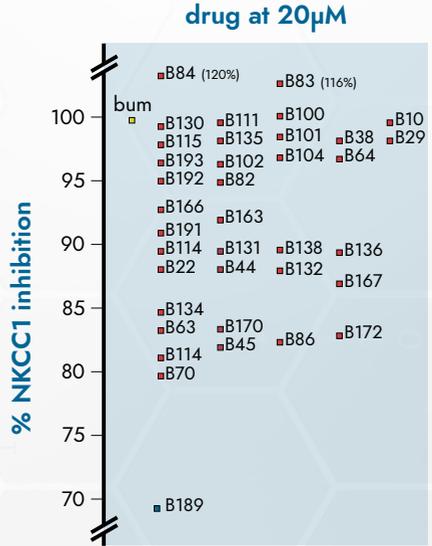
- > A unique repositioned and patented combo targeting invasion/migration & protumoral neuronal activity (Bumetanide anti-NKCC1) and synergic association with cytotoxicity of Mebendazole
- > Highly relevant Human tumoroid validation in freshly resected tumors
- > First in human compassionate safety and clinical response in human GBM: Phase I-2 in 2025
- > Collaboration with Prof F Berger -oncologist, director of the brain tech LabU1205- INSERM



# SECOND GENERATION PROPRIETARY NKCC1 INHIBITORS TO TREAT BRAIN TUMORS

> We have synthesized and patent protected 120 novel NKCC1 inhibitors having 80 to over 120% Bumetanide efficacy to block NKCC1 on GBM /neuronal primary cell cultures !

> In freshly resected tumors or temporal lobe epileptic foci, the combo like the new molecules have powerful anti-epileptic actions

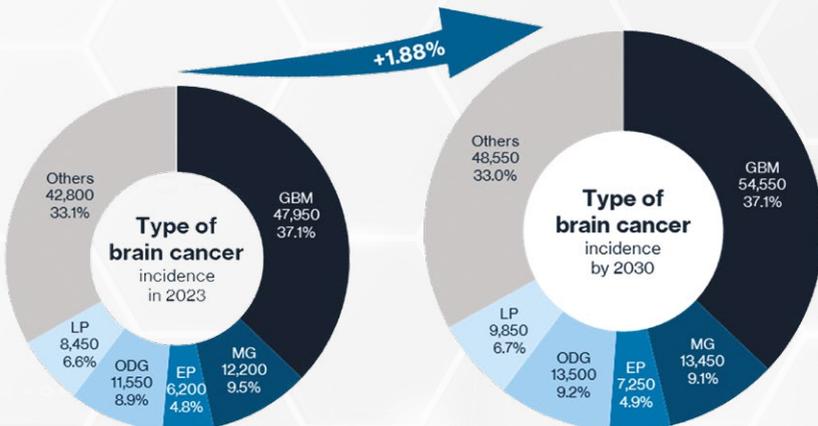
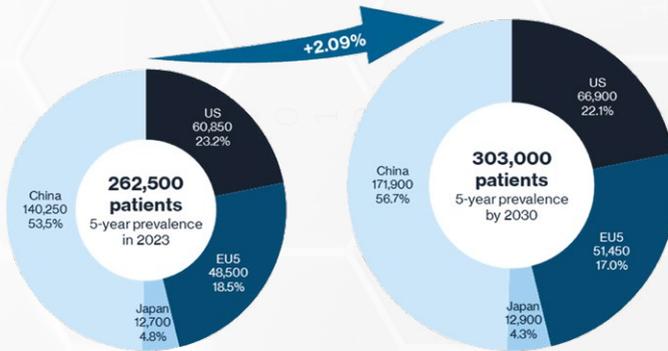
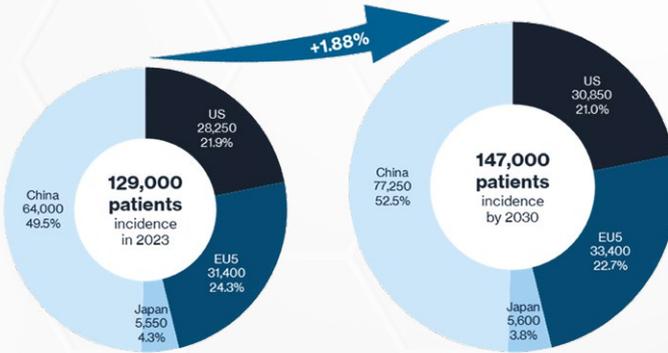


# OUR AIMS: A DUAL STRATEGY TO TREAT BRAIN TUMORS

- › Phase 2/3 clinical trials with Bumetanide & Mebendazole
- › Selecting the best Novel NKCC1 Inhibitors to IND-enabling studies and phase 1
- › We have a collection of proprietary powerful NKCC1 inhibitors
- › Large body of evidence suggests that NKCC1 inhibitors are putative treatments for many other disorders including brain trauma, epilepsies, CVI, Alzheimer disease, chronic pain, autism & developmental disorders, various cancers etc

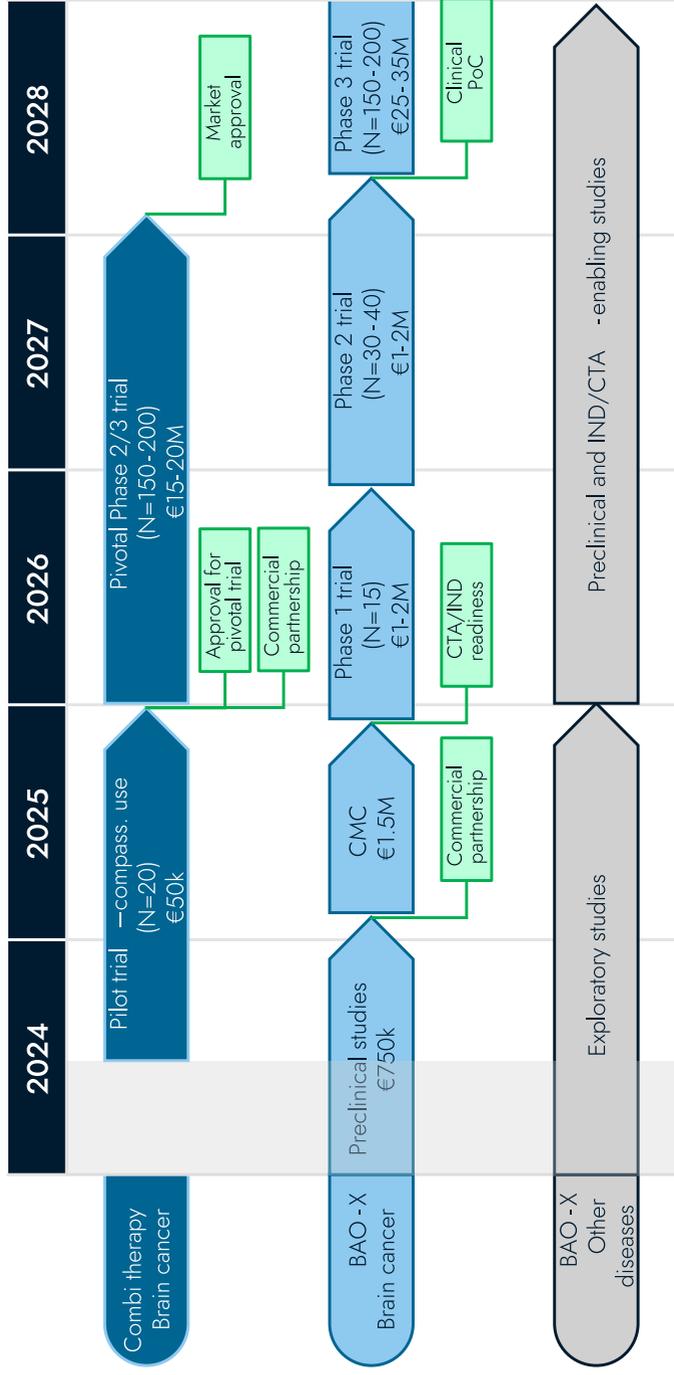


# STRIVING TO TACKLE THE UNMET NEEDS TO TREAT BRAIN TUMORS



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

# A DUAL STRATEGY FOR CAPTURING THE MARKET



# CONTACT



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