

A BREAKTHROUGH THERAPEUTIC SOLUTION PROTECTING AGAINST THE DEVELOPMENT OF THE POST-TRAUMATIC AND POST-STROKE EPILEPSY



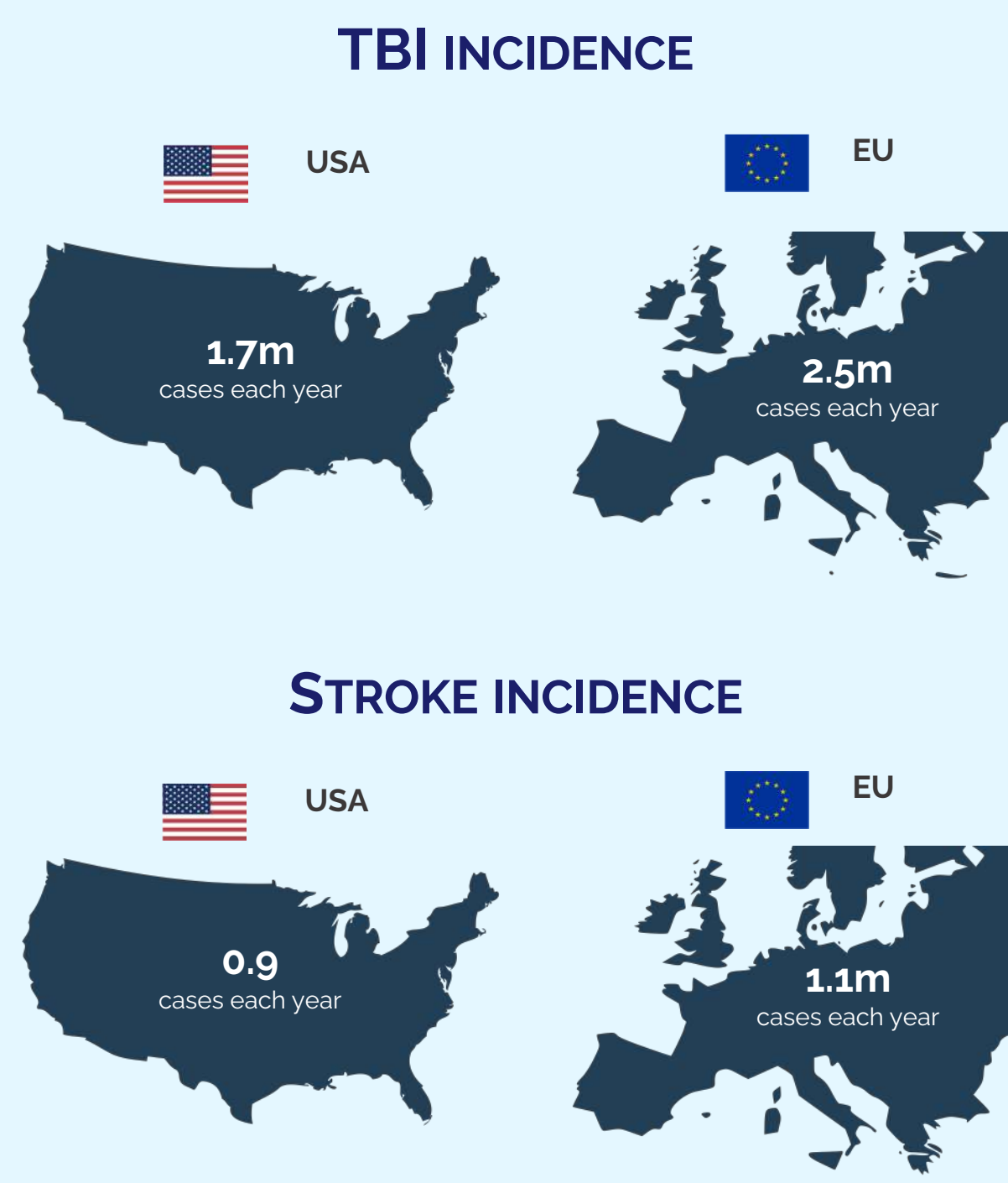
Pikralida

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EPIFIX PROJECT

- Our goal is to develop a breakthrough therapeutic solution protecting against the development of post-traumatic and post-stroke epilepsy.
- The biological target we intend to modulate is the enzymatic protein matrix metalloprotease 9 (MMP-9).
- PKL-021, a low molecular weight chemical compound and potent MMP-9 inhibitor, was selected as a development candidate due to its good pharmacokinetic properties, oral bioavailability, ability to cross brain-blood barrier, and proven *in-vivo* efficacy in animal models



BACKGROUND – EPILEPSY

- Epilepsy is a chronic neurological disease with recurrent epileptic seizures, which are an expression of transient brain dysfunction resulting from excessive, sudden, and spontaneous bioelectrical discharges in nerve cells.
- Currently, for about 30% of epilepsy cases there is no cure available - no drugs inhibiting epilepsy development have been developed so far.
- The development of epilepsy is a common complication after traumatic brain injury or stroke. Based on the current estimations, 4.2 million head injuries and up to 2.0 million strokes occur annually in Europe and the United States. Each of these events can initiate epileptogenesis leading, in the consequence, to the development of epilepsy.
- Various social and cultural aspects are harmful, and are a source of stigma.

MECHANISM OF ACTION

- Extensive research by the group of prof. Leszek Kaczmarek (Neurobiology Laboratory at the Nencki Institute of Experimental Biology PAS) and other research groups, have shown that following a severe head injury or stroke, there is a short-term increase in the activity of an enzymatic protein, matrix metalloproteinase 9 (MMP-9) in the proximity of the injury, which may initiate epileptogenesis.
- Short-term application of PKL-021 is expected to efficiently block excessive activity of the MMP-9 enzyme in the brain and suppress epileptogenesis as a result.

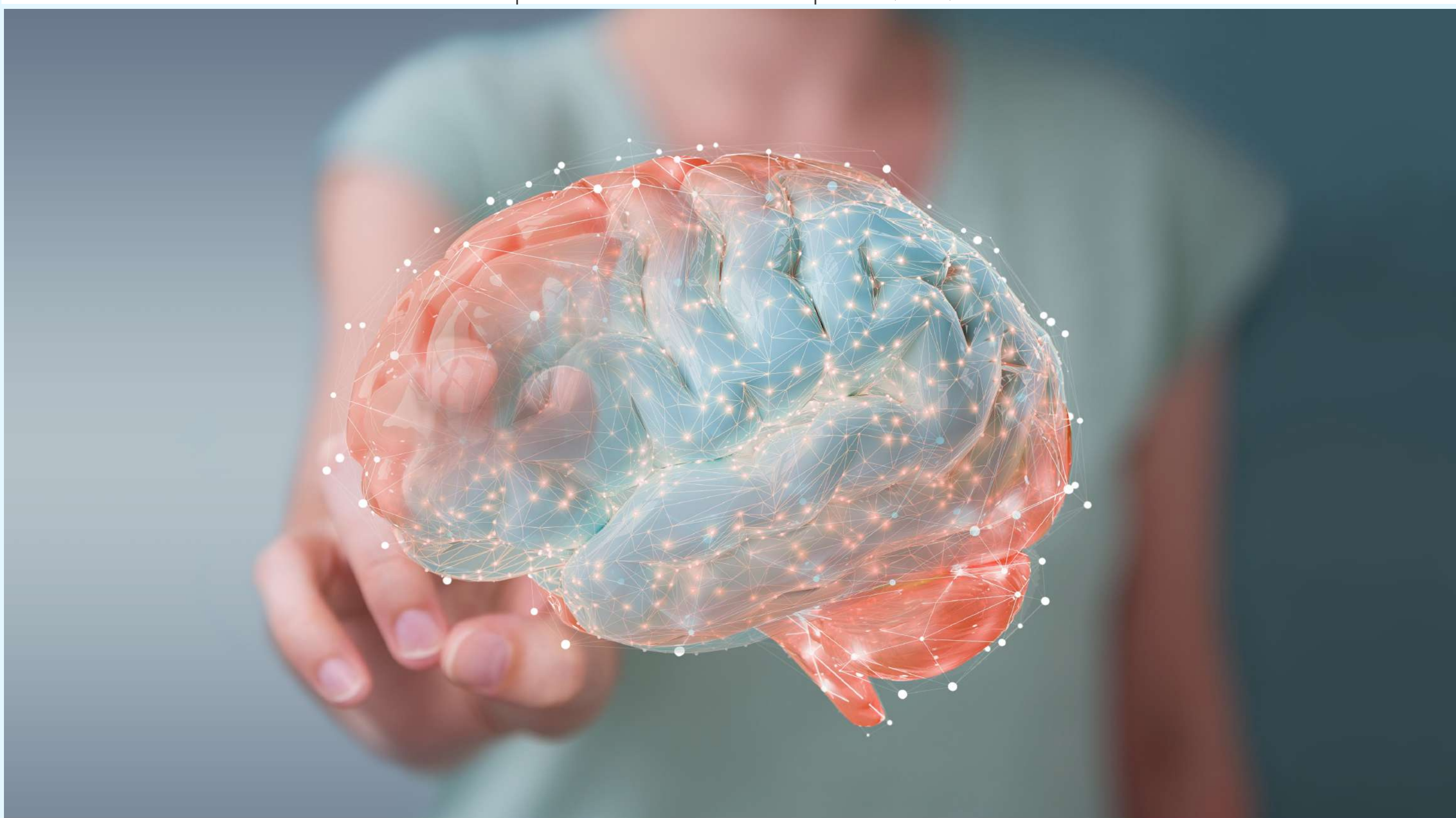
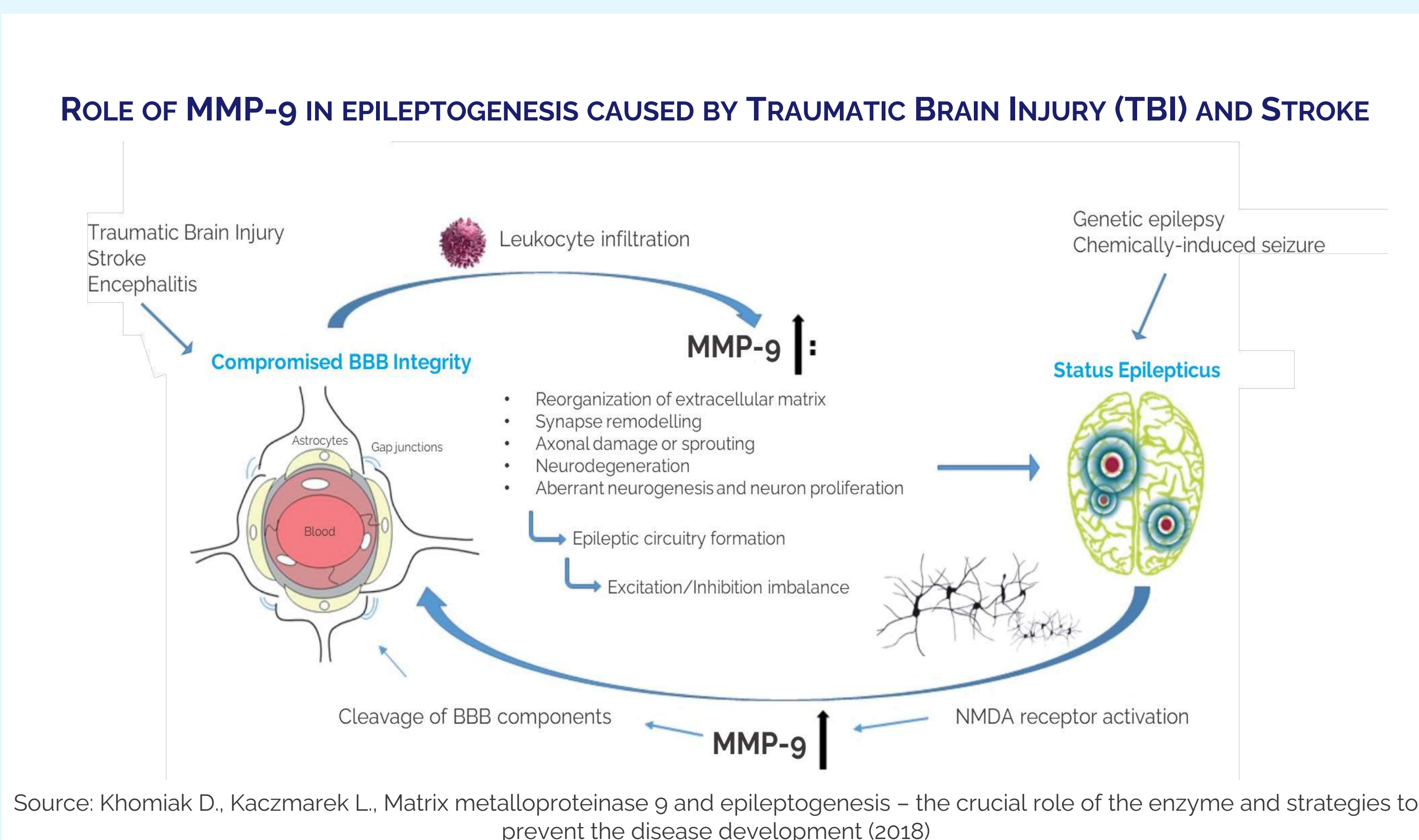
PKL-021 AS A DRUG REPOSITIONING

PKL-021 is an example of the drug repositioning strategy, one of the recommended actions in the Pharmaceutical Strategy for Europe.

THE EPIFIX PROJECT IS CURRENTLY AT THE PRE-CLINICAL STAGE

The ongoing and future activities include:

- Established efficient process for the synthesis of PKL-021 and GMP manufacturing of several kg of substance,
- Selected GMP manufacturer: Polpharma - tech transfer in progress,
- Formulation development and GMP manufacturing of investigational medicinal product,
- Assessment of *in-vivo* efficacy in additional animal models of epileptogenesis,
- Assessment of compound safety pharmacology and toxicology,
- Preparation and submission of regulatory documentation supporting initiation of clinical trials,
- Phase I SAD & MAD clinical trials (PK & safety assesment in HV).



DEVELOPMENT OF PKL-021 - TIMELINE

Year	2022				2023			
Quarter	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
GMP manufacturing of drug substance		█	█	█				
Scientific Advice			█					
Preclinical Safety Assessment Program		█	█	█				
Formulation development - tablets		█	█	█				
GMP manufacturing of drug product				█				
CTA preparation and submission				█	█	█	█	
Phase I clinical trial							█	█

The project is jointly carried out by Pikralida sp. z o. o. and the Nencki Institute of Experimental Biology and co-financed from the European Funds. Project title „Utilization of a matrix metalloprotease inhibitor to develop an innovative therapeutic method that prevents the development of post-traumatic and post-stroke epilepsy” (Project no. POIR.01.01.01-00-0235/20)



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Smart Growth



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