# *KURZPROTOKOLL*
# *X-TOLE*

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| **Öffentlicher Titel** | Phase II Studie zu XEN1101 als Begleittherapie bei fokaler Epilepsie |
| **Wissenschaftl. Titel** | A Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Safety, Tolerability and Efficacy of XEN1101 as Adjunctive Therapy in Focal-onset Epilepsy, with an Open-label Extension |
| **Kurztitel** | X-TOLE |
| **Studienart** | multizentrisch, prospektiv, Therapiestudie, randomisiert, doppelblind, mehrarmig |
| **Studienphase** | Phase II |
| **Erkrankung** | Nervensystem: Epilepsie |
| **Einschlusskriterien** | - Be properly informed of the nature and risks of the study and give informed consent in writing, prior to entering the study<br>- BMI <40 kg/m2<br>- Diagnosis (>=2 years) of focal epilepsy according to the International League Against Epilepsy [ILAE] Classification of Epilepsy (2017)<br>- Treatment with a stable dose of 1 to 3 allowable current AEDs for at least one month prior to screening, during baseline, and throughout the DBP<br>- Must be willing to comply with the contraception requirements<br>- Able to keep accurate seizure diaries<br>- ADDITIONAL CRITERIA FOR THE DBP:<br>- During the 8-week Baseline period preceding the randomization visit (V3), patients must have a documented seizure frequency of >=4 focal seizures per 28 days on average<br>- eDiary was completed a min of 80% of all days (i.e., >=45 days) during the 8 week Baseline period as evidence of adequate compliance<br>- Patients should not be seizure-free for more than 21 consecutive days during the 8-week Baseline period<br>- Patient does not show retinal macular disease, or retinal pigment epithelium abnormality on the dilated ophthalmic exam prior to randomization<br>- OPEN-LABEL EXTENSION:<br>- Be properly informed of the nature and risks of the study and give informed consent in writing<br>- Must have met all eligibility requirements and completed the DBP (to Visit 8 with a minimum of 80% compliance with eDiary entries and IMP), did not terminate early, patient had no important protocol deviations (e.g., that may impact patient safety or data integrity) that in the opinion of Sponsor should preclude participation in the OLE, and had no adverse events that, in the opinion of the Investigator, would preclude the patient's entry into the OLE<br>- Patient is expected to experience benefit from their participation, in the opinion of the Investigator<br>- Must be willing to comply with the contraception requirements as defined in the protocol<br>- Males must agree not to donate sperm until 6 months after the last dose of study drug. Females must agree not to donate ova until 6 months after the last dose of study drug |
| **Ausschlusskriterien** | - History of pseudoseizures, psychogenic seizures, primary generalized seizure, or focal aware non-motor seizures only<br>- Presence or previous history of Lennox-Gastaut syndrome<br>- Seizures secondary to other diseases or conditions<br>- History of repetitive seizures within the last 12 months where the individual seizures cannot be counted |

- History of neurosurgery for seizures <1 year prior to enrollment, or radiosurgery <2 years prior to enrollment
- Schizophrenia and other psychotic disorders, or active suicidal plan/intent in the past 6 months, or a history of suicide attempt in the last 2 years, or more than 1 lifetime suicide attempt
- History or presence of any significant medical or surgical condition or uncontrolled medical illness at screening, or history of cancer within the past 2 years, with the exception of appropriately treated basal cell or squamous cell carcinoma
- Any clinically significant abnormalities on pre-study physical examination, vital signs, laboratory values or ECG indicating a medical problem that would preclude study participation including but not limited to: a. History of presence of long QT syndrome; QTcF > 450 msec at baseline; family history of sudden death of unknown cause b. History of skin or retinal pigment epithelium abnormalities caused by ezogabine
- Use of vigabatrin in the last 5 years without stable visual fields tested twice over the 12 months after the last dose of vigabatrin (patients stopping vigabatrin more than 5 years prior to screening, must have no vigabatrin-related visual field abnormalities confirmed by examination within the past 6 months - concomitant use of vigabatrin is not allowed)
- If felbamate is used as a concomitant AED, patients must be taking it for at least 2 years, with a stable dose for >=49 days and acceptable hematology and LFT values (or discontinued felbamate no less than 49 days) prior to Screening
- Have had multiple drug allergies or a severe drug reaction to an AED(s), including dermatological (e.g., Stevens-Johnson syndrome), hematological, or organ toxicity reactions
- Current use of a ketogenic diet
- OPEN-LABEL EXTENSION:
- Patients who met any of the withdrawal criteria in the DBP
- Any medical condition, personal circumstance, or ongoing adverse event that in the opinion of the Investigator exposes the patient to unacceptable risk by participating in the OLE, or prevents adherence to the protocol
- Females who are pregnant, breastfeeding or planning to become pregnant until 6 months after the last dose of study drug
- Patients planning to enter a clinical trial with a different investigational drug or plan to use any experimental device for treatment of epilepsy or any other medical condition

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| **Alter** | 18 Jahre und älter |
| **Prüfzentren** | **Epilepsiezentrum** (Rekrutierung beendet)<br>Schleusenweg 2-16<br>60528 Frankfurt am Main<br>Prof. Dr. med. Felix Rosenow<br>Tel: 069 6301-7466<br>Felix.Rosenow@unimedizin-ffm.de |
| **Sponsor** | Xenon Pharmaceuticals Inc. |
| **Registrierung in anderen Studienregistern** | EudraCT 2018-003221-29<br>ClinicalTrials.gov NCT03796962 (primäres Register) |