CRESTONE: A Phase 2 Study of Seribantumab in Adult Patients With Neuregulin-1 (NRG1) Fusion Positive Locally Advanced or Metastatic Solid Tumors

Clinicaltrials.gov site: https://www.clinicaltrials.gov/ct2/show/NCT04383210

Website: https://nrg1fusion.com/

Contacts:

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VP, Medical Affairs	716-371-1125	medicalaffairs@elevationoncology.com

Study Locations:

38 locations across US with ongoing global expansion

CRESTONE

Find trials. ClinicalTrials.gov. Retrieved August 1, 2022, from https://clinicaltrials.gov/ct2/search

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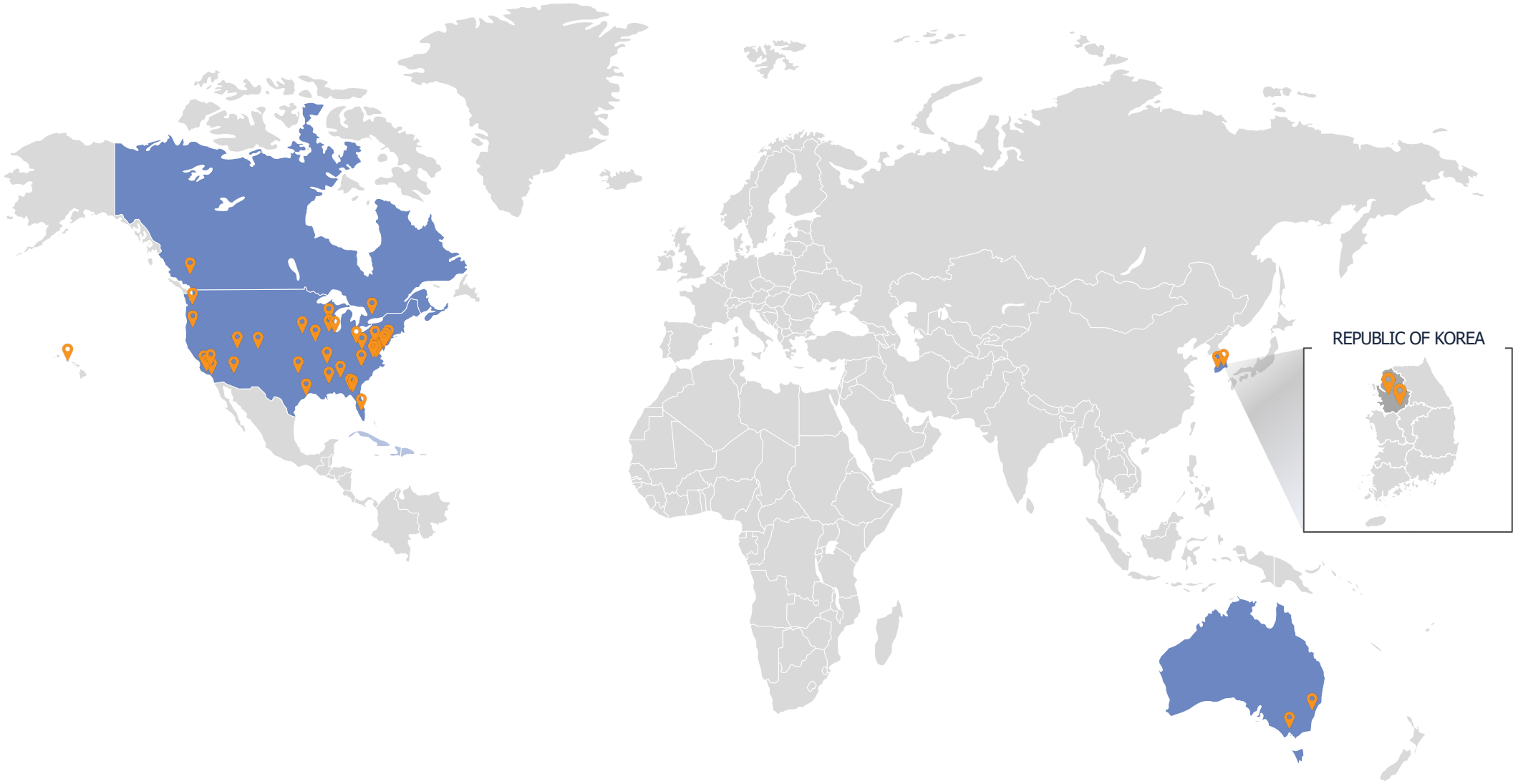
CRESTONE Clinical Trial Locations



Find trials. ClinicalTrials.gov. Retrieved August 1, 2022, from https://clinicaltrials.gov/ct2/search
Map courtesy of Elevation Oncology

Inclusion Criteria

To be eligible for participation in the study, patients must meet the following inclusion criteria:

- Locally-advanced or metastatic solid tumor with an NRG1 gene fusion identified through molecular assays, such as PCR, NGS (RNA or DNA) or FISH, by a CLIA-certified or similarly accredited laboratory
- Availability of fresh or archived FFPE tumor sample to be submitted to a central laboratory for confirmation of NRG1 gene fusion status
- Patients should have received a minimum of one prior standard therapy appropriate for their tumor type and stage of disease, progressed or been nonresponsive to these available therapies, with no further available curative therapy options
- ≥18 years of age
- ECOG performance status (PS) 0, 1 or 2
- Patients must have at least one measurable extra-cranial lesion as defined by RECIST v1.1
- Adequate hepatic function defined as:
- Serum AST and serum ALT < 2.5 × upper limit of normal (ULN), or AST and ALT < 5 × ULN if liver function abnormalities due to underlying malignancy
- Total bilirubin < 2.0 ULN. Subjects with a known history of Gilberts Disease and an isolated elevation of indirect bilirubin are eligible
- Adequate hematologic status, defined as:
  - Absolute neutrophil count (ANC) ≥1.5 × 10^9/L not requiring growth factor support for at least 7 days prior to Screening, and
  - Platelet count ≥100.0×10^9/L not requiring transfusion support for at least 7 days prior to Screening
- Able to provide informed consent or have a legal representative able and willing to do so
- Ability to comply with outpatient treatment, laboratory monitoring, and required clinic visits for the duration of study participation
- Willingness of men and women of reproductive potential to observe conventional and effective birth control for the duration of treatment and for 3 months following study completion; this may include barrier methods such as condom or diaphragm with spermicidal gel.

Find trials. ClinicalTrials.gov. Retrieved August 1, 2022, from https://clinicaltrials.gov/ct2/search

Exclusion Criteria

- Known, actionable oncogenic driver mutation other than NRG1 fusion where available standard therapy is indicated
- Life expectancy < 3 months
- Pregnant or lactating
- Prior treatment with ERBB3/HER3 directed therapy (Cohort 1 only)
- Prior treatment with pan-ERBB or any ERBB/HER2/HER3 directed therapy (Cohort 1 only)
- Symptomatic or untreated brain metastases (Note: Patients with asymptomatic brain metastases treated with radiation or surgery and without evidence of progression by imaging at screening are eligible to participate in the study. Patients requiring ongoing corticosteroids to treat brain metastases will not be eligible).
- Received other investigational agent or anticancer therapy within 28 days prior to planned start of seribantumab or 5 half-lives, whichever is shorter
- Prior to initiation of seribantumab treatment, patients must have recovered from clinically significant toxicities from prior anticancer or investigational therapy
- Any other active malignancy requiring systemic therapy
- Known hypersensitivity to any of the components of seribantumab or previous CTCAE grade 3 or higher hypersensitivity reactions to fully human monoclonal antibodies
- Clinically significant cardiac disease, including symptomatic congestive heart failure, unstable angina, acute myocardial infarction within 12 months of planned first dose, or unstable cardiac arrhythmia requiring therapy (including torsades de pointes)
- Active uncontrolled systemic bacterial, viral, or fungal infection
- Patients who are not appropriate candidates for participation in this clinical study for any other reason as deemed by the investigator

Find trials. ClinicalTrials.gov. Retrieved August 1, 2022, from https://clinicaltrials.gov/ct2/search

eNRGy: A Study of Zenocutuzumab (MCLA-128) in Patients With Solid Tumors Harboring an NRG1 Fusion

Clinicaltrials.gov site: https://www.clinicaltrials.gov/ct2/show/NCT02912949

Website: https://nrg1.com/clinical-trial/

Contacts:

Merus Inquiries 1-833-NRG-1234

Study Locations:

35 locations across US, Canada, France, Israel, Italy, Japan, Republic of Korea, Netherlands, Norway, Singapore, Spain, and Taiwan

eNRGy Clinical Trial

Find trials. ClinicalTrials.gov. Retrieved August 1, 2022, from https://clinicaltrials.gov/ct2/search

eNRGy Clinical Trial Locations

eNRGy Global Clinical Trial Locations. eNRGy Clinical Trial for Zenocutuzumab (MCLA-128). https://nrg1.com/clinical-trial/. Accessed August 1, 2022.

Inclusion Criteria

- At least one measurable lesion according to RECIST v1.1 OR evaluable disease for a limited number of patients (up to 10) in Group H;
- Performance status of ECOG 0 or 1;
- Estimated life expectancy of at least 12 weeks;
- Toxicities incurred as a result of previous anti-cancer therapy resolved to ≤Grade 1;
- Treatment with anti-cancer medication or investigational drugs within the following intervals before the first dose of MCLA-128:
- >14 days or >5 half-lives prior to study entry, whichever is shorter.
- >14 days for radiotherapy.
- Recovery from major surgery or other complication to ≤ Grade 2 or baseline ;
- Absolute neutrophil count ≥1.5 x 10^9/L without colony stimulating factor support;
- Platelets ≥100 x 10^9/L;
- Hemoglobin ≥8 g/dL or ≥2.2 mmol/L;
- Alanine aminotransferase (ALT), aspartate aminotransferase (AST) ≤3 x upper limit of normal (ULN) and total bilirubin ≤1.5 x ULN; in cases of metastatic liver involvement, ALT/AST ≤5 x ULN and total bilirubin ≤2 x ULN will be allowed; in cases of antecedents of Gilbert's syndrome when total bilirubin ≤3.0 x ULN or direct bilirubin ≤1.5 x ULN will be allowed;
- Estimated glomerular filtration rate (GFR) of >30 mL/min
- Able to provide a tumor biopsy sample (fresh strongly preferred or else archival);
- Not pregnant or nursing
- Fertile patients must use effective contraception during and for 6 month after completion of study therapy;
- Patients must have received prior standard therapy appropriate for their tumor type and stage of disease, or in the opinion of the Investigator, would be unlikely to tolerate or derive clinically meaningful benefit from appropriate standard of care therapy;
- Locally-advanced unresectable or metastatic solid tumor malignancy with documented NRG1 gene fusion, identified through molecular assays such as PCR, next generation sequencing-based assays [DNA or RNA], or FISH as routinely performed at CLIA or other similarly-certified laboratories.

Find trials. ClinicalTrials.gov. Retrieved August 1, 2022, from https://clinicaltrials.gov/ct2/search

Exclusion Criteria

- Pregnant or lactating;
- Presence of an active uncontrolled infection or an unexplained fever;
- Known hypersensitivity to any of the components of MCLA-128;
- Known HIV, active Hepatitis B or Hepatitis C; patients treated for Hepatitis C and have undetectable viral loads are eligible
- Known symptomatic or unstable brain metastases;
- Patients with leptomeningeal metastases
- Presence of congestive heart failure or Left Ventricular Ejection Fraction <50% or history of significant cardiac disease, unstable angina, myocardial infarction or ventricular arrhythmia requiring medication.
- Previous or concurrent malignancy (excluding non-basal cell carcinoma of skin or carcinoma in situ of the uterine cervix) unless the tumor was treated with curative intent more than 2 years prior to study entry;
- Presence of any other medical or psychological condition deemed by the Investigator to be likely to interfere with a patient's ability to sign informed consent, cooperate or participate in the study, or interfere with the interpretation of the results.

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