Rare Disease Clinical Trials

Module 1: Researching clinical trial opportunities for patients

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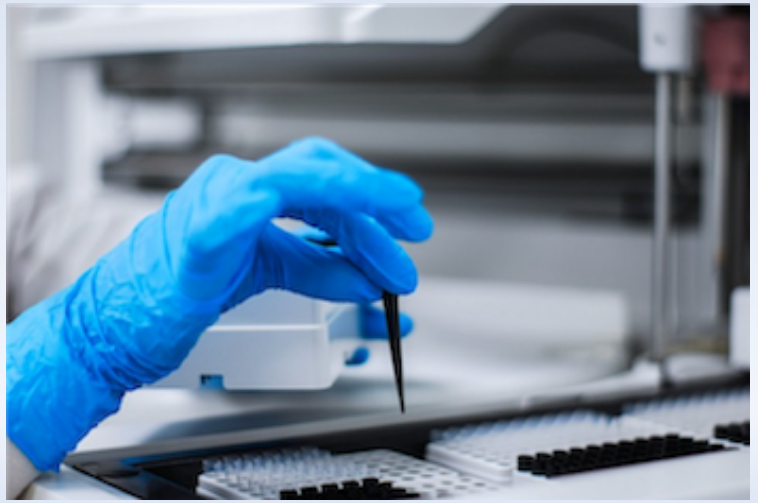
What are Clinical Trials?

Definition

- Research investigations involving humans to prevent, detect, treat, or undertand disease processes or medical conditions
- **Non-interventional**
  - Prevention
  - Screening
  - Diagnostic
  - National history
  - Behavioral
  - Quality of life
- **Interventional**
  - Phase 1, 2, and 3



Common vs Rare Diseases

	Common Disease	Rare Disease
Phase 1 Phase 2 Phase 3	N = 10-100 100-500 500-5000	5-20 5-40 10-500
Inclusion Criteria	Strict	Strict
Exclusion Criteria	Strict	Strict
Number of locations	Numerous	Few
Recruiting patients	Easier	More Difficult

Treatment Trials

	Participants	Main Purpose
Preclinical	Animals	Does the treatment work as hypothesized?
Phase 1	Healthy volunteers or individuals with a specific disease	Does the treatment work in humans like it did in animals?
Phase 2	Individuals with a specific disease	What is the best dose of the treatment (focus on safety)?
Phase 3	Individuals with a specific disease	Using a specific dose, is the treatment safe and effective?

Why join a clinical trial?

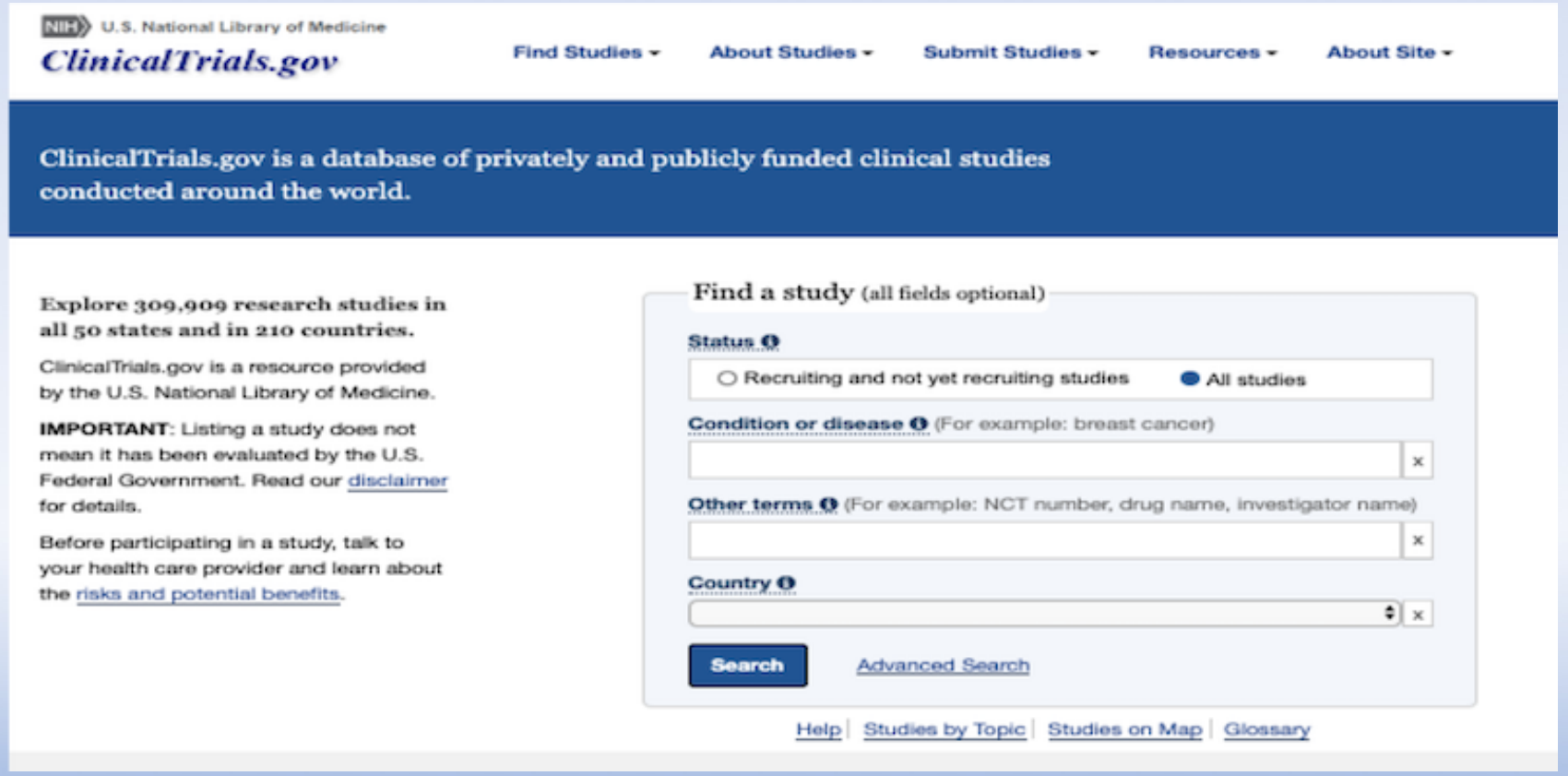
- Advance medicine (not all clinical trials need to be interventional trials)
- Currently there is no treatment available
- Treatment is available but ineffective
- Treatment is available but has safety/quality of life concerns
- Access to experimental treatment at a reduced or no cost
- Advances will occur faster if more people participate
- Advances will not occur if people do not participate

What is expanded access?

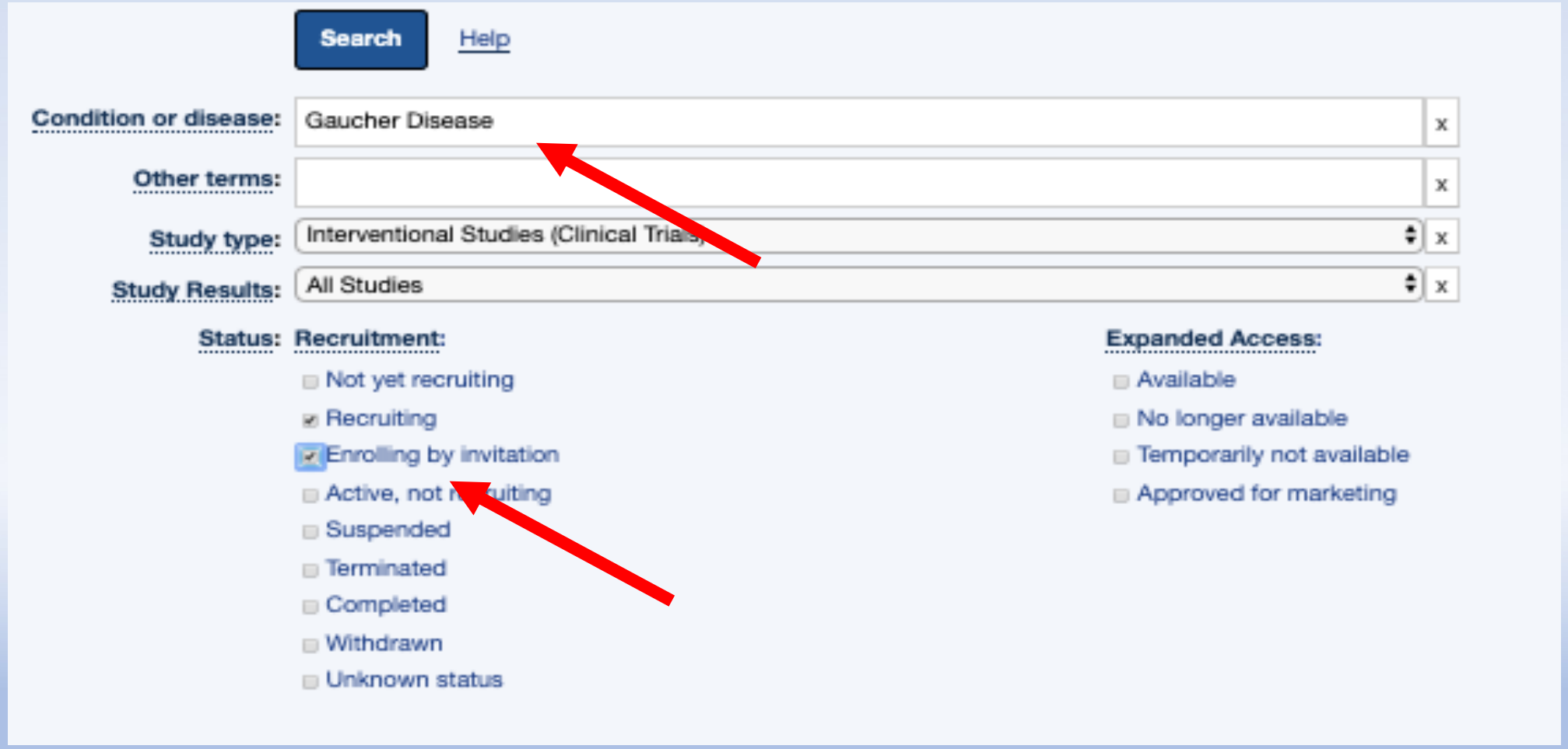
- FDA program designed to allow some patients access to experimental treatment. Usually, it is for patients that do not qualify for a clinical trial or do not have a clinical trial to participate in
- Patient must have a serious or life-threatening disease with no treatment options available (other than the experimental drug)
- FDA reviews each request individually
  - Non-emergency – FDA responds within 30 days
  - Emergency – FDA responds within hours

https://www.fda.gov/news-events/expanded-access/expanded-access-information-physicians

How to research clinical trials (clinicaltrials.gov)



Advanced Search / Disease / Status



Results

Row	Saved	Status	Study Title	Conditions
1	☐	Recruiting	Role of Oxidative Stress and Inflammation in Type 1 **Gaucher Disease** (GD1)	• **Gaucher Disease** Type 1
2	☐	Recruiting	Study of the Effect of Velaglucerase Alfa (VPRIV®) on Bone-related Pathology in Treatment-naïve Participants With Type 1 **Gaucher Disease**	• **Gaucher Disease**
3	☐	Recruiting	GZ/SAR402671 in Combination With Cerezyme in Adult Patients With **Gaucher Disease** Type 3	• **Gaucher Disease** Type 1 • **Gaucher Disease** Type 3

Inclusion Criteria is Extensive

Inclusion criteria:

- The patient must provide written informed consent prior to any study-related procedures being performed.
- The patient has a clinical diagnosis of Gaucher Disease Type 1 (GD1) or Gaucher Disease Type 3 (GD3) and documented deficiency of acid beta-glucosidase activity.
- The patient has received treatment with enzyme replacement therapy for at least 3 years. For at least 6 months prior to enrollment, the patient has received Cerezyme at a stable monthly dose and must continue at the same monthly dose during the study.
- The patient has reached Gaucher disease therapeutic goals defined as all of the following:
- Hemoglobin level of ≥11.0 g/dL for females and ≥12.0 g/dL for males.
- Platelet count ≥100 000/mm3.
- Spleen volume <10 multiples of normal (MN), or total splenectomy (provided the splenectomy occurred >3 years prior to randomization).
- Liver volume <1.5 MN.
- No bone crisis and free of symptomatic bone disease such as bone pain attributable to osteonecrosis and/or pathological fractures within the last year.
- The patient, if female and of childbearing potential, must have a negative pregnancy test [urine beta-human chorionic gonadotropin (β-hCG)] at baseline.
- If the patient has a history of seizures, except for myoclonic seizures, they are well controlled under appropriate medication not identified as a strong or moderate inducer or inhibitor of CYP3A.
- Adult GD1 cohort only:
- -GD1 Patient is ≥18 and ≤40 years of age.
- Adult GD3 cohort only:
- GD3 Patient is ≥18 years of age.
- The patient is willing to abstain from consumption of grapefruit, grapefruit juice, or grapefruit containing products for 72 hours prior to administration of the first dose of GZ/SAR402671 and for the duration of the 156 week treatment period.
- Oculomotor apraxia characterized by a horizontal saccade abnormality.
- Cerezyme treatment every 2 weeks (minimum dose 30 U/kg every 2 weeks).
- Female patients of childbearing potential and male patients must be willing to practice true abstinence in line with their preferred and usual lifestyle, or use 2 acceptable effective methods of contraception for the duration of the study and for at least 6 weeks for females and 90 days for males following their last dose of study drug

Exclusion Criteria is Extensive

Exclusion criteria:

- Substrate reduction therapy or chaperone therapy for GD within 6 months prior to enrollment.
- The patient has had a partial or total splenectomy within 3 years prior to randomization.
- The patient is blood transfusion-dependent.
- Prior esophageal varices or liver infarction or current liver enzymes (alanine aminotransferase [ALT]/ aspartate aminotransferase [AST]) or total bilirubin >2 times the upper limit of normal, unless the patient has a diagnosis of Gilbert Syndrome.
- Clinically significant congenital cardiac defect, coronary artery disease, valve disease or left sided heart failure; clinically significant arrhythmias or conduction defect.
- The patient has any clinically significant disease, other than GD, including cardiovascular, renal, hepatic, gastrointestinal, pulmonary, neurologic, endocrine, metabolic (e.g., hypokalemia, hypomagnesemia), or psychiatric disease, other medical conditions, or serious intercurrent illnesses that may preclude participation.
- The patient has received an investigational product within 30 days prior to enrollment.
- The patient has a history of cancer, with the exception of basal cell carcinoma.
- The patient has myoclonic seizures.
- The patient is pregnant or lactating.
- The patient has, according to World Health Organization (WHO) Grading, a cortical cataract >one-quarter of the lens circumference (Grade cortical cataract-2) or a posterior subcapsular cataract >2 mm (Grade posterior subcapsular cataract-2). Patients with nuclear cataracts will not be excluded.
- The patient requires use of invasive ventilatory support.
- The patient requires use of noninvasive ventilator support while awake for longer than 12 hours daily.
- The patient is unable to receive treatment with Cerezyme due to a known hypersensitivity or is unwilling to receive Cerezyme treatment every 2 weeks.
- The patient is currently receiving potentially cataractogenic medications as listed in Section 8.8.2.
- The patient has received strong or moderate inducers or inhibitors of Cytochrome p450 Isoform 3A within 30 days or 5 half-lives from screening, whichever is longer, prior to enrolment in Part 2. This also includes the consumption of grapefruit, grapefruit juice, or grapefruit containing products within 72 hours of starting GZ/SAR402671 administration in Parts 2 and 3.
- The patient is scheduled for in-patient hospitalization including elective surgery, during the study.
- The patient has had a major organ transplant (e.g., bone marrow or liver).
- The patient, in the opinion of the investigator, is unable to adhere to the requirements of the study or unable to undergo study assessments (e.g., contraindications for magnetic resonance imaging).
- The above information is not intended to contain all considerations relevant to a patient's potential participation in a clinical trial.

Contact information

Contacts

Contact: Trial Transparency email recommended (Toll free number for US & Canada) 800-633-1610 ext 1 then # Contact-Us@sanofi.com

Locations

United States, Connecticut

Investigational Site Number 840002 **Recruiting**
New Haven, Connecticut, **United States**, 06520

United States, Texas

Investigational Site Number 840[illegible] **Recruiting**
Dallas, Texas, **United States**, 75226

Germany

Investigational Site Number 276001 **Active, not recruiting**
Mainz, Germany, 55131

Japan

Investigational Site Number 392001 **Active, not recruiting**
Minato-Ku, Japan

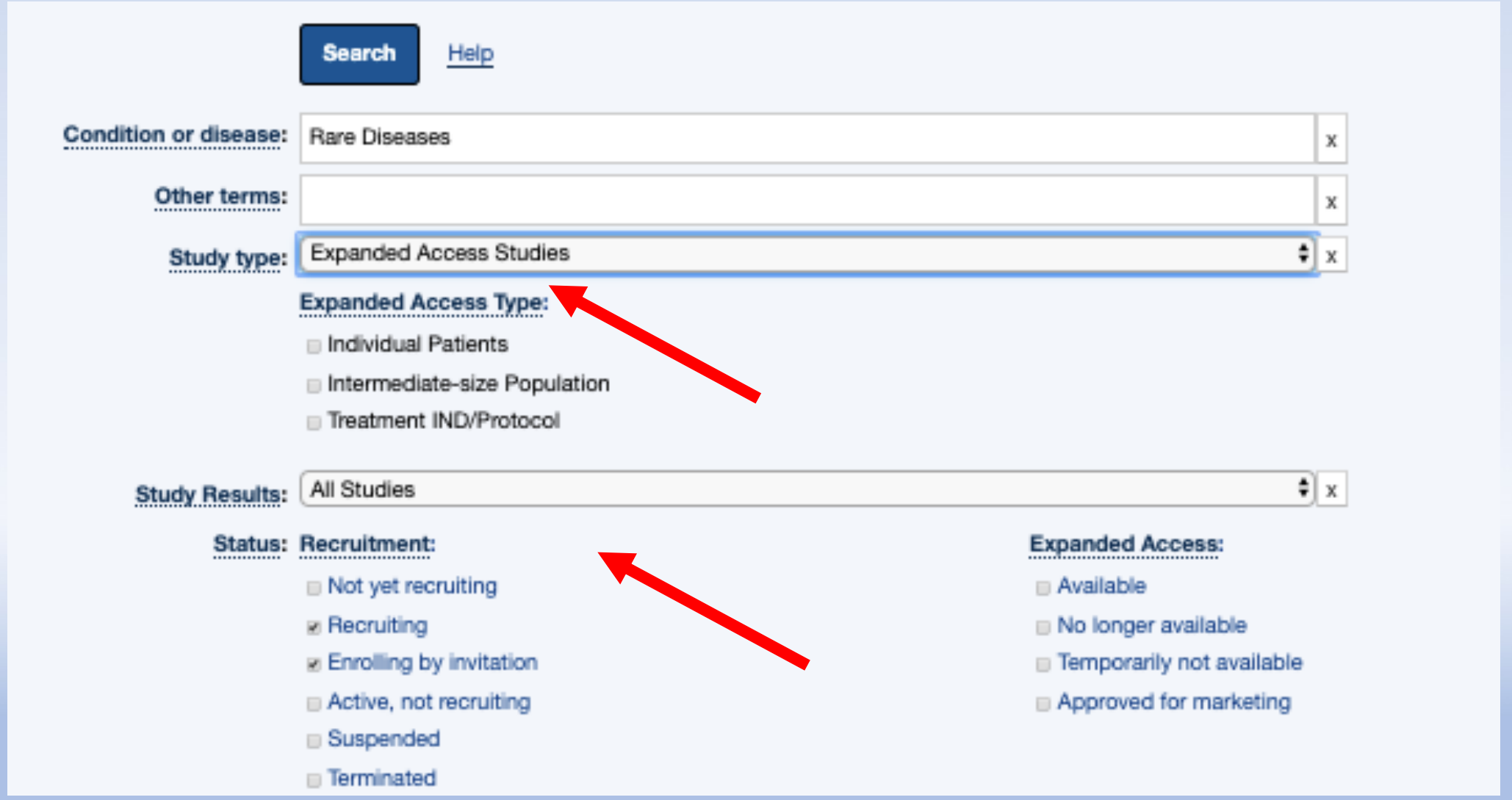
United Kingdom

Investigational Site Number 826003 **Recruiting**
Cambridge, United Kingdom, CB2 OQQ

Investigational Site Number 826001 **Recruiting**
London, United Kingdom, NW1 2PJ

Investigational Site Number 826002 **Recruiting**
Salford, United Kingdom, M6 8HD

Expanded Access



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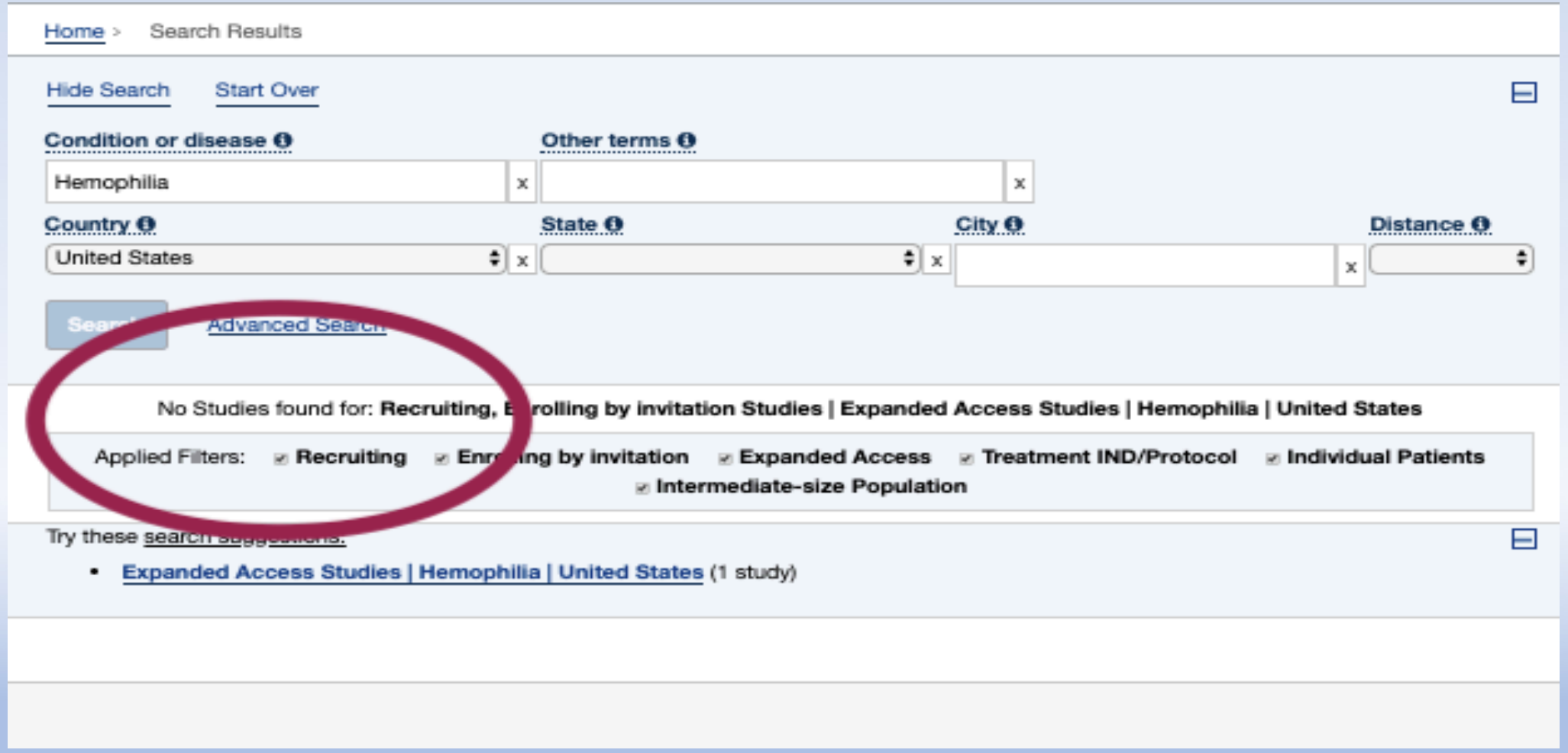

Summary

- Do your homework
- Not all trials are treatment trials
- Clinicaltrials.org
- Expanded access
- If a clinical trial is appropriate, set up an appointment with your patient and their caregiver to discuss
  - please see modules 2 and 3 for more information about discussing clinical trials with patient/caregiver