NAAF Webinar Series: Patient Guide to Clinical Trials and Drug Development: Phases and Terminology Explained

Presented by:

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My Background

- I am a mom to two awesome alopecians- Connolly and Damon
  - Connolly is now 14, and was diagnosed with AA at age 3
  - Damon is now 8, and was diagnosed with AA at age 18 months
- I have 20 years of clinical operations and clinical program management experience
  - I serve as the operational strategy, direction and oversight of clinical programs at a biotech company
  - In developing clinical trial protocols, I am the voice of the site and the patient
  - In 2022 I spoke at the ASGCT Annual Conference on “Diversity in Research”
  - In 2018 I was named PharmaTimes Clinical Researcher of the Year (CROY) Gold Medal Winner
- I have a Master of Public Health (MPH) degree from Johns Hopkins

What are clinical trials? Why do we need them?

Clinical trials are research studies performed **in people** that are aimed at evaluating a medical, surgical or behavioral intervention.

They are the primary way that researchers find out if a new treatment is

SAFE

EFFECTIVE

What makes a clinical trial reliable?

- Rigorous science
- Reproducibility
- Regulation
  - Federal law (eg, FDA)
  - International guidance

Two of the cornerstones of science advancement are **rigor** in designing and performing scientific research and the **ability to reproduce** biomedical research findings. The application of rigor ensures robust and unbiased experimental design, methodology, analysis, interpretation, and reporting of results. When a result can be reproduced by multiple scientists, it validates the original results and readiness to progress to the next phase of research. This is especially important for clinical trials in humans, which are built on studies that have demonstrated a particular effect or outcome.

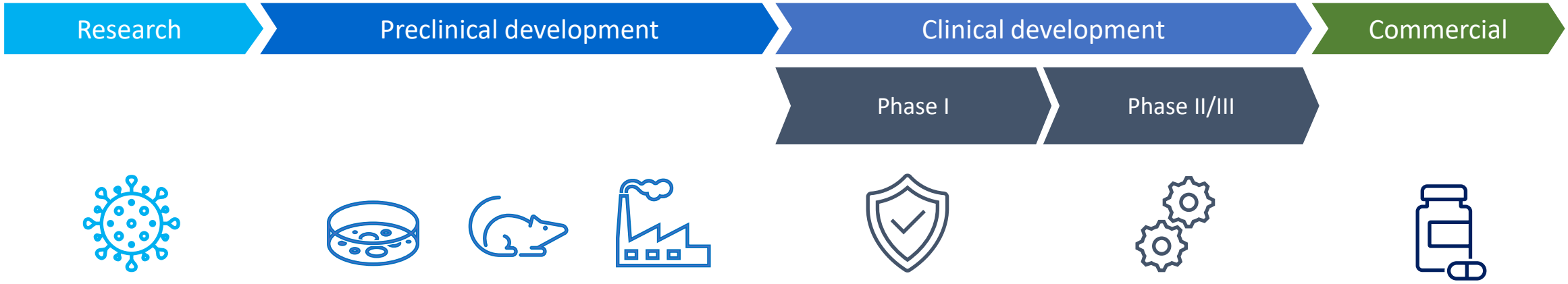
—Francis S. Collins, MD, PhD, NIH Director

What role do patients play in drug development?

Voice of the Patient in Developing New Therapeutics

Industry	Patient	Regulatory Agencies
Develop New Therapies	**Hear My Voice**	**Provide Framework**

Drug development is a complex and dynamic process



What are clinical trial phases?

IND Submission → **Phase 1 – 3 Clinical Trials** → Marketing Application, Review & Approval → Product Launch → **Post-Marketing Surveillance**

Human Pharmacology/
First in Human (FIH)

- Purpose:
  - Safety and tolerability
  - Pharmacokinetics (ADME)
  - Pharmacodynamics
- Dosing:
  - Dose finding/ranging, often starting at a sub-therapeutic dose
  - Open-label
- Study Length: Several months
- Study sites: 1-10 clinical sites
- Participants: 20-100 healthy volunteers, or people with the disease/condition (where necessary, eg oncology)

~70% of drugs move onto the next phase

Source: https://www.fda.gov/patients/drug-development-process/step-3-clinical-research

What are clinical trial phases?

Therapeutic Exploratory

- Purpose:
  - Safety and tolerability
  - Efficacy
  - Proof of Concept (POC)
- Dosing:
  - Typically open-label
  - Can be blinded, comparative
- Study Length: Several months to 2 years
- Study sites: 5-50 clinical sites
- Participants: 100-500 people with the disease/condition

~33% of drugs move onto the next phase

Source: https://www.fda.gov/patients/drug-development-process/step-3-clinical-research

What are clinical trial phases?

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Therapeutic Confirmatory

- Purpose:
  - Efficacy
  - Monitoring for adverse reactions
- Dosing:
  - Blinded
  - Comparative
- Study Length: 1-4 years
- Study sites: >50 clinical sites
- Participants: 300-3,000 people with the disease/condition

~25-30% of drugs move onto the next phase

Source: https://www.fda.gov/patients/drug-development-process/step-3-clinical-research

What are clinical trial phases?

Phase 1

Human Pharmacology/ First in Human (FIH)

- Purpose:
  - Safety and tolerability
  - Pharmacokinetics (ADME)
  - Pharmacodynamics
- Dosing:
  - Dose finding/ranging, often starting at a sub-therapeutic dose
  - Open-label
- Study Length: Several months
- Study sites: 1-10 clinical sites
- Participants: 20-100 healthy volunteers, or people with the disease/condition (where necessary, eg oncology)

~70% of drugs move onto the next phase

Phase 2

Therapeutic Exploratory

- Purpose:
  - Safety and tolerability
  - Efficacy
  - Proof of Concept (POC)
- Dosing:
  - Typically open-label
  - Can be blinded, comparative
- Study Length: Several months to 2 years
- Study sites: 5-50 clinical sites
- Participants: 100-500 people with the disease/condition

~33% of drugs move onto the next phase

Phase 3

Therapeutic Confirmatory

- Purpose:
  - Efficacy
  - Monitoring for adverse reactions
- Dosing:
  - Blinded
  - Comparative
- Study Length: 1-4 years
- Study sites: >50 clinical sites
- Participants: 300-3,000 people with the disease/condition

~25-30% of drugs move onto the next phase

Phase 4

Post Marketing Surveillance

- Purpose:
  - Safety surveillance (pharmacovigilance)
  - Real World Evidence (RWE) and outcomes data gathering
- Dosing: Therapeutic dosing
- Study Length:
  - Several years
  - Dependent upon regulatory commitments
- Study sites: Hundreds – thousands of sites
- Participants: Several thousand people with the disease/ condition

For every 100 drugs entered into Phase 1 trials, fewer than 10 will receive regulatory approval

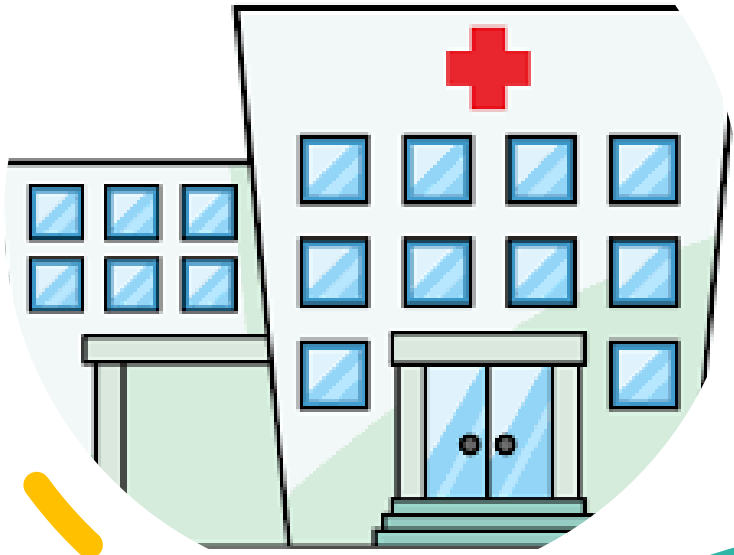
Source: https://www.fda.gov/patients/drug-development-process/step-3-clinical-research

How is the safety of clinical trial participants protected?

Researchers follow a strict set of rules to ensure that participants are safe. The rules are enforced by the US federal government via the FDA.

Study Protocol	Institutional Review Board (IRB)	Data and Safety Monitoring Committee
• Each clinical trial follows a carefully crafted study plan called a protocol. This describes what the researchers will do • The principal investigator is responsible for ensuring that the protocol is followed	• An IRB at each site must approve every clinical trial in the United States • IRB is made up of doctors, scientists and lay people • The IRB regularly reviews the study and its results • The IRB ensures that risks (or potential harm) to participants are as low as possible	• Some (but not all) clinical trials are supervised by this committee • The committee is made up of experts in your condition who periodically review results as the study progresses • If they find that the experimental treatment is not working or is harming patients, they will stop the trial immediately

Clinical Trial Roles and Responsibilities



Sponsor (eg Pharma/ Biotech)

- Design medically and scientifically sound clinical protocols
- Provide medical oversight and expertise
- Monitor safety

Patient

- Understand risk
- Participate in the informed consent process
- Participate in clinical trial assessments

Investigator

- Medical care of patients
- Ensure compliance with clinical protocol

Investigational Review Board (IRB)

- Safeguards the rights, safety, and well-being of trial participants

Participating in a clinical trial may have risks, but it may also have benefits

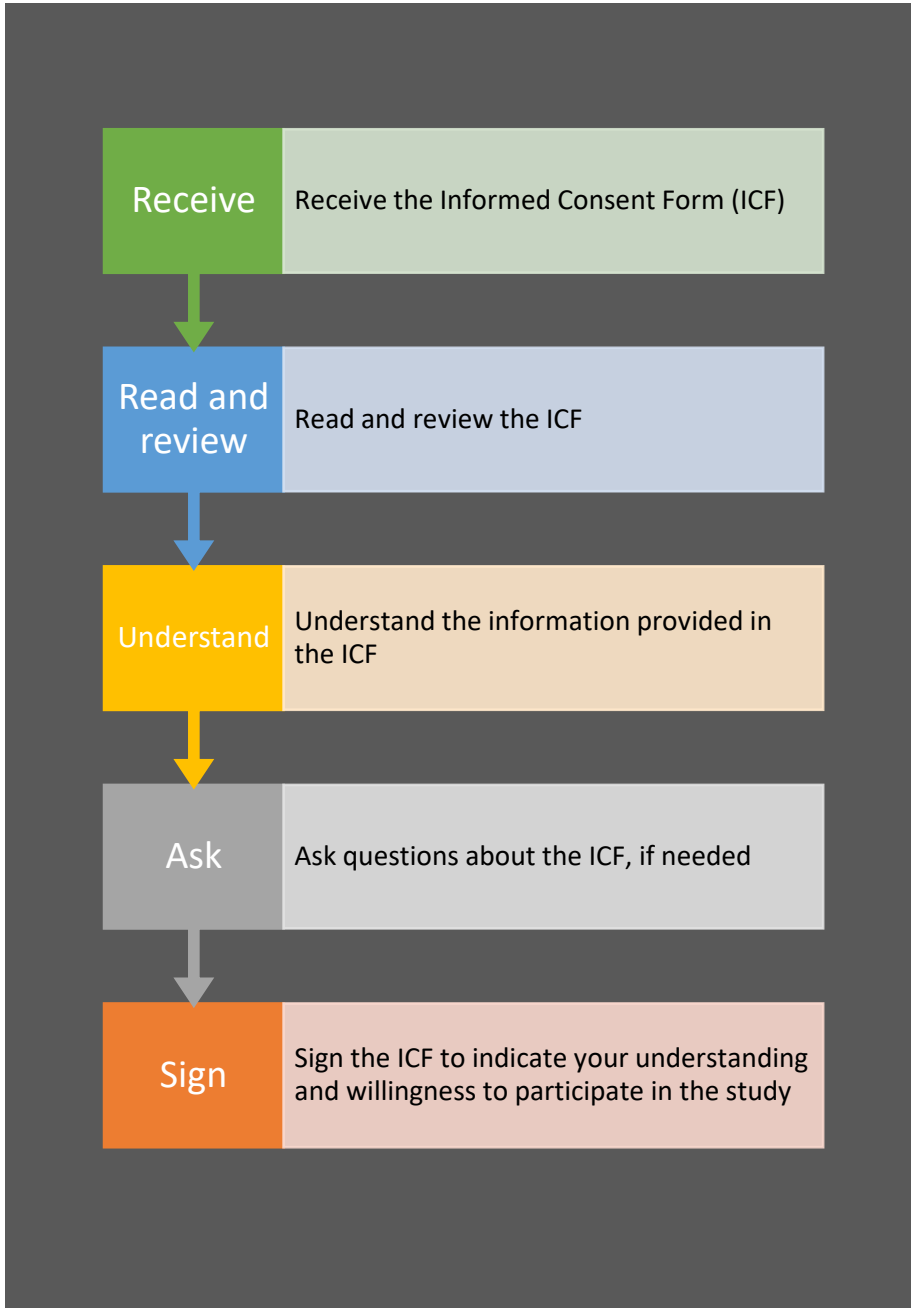
Potential Benefits	Potential Risks
You may receive a new treatment before it is available widely	The new treatment may cause serious side effects or be uncomfortable
You play an active role in driving your healthcare	The new treatment may not work, or it may not be better than what is already available
Researchers may provide you with medical care as a part of your treatment	You may NOT be a part of the experimental group, and you may not receive the new treatment. This means that you might receive a placebo or standard of care treatment
You may have the chance to help others get a better treatment for their health concerns in the future	The clinical trial may be an inconvenience to you. Required appointments and procedures may take a lot of time, or require you to travel to the investigator site many times

What is a placebo?

- An **inactive** substance or other intervention that looks the same as, and is given the same way as, an active drug or treatment being tested.
- The effects of the active drug or other intervention are compared to the effects of the placebo.

What is an informed consent?

- Informed consent is a process that helps protect participants
- Before joining a clinical trial, you will be told what to expect as a participant, and all the things that might happen. For example, the principal investigator will explain possible side effects or other risks
- By signing an Informed Consent Form (ICF), you show that you have been told all the details of the study
- The ICF is NOT a contract
- You can leave the clinical trial at any time and for any reason
- Researchers must keep health and personal information private



What questions should I ask my doctor?

- What is the purpose of the trial?
- What kind of treatments and tests are involved in the trial?
- Have similar studies already been done and what were the results?
- What are the possible risks or side effects of this treatment?
- How will my medical information and privacy be protected?
- How long will the trial last?
- How will the trial affect my daily life? How often will I need to come to the clinic?
- Who will fund this study?
- Do I have to pay for any of the treatments? What costs will my health insurance cover?
- Is there a chance I will receive placebo, and if so, will the new treatment be given should it prove to be better than current treatments?
- If I benefit from this therapy, will I be allowed to continue receiving it after the trial ends?
- Who will oversee my care while I am participating in the trial?
- Will I be able to take my regular medications while participating in the trial?

Do I have to pay for any of the treatments?

- Most clinical trials are paid for by private industry or the federal government.
- Typically, you will NOT be asked to pay for participation in a clinical trial.
- You may receive compensation for clinical trial participation, e.g., for travel.
- Your health insurance may pay for ‘standard of care’ treatment costs.

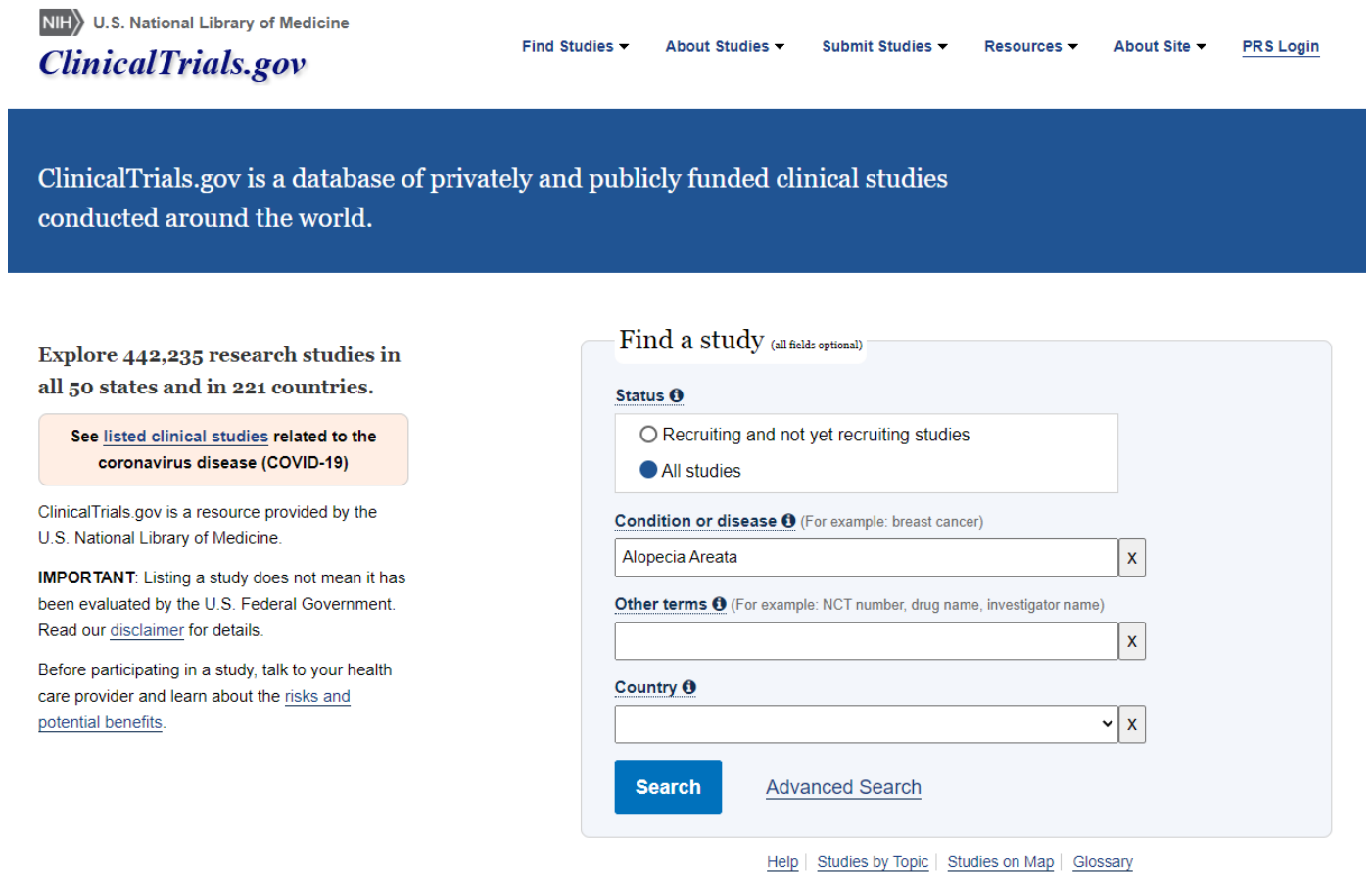
Be suspect if you are asked to pay to participate in a clinical trial.

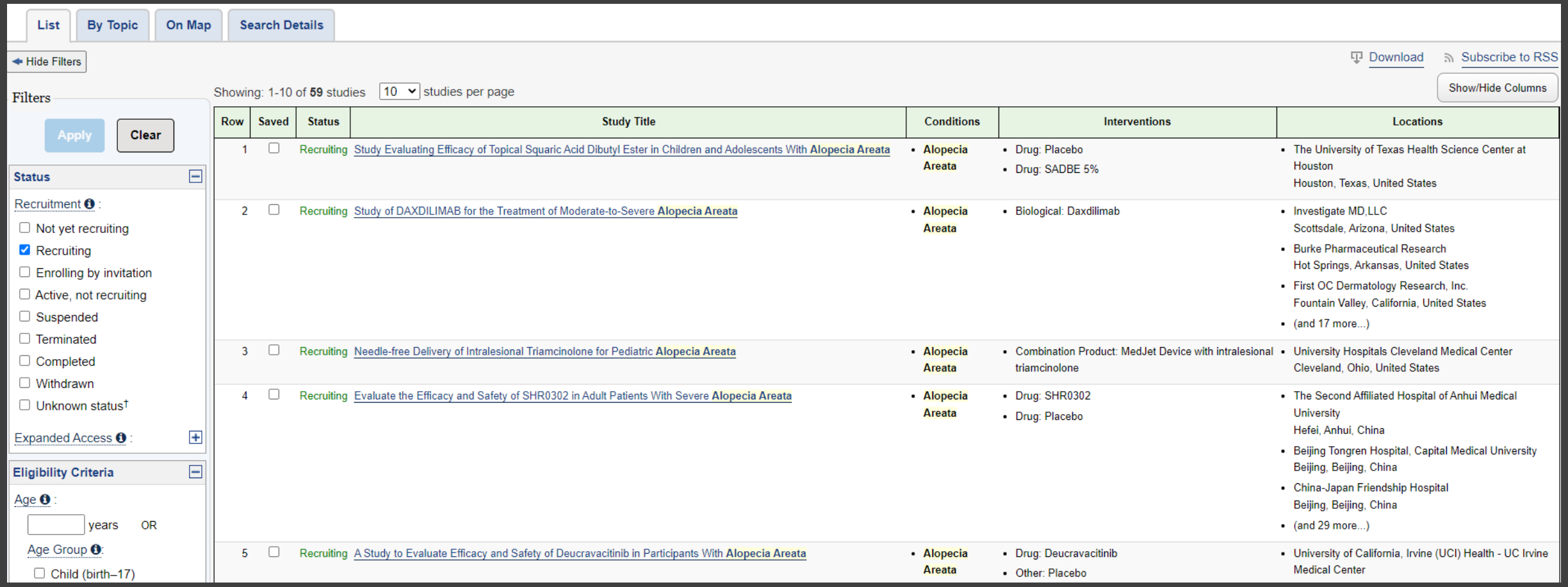
Where do I find information about ongoing and upcoming clinical trials?

- Clinical Trials.gov
  - www.clinicaltrials.gov
  - A service provided the National Institutes of Health (NIH)
  - Provides patients, family members and members of the public easy and free access to information on clinical trials
  - Includes federal and private studies nationwide
- Patient advocacy and support organizations such as NAAF
  - www.naaf.org/research/clinical-trials
  - NAAF posts some clinical trial announcements for studies seeking to recruit people with alopecia areata
  - The NAAF website also links to Clinical Trials.gov

ClinicalTrials.gov

- On landing page, you can search by:
  - Condition/disease
  - Other terms (such as study or sponsor names)
  - Country



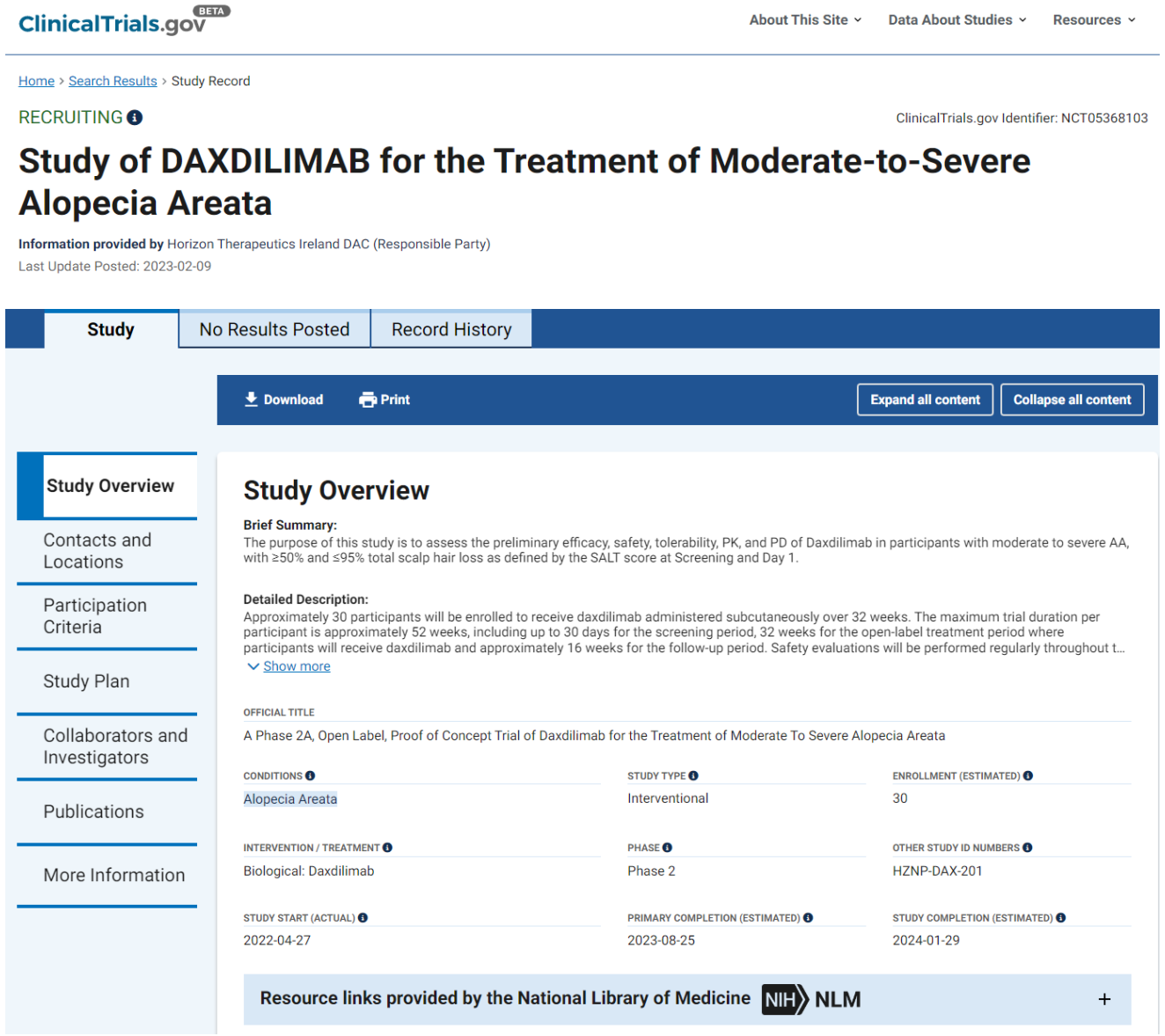


ClinicalTrials.gov

- Within returned results, use search boxes on right to refine results.
- Click on ‘Study Title’ to read details about the clinical trial.

ClinicalTrials.gov

The study record page contains information about the study plan, participation criteria, locations, and more.



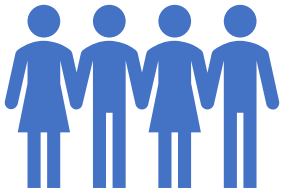
The FDA has a growing focus on diversity, inclusion & equity

- FDA focus on health equity- new draft guidance released April 2022
  - Submit “race and ethnic diversity plan” early in clinical development
    - Set enrollment goals
    - Correct for underrepresentation in clinical trials
  - Establishes the ‘Diversity in Clinical Trials Initiative’ to support via public education and outreach

Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials
Guidance for Industry

DRAFT GUIDANCE

How does my participation in a clinical trial help the alopecia areata community?



Helping Others

Participating in a clinical trial may help people with alopecia areata have better outcomes

Contribute to moving science forward

Personal

Participating in a clinical trial may offer you access to the newest treatment

Conclusions

- It is through clinical trials that safe and effective drugs, therapies and potentially a cure for alopecia areata will be discovered.
- By participating in a clinical trial, you play an important role in the fight to develop effective treatments and potentially identify a cure for alopecia areata.
- The decision to participate, however, is very personal and should be made only after speaking with your health care provider and other individuals you trust.
- You can stop participation in a clinical trial at any time if new concerns arise or you lose confidence that its potential benefits outweigh its risks.

Thank you!

“Research participants are giving a gift to society.”

- Liz Martinez, Johns Hopkins Medicine Research Participant Advocate