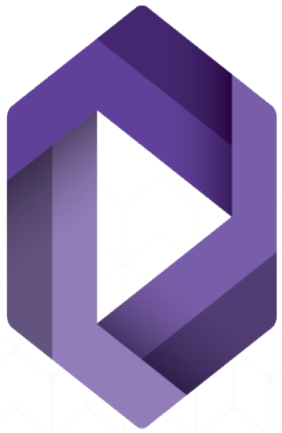

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Current Alzheimer's Disease Clinical Research at SIU Medicine

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Center for Clinical Research

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FORWARD. FOR YOU.

CURRENT RESEARCH NUMBERS IN THE NEUROLGY DEPARTMENT AT SIU

Alzheimer's Disease – 6 open (3 Pending)

Parkinson's Disease and Movement disorders – 4 open (2 Pending)

Neurocritical Care – 1 open (0 Pending)

Neurosurgery – 1 open (1 Pending)

Neuromuscular – 1 open (0 Pending)

Seizure – 4 open (3 Pending)

Stroke – 1 open (0 Pending)

WHAT IS A CLINICAL TRIAL?

- A clinical trial is a research study that tests a medicine or therapy in people.
- Clinical trials can also be called clinical studies or clinical research.
- Clinical research helps us answer questions about the medicine being studied.
  - Does the medicine work?
  - Is the medicine safe?
- The medicines inside your medicine cabinet have one big thing in common; before reaching you, they went through years of research studies to ensure that they were safe for you to take.

VALUE OF A CLINICAL TRIAL

- They play an important role in the development of new medical breakthroughs.
- They are needed to make sure new approaches are safe and effective for the human body.
- They may show that one treatment is effective over a previously used treatment.
- They may reduce the burdens of disability and illness.
- Without clinical trials, it would be impossible to develop new medicines, treatments, and most importantly cures!

CLINICAL TRIAL PHASES

Phase I	Phase II	Phase III	Phase IV
20-80 participants	**100-300 participants**	**1,000-3,000 participants**	**Thousands of participants**
Up to several months	Up to (2) years	One (1) - Four (4) years	One (1) year +
Studies the safety of medication/treatment	Studies the efficacy	Studies the safety, efficacy and dosing	Studies the long-term effectiveness; cost effectiveness
70% success rate	33% success rate	25-30% success rate	70-90% success rate

https://www.cern-foundation.org/education/clinical-trials/clinical-trial-phases

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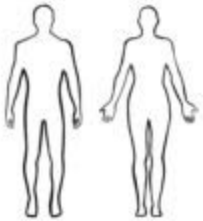
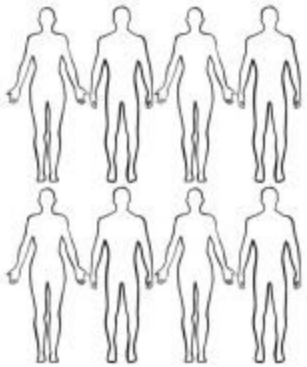
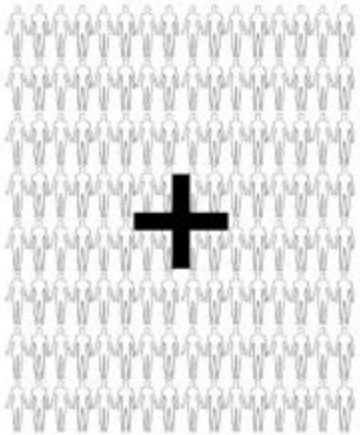
PRECLINICAL	PHASE I	PHASE II	PHASE III	PHASE IV
				
Laboratory Research determines if treatment is useful and safe	6-10 Participants Understand effects of treatment in humans	20-50 Participants Evaluate safety and efficacy of treatment	100-200 Participants Confirm benefit and safety of treatment	200+ Participants Evaluate long-term effects of treatment

https://gene.vision/knowledge-base/clinical-trials/

IMPORTANT TERMS

Double-Blind Study– A type of clinical trial in which neither the participants nor the research team knows which treatment or intervention participants are receiving. The results are less likely to be biased.

Open-Label Extension Study (OLE) – Patients who have participated in the entire double-blind trial are then eligible to participate in an open-label treatment phase where everyone is receiving the drug.

Placebo – May resemble the study drug, but is not active drug. The placebo has no known therapeutic value.

Inclusion Criteria – A type of eligibility criteria. These are the reasons that a person is allowed to participate in a trial.

Exclusion Criteria – Also a type of eligibility criteria. These are reasons that a person may not be allowed to participate in a trial.

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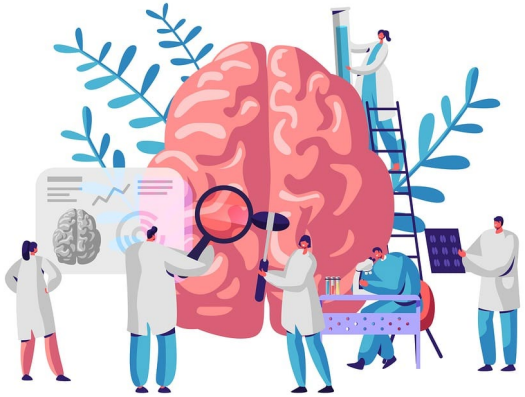
IMPORTANT CLINICAL TRIAL ROLES

Principal Investigator (PI) – The primary individual responsible for overseeing the preparation, conduct, and administration of a clinical trial. The PI prepares and carries out the clinical trial protocol.

Sub-Investigator (Sub-I) – A clinician appointed and supervised by the PI to assist in important trial related duties and decisions.

Clinical Research Coordinator (CRC) – A specialized research professional working with and under the direction of the PI. The CRC works with the PI, department, sponsor, and institutions to support all aspects of a study.

Research Nurse – A professional member of a research team who provides direct patient care for participants in clinical trials.



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THINGS YOU NEED TO KNOW ABOUT CLINICAL TRIALS

People participate for different reasons. Some common reasons for study volunteers to join a clinical trial include:

- to advance science and treatments
- to help others with the same condition or disease as them
- to potentially obtain new treatments before it is available to others

THINGS YOU NEED TO KNOW ABOUT CLINICAL TRIALS

- Everyone conducting a clinical trial has strict regulatory and ethical duties.
- Institutional Review Board (IRB) or Central IRB (CIRB), operate independently from the day-to-day conduct of research.
- The purpose of an IRB is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in research.

THINGS YOU NEED TO KNOW ABOUT CLINICAL TRIALS

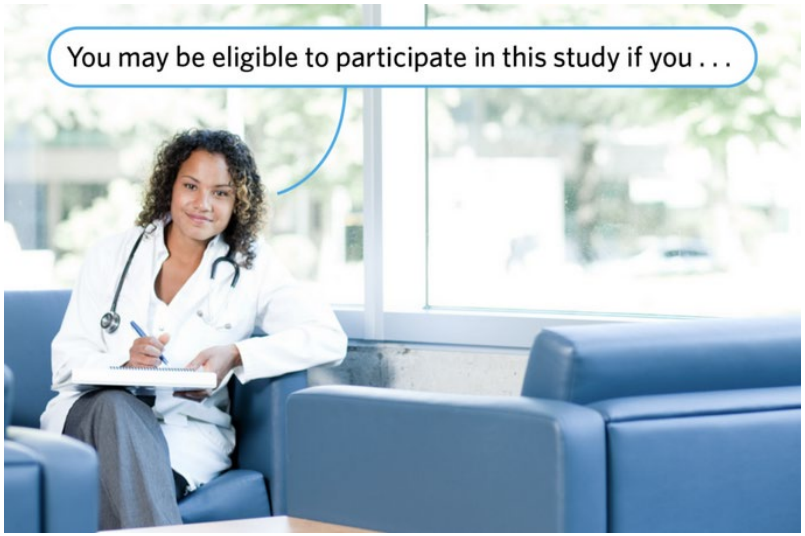
- Clinical trials are experiments, so the exact risks and benefits can be difficult to predict.
- Researchers only move forward with clinical trials when they are optimistic about the potential benefits and believe any risks for participants are acceptable.
- The risks and benefits are different for everyone.

THINGS YOU NEED TO KNOW ABOUT CLINICAL TRIALS

- For most clinical trials, the study medicine is provided and visits are conducted at no cost to the participant.
- Some clinical trials pay or reimburse participants.
- Payment for participation is not meant to entice subjects to participate - this could be seen as coercion.

THINGS YOU NEED TO KNOW ABOUT CLINICAL TRIALS

- For each trial, there is a set of criteria needed to prove whether a medicine works or not in a specific patient population.
- Trial criteria are based on things like age, gender, the type and stage of a disease, previous treatment history, and other medical conditions.



TYPICAL INCLUSION CRITERIA FOR ALZHEIMER'S STUDIES

- Age range (usually 55 to 85)
- Diagnosis of Alzheimer's disease or memory loss
- Generally in good health other than the illness being studied
- Caregiver is with the patient at least 10 hours a week and willing to accompany patients to all study visits
- Mini-Mental State Exam (MMSE) – score is 0 to 30
  - Mild studies – score of 25-30
  - Moderate studies – score of 14-24
  - Severe studies – score of 0-13

EXCLUSION CRITERIA (NOT AS TYPICAL)

- Must be able to tolerate MRIs/PET scans
- Body mass index usually within a certain range
- Cannot reside in a skilled nursing facility
- Poor venous access
- Any serious medical condition that in the opinion of the investigator precludes the patient's safe participation
  - Chronic kidney disease
  - Uncontrolled diabetes
  - Uncontrolled hypertension
  - Clinically significant, abnormal EKG at screening
  - History of cancer
  - History of stroke
  - Psychiatric disorders (i.e. major depressive disorder, schizophrenia, etc.)
  - Etc.

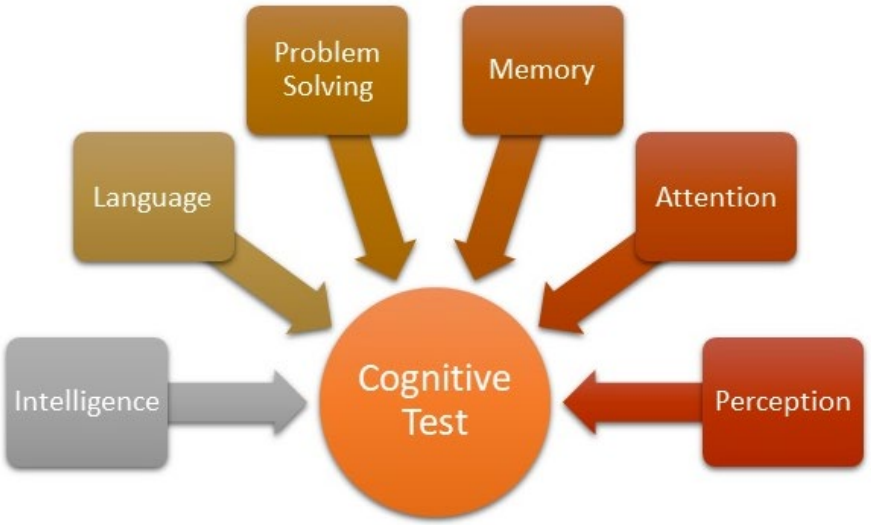
EXCLUSION CRITERIA (PROHIBITED MEDICATIONS)

- This can vary from study to study
- Stable dose of medicines for three months prior to joining study
- Most benzodiazepines are excluded
- Any drug that may have a sedating affect is often excluded

MMSE

- Used by neurologists, psychiatrists, geriatricians, and general practitioners.
- Takes 5-10 minutes to administer.
- Score is from 0-30 (30 being the maximum).
- MMSE measures orientation to time and place, immediate recall, short-term verbal memory, calculation, language, and construct ability (all important aspects of cognition).
- When used repeatedly, measures changes in cognitive status.
- Test has its' strengths and weaknesses, but it is still considered by many to be the "Gold Standard" of cognitive screens for both research and clinical use (Tombaugh et al, 1992).
- Changes over 1 year of 4 points or more are considered significant (Tangolos et al., 1996).

Mini Mental State Exam (MMSE)



Mini-Mental State Examination (MMSE)

Patient's Name: _____ Date: _____

Instructions: ***Ask the questions in the order listed. Score one point for each correct response within each question or activity.***

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day of the week? Month?"
5		"Where are we now: State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: _____
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, ...) Stop after five answers. Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

(Adapted from Rovner & Folstein, 1987)

Source: www.medicine.uiowa.edu/igec/tools/cognitive/MMSE.pdf

THE MOST IMPORTANT THING YOU NEED TO KNOW ABOUT CLINICAL TRIALS

- Participants can withdraw from a clinical trial at any time, for any reason.
- No matter the stage of the trial, participants have the right to change their mind.
- If a study participant decides to leave the study, the Principal Investigator will remove them from the trial in a safe manner.

ONGOING CONSENT

- During each encounter with the patient and their caregivers, researchers have the opportunity to continue the informed consent process (make sure subjects still understand why the study is being done).
- Discuss new information that may affect the patient's and caregiver's willingness to participate (new known risks or benefits, new alternative treatment options, updates to study schedule).
- Remind the patient and caregiver of the study goals and objectives

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CURRENTLY ENROLLING –

LIFT-AD

- Athira Pharma, Inc., Bothell, WA
- ATH-1017-AD-0201
- A Randomized, Placebo-Controlled, Double-Blind Study of ATH-1017 Treatment in Subjects with Mild to Moderate Alzheimer's Disease
- Phase 2
- 55 Centers in USA (might open in Australia)
- 375 participants – currently at >50% of target and now only enrolling those on no other drugs for treatment of Alzheimer's Disease

CURRENTLY ENROLLING –

LIFT AD

The main purpose of this study is to investigate the effectiveness of ATH-1017 at different doses compared to a placebo, for the treatment of Alzheimer's disease (AD) and to determine the safety and tolerability (whether side effects of a medicine can be handled by study subjects) of ATH-1017 compared to a placebo, when administered once a day for up to 26 weeks.

CURRENTLY ENROLLING –

LIFT AD

- Subjects and their trial partners will be required to sign an informed consent document and will be evaluated against the inclusion/exclusion criteria during a screening period.
- Those who meet all inclusion/exclusion criteria will be randomized in a ratio of 1:1:1 to three parallel arms, either to active treatment (ATH-1017 40 mg/day or ATH-1017 70 mg/day) or placebo (66% chance of receiving active medication).

CURRENTLY ENROLLING –

LIFT AD

- During the study, patients will undergo cognitive assessments, collection of laboratory samples, ECG monitoring, and a brain MRI.
- The Screening Period (to confirm eligibility) can last up to 28 days.
- The Treatment Period (where you will receive your assigned study medication) will last up to 26 weeks (approximately 6 months).
- The Post-treatment Follow-up Period (to check your overall health) may last up to 4 weeks or you may choose to go into the OPEN-LABEL EXTENSION period (more on that later).

CURRENTLY ENROLLING –

LIFT AD

- Study drugs will be administered by subcutaneous injection once-daily.
- The study partner will need to document all injections in a dosing diary.
- Subjects may experience risks and/or possible side effects while in the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors do not know all the side effects that may happen.

CURRENTLY ENROLLING –

LIFT AD

- There is no cost to the subject to participate – all study related visits, tests, etc. are covered by Athira.
- Subjects and caregivers each receive $78 per visit that is completed. This is distributed via a check mailed to their home.
- Sara Boarman, BS, is the Lead Coordinator for this study – you can reach her at sboarman93@siumed.edu or 217.545.6829.

CURRENTLY ENROLLING – LIFT AD – OPEN-LABEL EXTENSION

- Open-Label Extension (OLE) – only subjects who complete the 26 week blinded portion of study may *roll-over* into the OLE.
- The OLE is not blinded – Open-Label means everyone gets the real drug – no more possibility of placebo.
- This period runs 18 months – it is run similar to the blinded period (less cognitive testing).
- Subjects will receive a daily injection.
- You do not have to enroll in the OLE – it is optional.

CURRENTLY ENROLLING –
NEW IDEAS

- American College of Radiology
- New IDEAS: Imaging Dementia—Evidence for Amyloid Scanning Study
- A Study to Improve Precision in Amyloid PET Coverage and Patient Care
- Mild Cognitive Impairment or Dementia
- 7,000 persons may be enrolled – United States
- Will having the results of an amyloid PET scan change your doctors treatment plan?
- Radioactive tracer injected via IV – wait 45 minutes, then PET scan of brain completed.
- **Currently only enrolling minorities of color** – this is not expected to change in the near future.
- Must be a Medicare recipient – Medicare is paying for scan.
- $75 check comes to subject's home directly from ACR.
- NOT A TREATMENT STUDY.
- Contact Sara Boarman, BS, at 217.545.6829 or sboarman93@siumed.edu for more information.

NEW iDEAS
Brain Imaging Study for Alzheimer's

CURRENTLY ENROLLING –
CAREGIVER STUDY

- Caregiver Characteristics that may be associated with the optimal care of patients with Alzheimer's disease.
- Investigating various characteristics and features that may predict changes in caregiving over the course of three years. Couples will have a one-time visit at the clinic. During the one-time visit, the couple will be administered questionnaires, assessments, and physical measurements. After this visit, the caregiver will have a phone-call interview every two months, spanning three years. The caregiver will also complete two mail-in questionnaires every six months and a depression screening.
- We hope to enroll 217 couples.
- Each enrolled couple that completes the one-time visit and mail-in questionnaires will be paid $150. An additional payment of $100 will be given each succeeding 12 months for the phone-call interviews and for completing and returning the two questionnaires. A total payment of $450 will be paid to couples who complete the full three years. Payment will be given as a check mailed to your home address.
- Contact Stephanie Kohlrus, BA, CCRP, at 217.545.3013 or skohlrus@siumed.edu for more information.

ONGOING – NOT ENROLLING

TRAILBLAZER-2

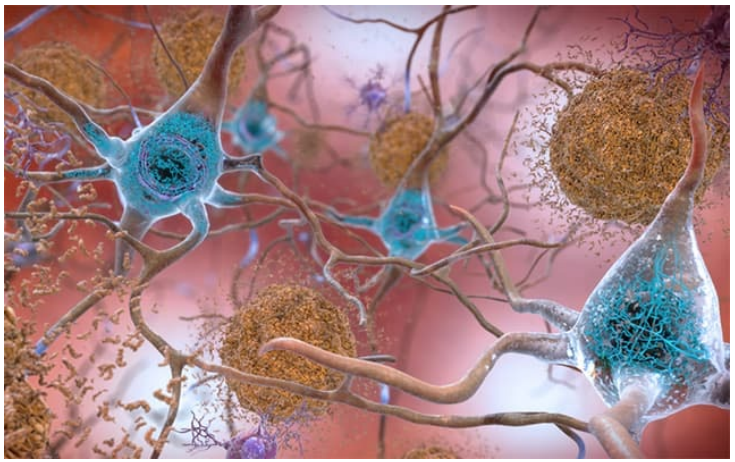
Lilly I5T-MC-AACI

- Assessment of safety, tolerability, and efficacy of donanemab in early symptomatic Alzheimer's disease.
- Phase 3
- Infusion every four weeks at SCI
- 1800 subjects world-wide
- Six subjects were enrolled locally
- 78 weeks blinded with the option to roll over into an open-label period (currently all subjects are in the open-label period

ONGOING – NOT ENROLLING

TRAILBLAZER-2

During the study, patients will undergo cognitive assessments, collection of laboratory samples, ECG monitoring, brain magnetic resonance imaging (MRI) and positron emission tomography (PET) scans, and will receive either the study drug or placebo by intravenous (IV) infusion once every 4 weeks at an infusion center.



ONGOING – NOT ENROLLING

TRAILBLAZER-2

- June 2021 - Lilly's donanemab receives U.S. FDA's Breakthrough Therapy designation for treatment of Alzheimer's disease.
- The Breakthrough Therapy designation aims to expedite the development and review of drugs that are intended to treat a serious condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over already available therapies that have received full FDA approval.

ONGOING – NOT ENROLLING

LAURIET

Genentech GN40040

- A Phase II, multicenter, randomized, double-blind, placebo-controlled, parallel-group, efficacy, and safety study of MTAU9937A in patients with moderate Alzheimer's disease.
- 260 subjects – 50 study centers
- One subject enrolled locally – currently in the OLE portion of the study
- 3.5 year study
- Infusion administered every four weeks – at Springfield Memorial Hospital.
- If it works, MTAU9937A may slow down how fast the disease progresses.

CLINICAL TRIALS WEBSITE

- http://clinicaltrials.gov
- This is a worldwide database of privately and publicly funded clinical trials.
- Currently there are 425,817 research studies in all 50 states and 221 countries.
  - Search for Alzheimer's disease turned up 2,910 results.
  - Search for Dementia turned up 4,224 results.

NEUROSCIENCES RESEARCH AT SIU (NEUROLOGY STUDIES)

- https://www.siumed.edu/neuro/research.html
- If you would like to enroll in our clinical trials, please complete the patient survey located at: https://www.siumed.edu/ccr/enroll-clinical-trial

CARING FOR THE CAREGIVER

"This disease [Alzheimer's] plays havoc with not only the patient, but also the caregiver. The caregiver is really the second patient."

— Meryl Comer, Caregiver & Author

"There are only four kinds of people in this world—those who have been caregivers, those who are currently caregivers, those who will be caregivers and those who need caregivers."

— Former First Lady, Rosalynn Carter

CARING FOR THE CAREGIVER CONTINUED…

- Help the caregivers gain an understanding of the patient's diagnosis
- Help the caregivers to not neglect their own needs (Caregiver burnout)
- Listen to the caregiver, but also pay attention to any nonverbal cues (fatigue, physical pain, etc.)

“I open my heart to those who give comfort and care. Today I express gratitude for those, who out of necessity, find themselves caring for others. In prayer, I appreciate each caregiver, grateful that their loving service makes life sweeter and better for those they serve. Their healing touch soothes, their emotional comfort heals, their prayerful support shines great light for those who need it.”

“Everyone can be a caregiver to the world community by expressing tender care and mercy each day in every word and action. I may have no idea of the difficulties that someone may be going through, but my one act of kindness may provide a lifeline for that person going forward. As I care for others, I become one in purpose with all who are giving from their hearts of goodwill.”

OUR CLINICAL RESEARCH TEAM

Jennifer Arnold, MD, PhD – Principal Investigator

Tom Ala, MD – Principal Investigator/Sub-Investigator

Cindy Womack, DNP – Sub-Investigator

Charlene Young, FNP-BC – Sub-Investigator

Amber Fifer, PharmD, ACRP-CP – Research Assistant Professor of Neurology and Psychiatry

Barbara Lokaitis, BA, CCRP – Senior Clinical Research Coordinator

Stephanie Kohlrus, BA, CCRP – Clinical Research Coordinator

Ann Jirmasek, MS, LPC – Rater

Amy Richey, LPN - Rater

OUR CLINICAL RESEARCH TEAM

Sara Boarman, BS – Clinical Research Specialist
Rylee Manka, BA – Clinical Research Specialist
Stephanie Rasmussen, RN, BSN – Research Nurse
Mary (Missy) Cartwright, RN, BSN – Research Nurse
Andre Catalano, PharmD, MBA – Post-Doctoral Fellow
Megan Meinke, MD – Post-Doctoral Fellow

SIU Medicine

Neuroscience Institute

Dale and Deborah Smith Center for Alzheimer's Research and Treatment

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