ARC TALKS
WEBINAR SERIES

AL Amyloidosis Clinical Trial Updates

April 15 | 12pm - 1pm ET

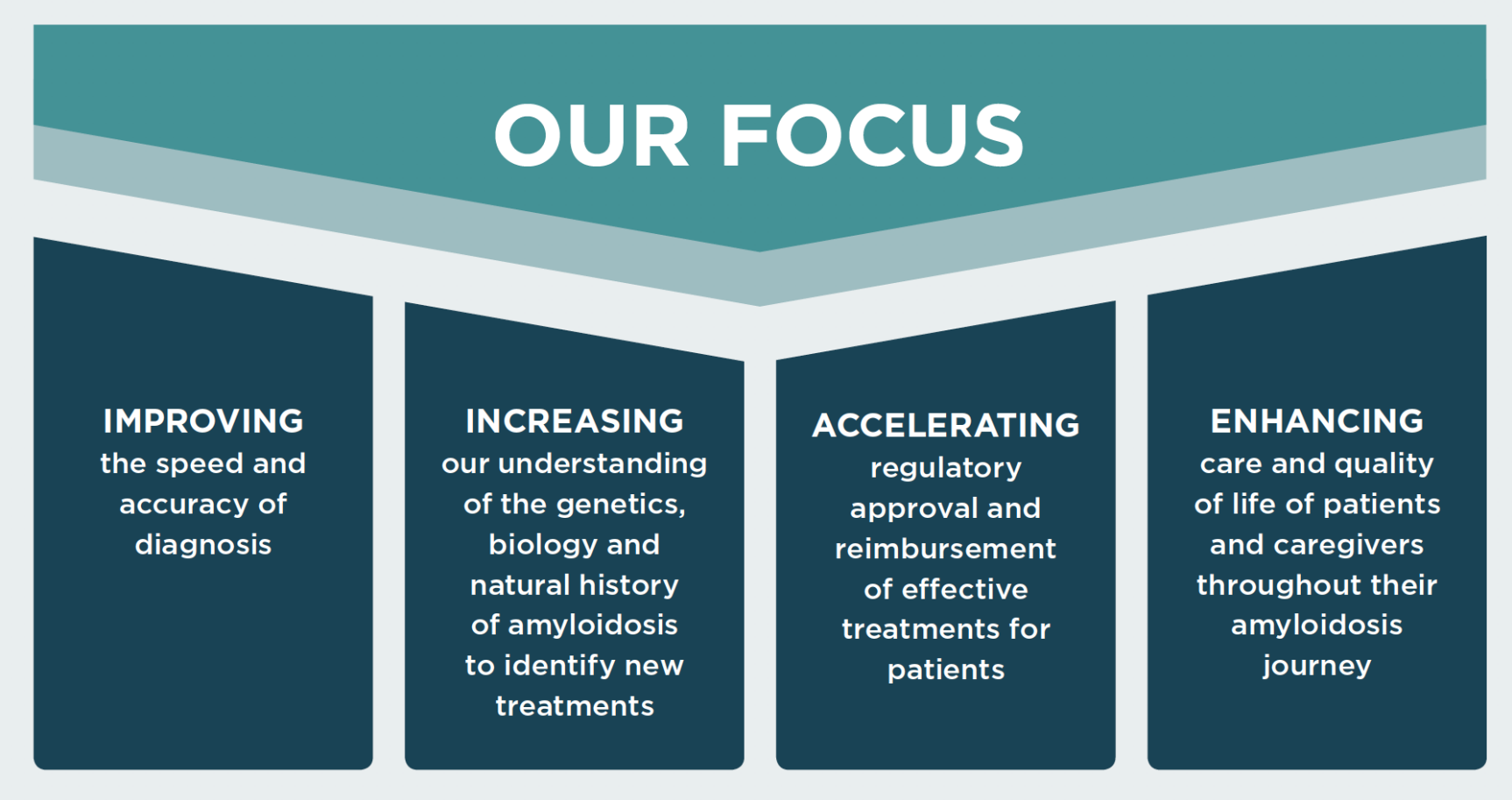
Kristen Hsu

Executive Director of Research
Amyloidosis Research Consortium

About ARC

Amyloidosis Research Consortium

ARC's mission is to improve and extend the lives of those with amyloidosis



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Before We Begin

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This webinar is recorded. We will post the webinar on our website so you can view it again later.

Submit your questions anytime via the Q&A box. We will try to answer them at the end.

If you are having trouble with the audio using your computer, you can dial in (check your email for info).

Amyloidosis Research Consortium

Clinical Trial Updates for the AL Amyloidosis Community

Kristen Hsu, Executive Director of Research

If you are here to learn about ATTR clinical trials…

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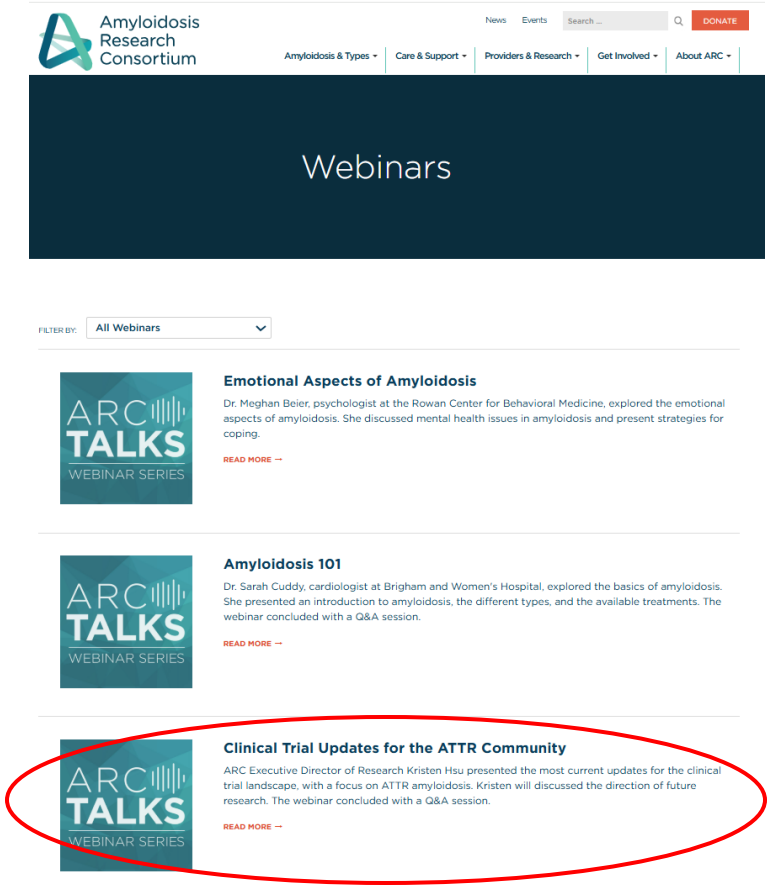
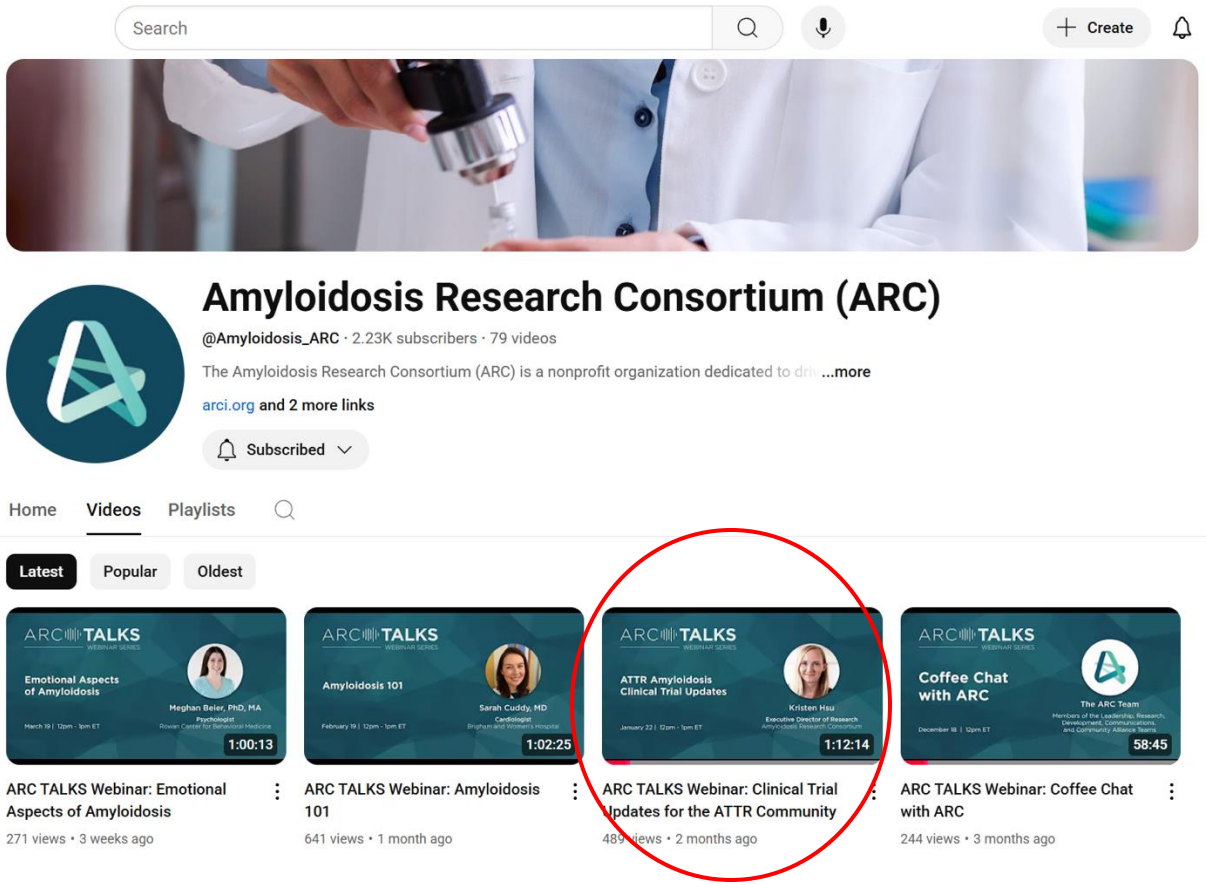
…check out our January webinar focusing on ATTR amyloidosis clinical trials on our website or YouTube channel.
Our next ATTR amyloidosis clinical trials webinar is planned for July 2025

https://arci.org/resources-category/webinars/



https://www.youtube.com/@Amyloidosis_ARC



What is a Clinical Trial?

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- A clinical study is research study involving human volunteers (also called participants) that is intended to add to medical knowledge.
- There are two types of clinical studies: interventional studies (also called **clinical trials**) and observational studies.

Interventional

A type of clinical study in which participants are assigned to groups that receive one or more intervention/treatment (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study's protocol. Participants may receive diagnostic, therapeutic, or other types of interventions.

Observational

A type of clinical study in which participants are identified as belonging to study groups and are assessed for biomedical or health outcomes. Participants may receive diagnostic, therapeutic, or other types of interventions, but the investigator does not assign participants to a specific interventions/treatment.

Clinicaltrials.gov/study-basics/glossary

Clinical Trial Phases

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- Trials are divided into different stages, called phases.
- Each trial phase has a specific purpose and is designed to answer certain questions:

Phase 1	Phase 2	Phase 3	Phase 4
Determines a safe dose of the treatment under study (study drug) and monitors how the new treatment affects the human body (i.e. how the drug is broken down and excreted by the body).	Gather preliminary data on whether the new treatment works in people wohave a certain condition/disease and continues to evaluate safety.	Confirms how well a treatment works, monitors side effects, and compares the new treatment with the current standard treatment or a control arm in a randomized controlled study.	Post regulatory approval, gathers more information on a drug or treatment after it has been marketed to see its effect in various populations and any side effects associated with long-term use.

- The pathway develop a new drug is not always linear. This is especially true in rare disease!

What's involved?

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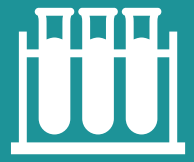
- Most studies are interventional studies.
- These will require administration of the study drug or treatment and a sequence of monitoring visits.
- Monitoring usually takes place under clinical conditions (in a clinic), and on rare occasions may require overnight stays.

Clinical Examinations



Blood and Urine Lab Tests

Questionnaires

Functional Tests

Imaging Tests

What makes a study a good fit for me? How do I know it's safe?

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- Participating in a trial or study has many potential benefits and also some possible risks.

Potential Benefits

- Treatment with investigational drugs that may not be available anywhere else
- Care from a research team
- Opportunity to learn more about your disease and how to manage it.
- Helping scientists better understand your disease and to advance treatments and ways to prevent it in the future

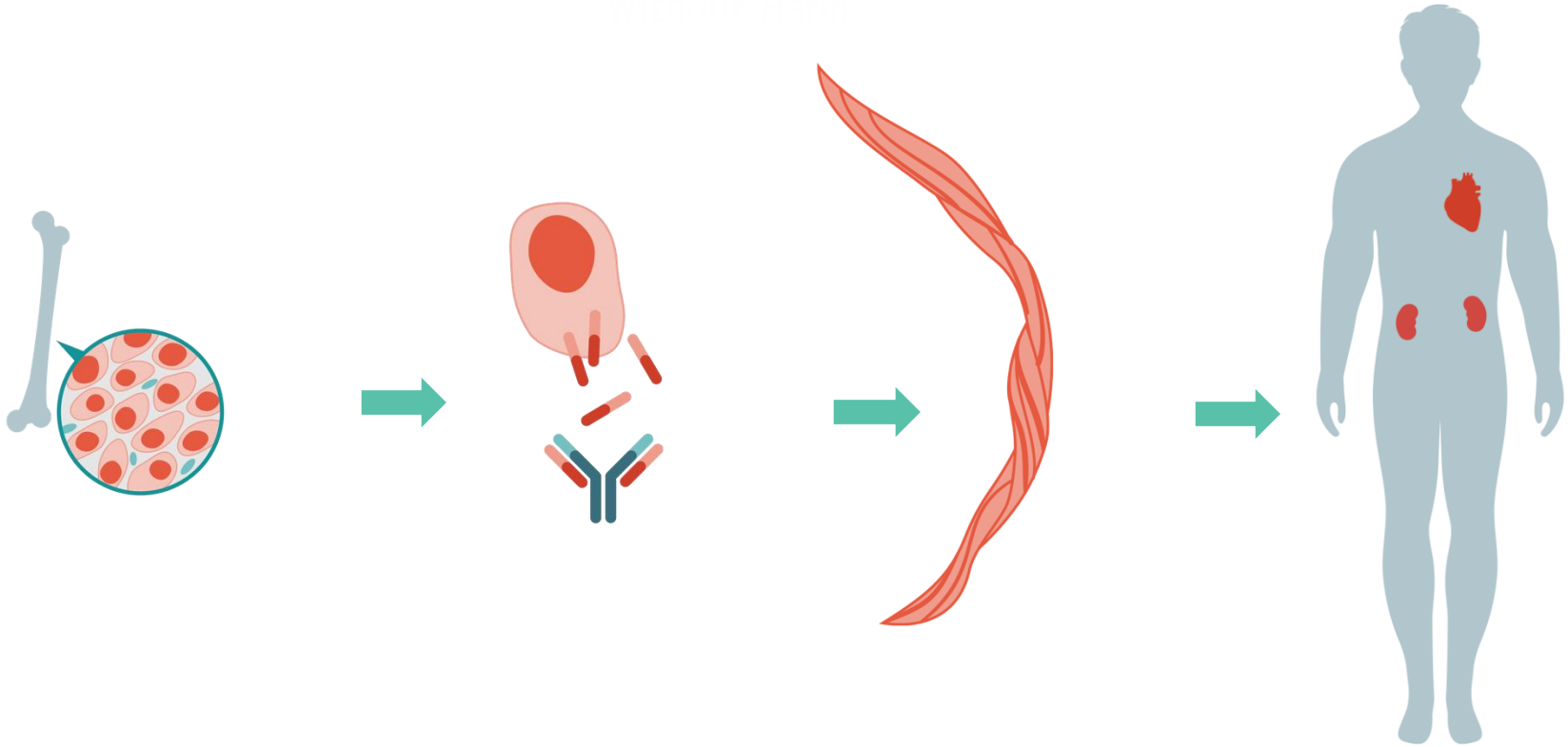
Potential Risks

- Clinical trials may involve a large time commitment and be inconvenient
- Study tests may pose a risk
- Study drug may pose risks, known and unknown
- The experimental treatment might not work
- Participants may be randomly assigned to receive a standard treatment or a placebo

- Potential benefits and risks should be discussed carefully with study doctors and their teams.

AL Amyloidosis Clinical trials

Investigative approaches to treating AL Amyloidosis....



...are like treating a clogged bathtub

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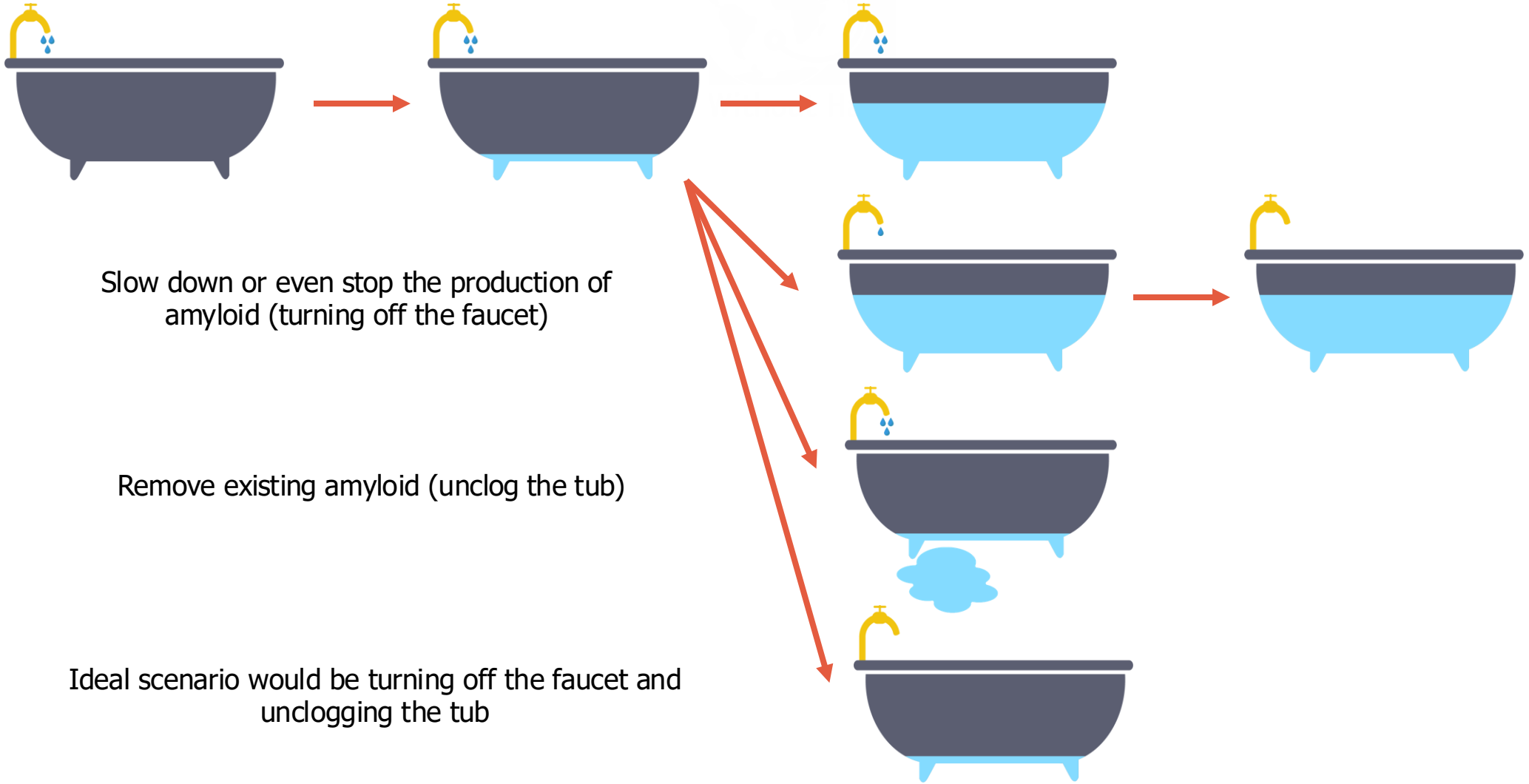

Slow down or even stop the production of amyloid (turning off the faucet)

Remove existing amyloid (unclog the tub)

Ideal scenario would be turning off the faucet and unclogging the tub

Investigative Approaches to Treat AL Amyloidosis

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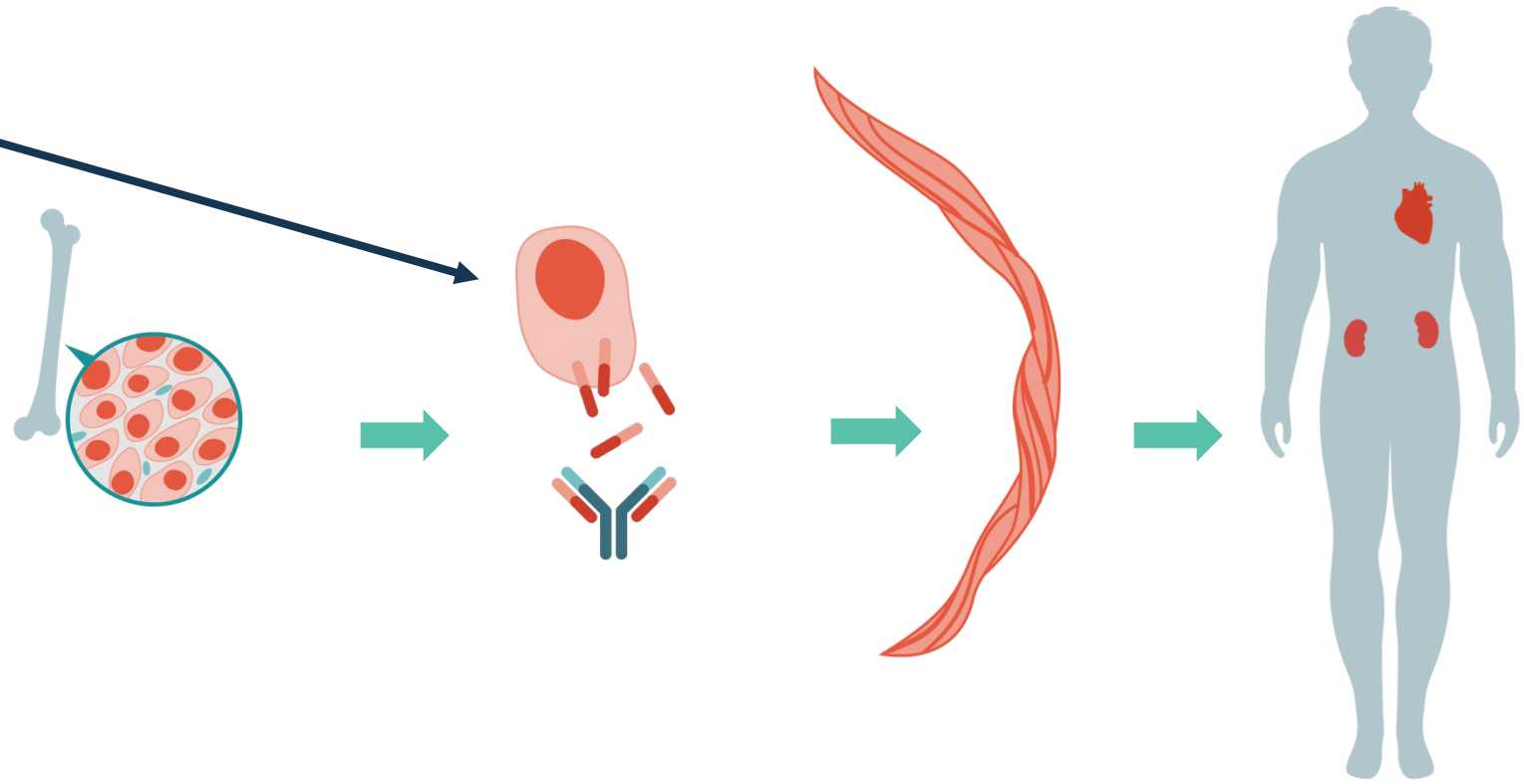
Anti-plasma cell therapies



Investigative Approaches to Treat AL Amyloidosis

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Anti-plasma cell therapies

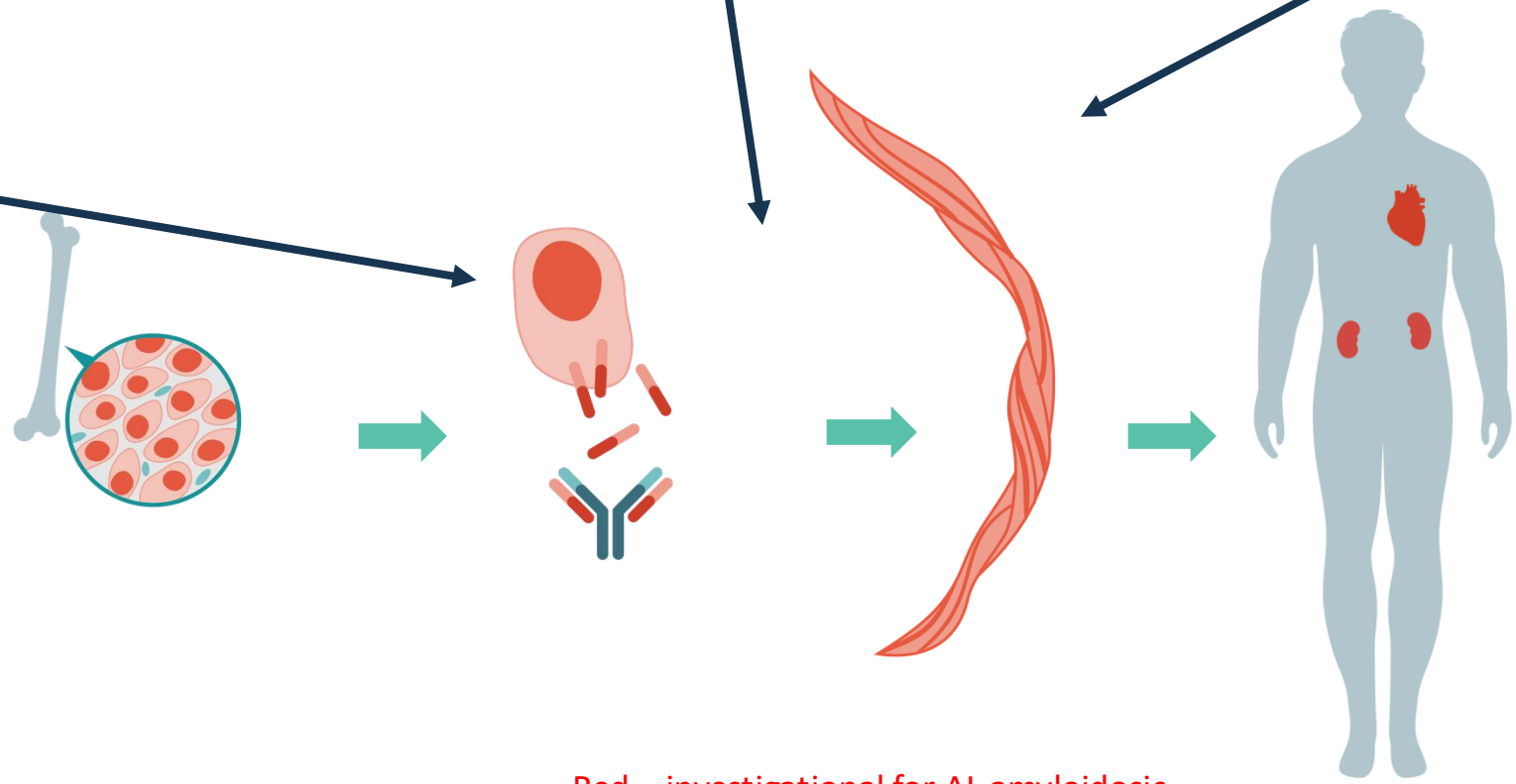
- Monoclonal antibodies
  - Daratumumab (Darzalex)
  - Isatuximab (Sarclisa)
  - Elotuzumab (Empliciti)
  - Belantamab mafodotin (Blenrep)
- BCL-2 Inhibitors
  - Venetoclax (Venclexta)
- Bispecific Antibodies and Cellular Therapies
  - Teclistimab (Tecvayli)
  - JNJ-79635322
  - Linvoseltamab
  - Etentamig (ABBV-383)
  - Elrantumab
  - CAR-T cells

Light chain Stabilizers

- Name TBD

Anti-Fibril Agents

- Anselamimab (CAEL-101)
- Birtamimab (NEOD001)
- AT-02



Red = investigational for AL amyloidosis

Recruiting Trials for Novel AL Therapies in 2025

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				Pre-clinical	Phase I	Phase II	Phase III	Commercial
Monoclonal Antibodies	Janssen	Daratumumab (Darzalex)	Approved (accelerated)					
	Sanofi	Isatuximab	Phase 2 IST recruiting					
	BMS	Elotuzumab	Phase 2 IST ongoing					
	GSK	Belantamab mafodotin	Phase 1/2 IST recruiting					
Bispecific Antibodies and Cellular Therapies	Janssen	Teclistimab	ISTs planned					
		JNJ-79635322 (trispecific)	Phase 1 planned					
	Regeneron	**Linvoseltamab**	**Phase 1 recruiting**					
	AbbVie	**Etentamig (ABBV-383)**	**Phase 1 recruiting**					
	Pfizer	Elrantumab	Phase 1/2 IST recruiting					
	Nexcella	**NXC-201**	**Phase 1 recruiting**					
BCL2 Inhibitors	AbbVie	Venetoclax	Phase 1/2 ISTs recruiting					
LC Stabilizer	Protego	TBD	Preclinical					
Anti-Fibril Agents	Prothena	**Birtamimab**	**Phase 3 recruiting, results Q2 2025**					
	Alexion/AZ	Anselamimab (CAEL-101)	Phase 3 results Q2/Q3 2025					
	Attralus	AT-02 (pan-amyloid)	Phase 1 ongoing					

LINKER-AL2 (linvoseltamab; BCMA-CD3 bispecific antibody)

Relapsed/refractory AL amyloidosis

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Study Phase	Phase 1/2
Purpose of the study	- Phase 1: Evaluate the safety of linvoseltamab and determine recommended Phase 2 dose - Phase 2: Evaluate the safety and efficacy of linvoseltamab
Primary endpoint	- Phase 1: Evaluate the safety of linvoseltamab and determine recommended Phase 2 dose - Phase 2: Evaluate the safety and efficacy of linvoseltamab
Key eligibility criteria	- Measurable disease (serum difference between involved and uninvolved free light chains (dFLC) concentration) - Patients with at least 1 prior line of therapy and still requires further treatment - NT-proBNP ≤8500 ng/L
Number of patients	220
Study Drug	linvoseltamab
Chance of receiving study drug?	All patients will receive study drug
How long?	~3 years

Recruiting LINKER-AL2 Countries (as of 4/14/25)

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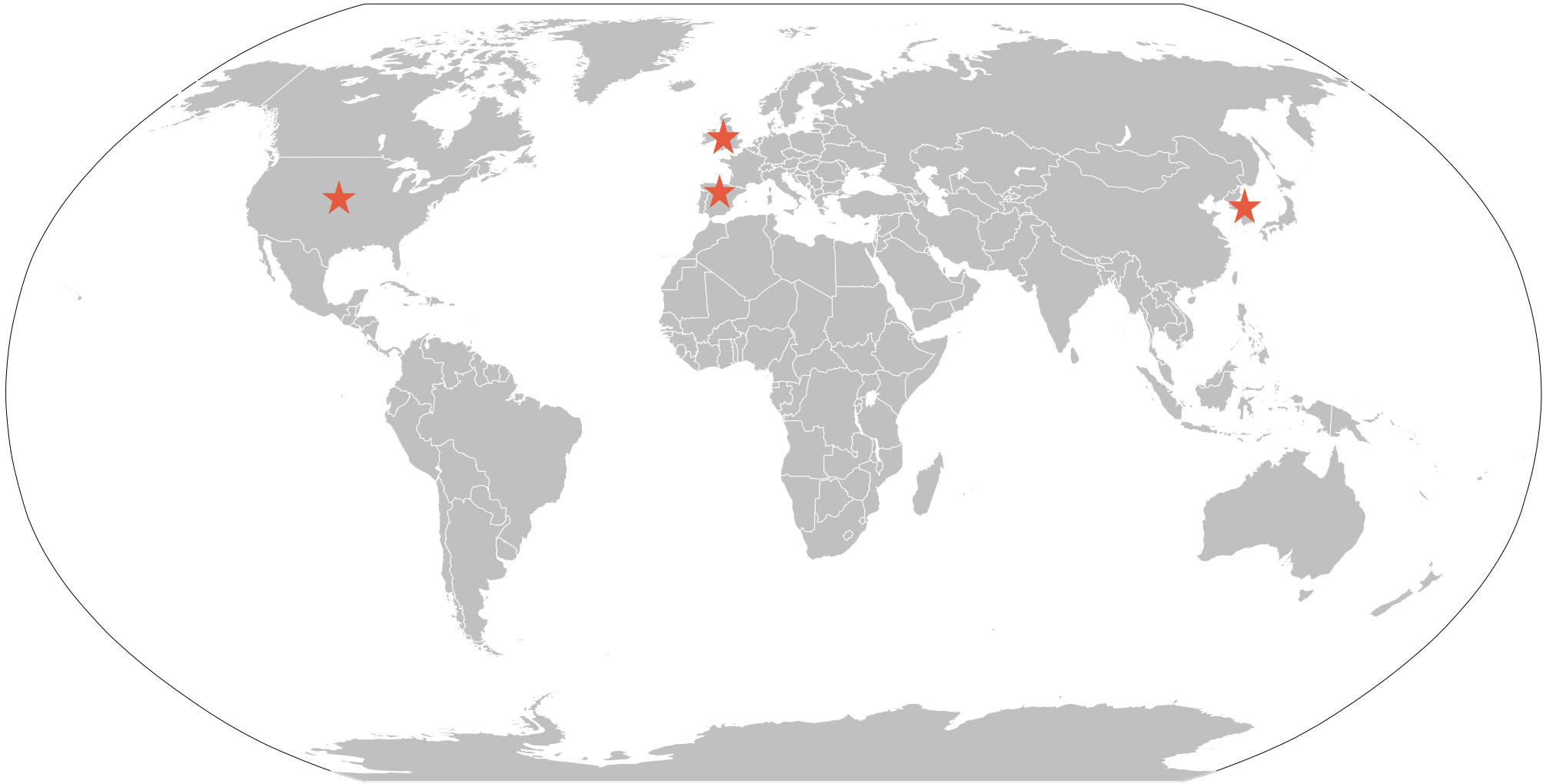

Recruiting LINKER-AL2 Centers (as of 4/14/25)

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Recruiting Centers:

- **California-** Duarte
- **Michigan**- Detroit
- **New York-** Buffalo
- **Texas**- Houston

ETENTAMIG (ABBV-383) study (BCMA-CD3 bispecific antibody)

Relapsed/refractory AL amyloidosis

Amyloidosis Research Consortium

Study Phase	Phase 1b
Purpose of the study	Safety evaluation and preliminary activity
Primary endpoint	Dose limiting toxicities and recommended dose of etentamig monotherapy in AL amyloidosis (Secondary: preliminary activity of Etentamig monotherapy in AL amyloidosis)
Key eligibility criteria	• Patients with at least 1 prior therapy that includes prior proteosome inhibitor and anti-CD38 • At least one organ historically involved • Measurable disease (difference between involved and uninvolved free light chains (dFLC)) >= 50 mg/L • Must not have other non-AL amyloid disease, plasma cell leukemia, multiple myeloma, Waldenstrom's macroglobulinemia
Number of patients	Approximately 76 patients
Study Drug	Infusions of etentamig every 4 weeks
Chance of receiving study drug?	All patients will receive study drug
How long?	Up to 2 years

Recruiting Etentamig Countries (as of 4/14/25)

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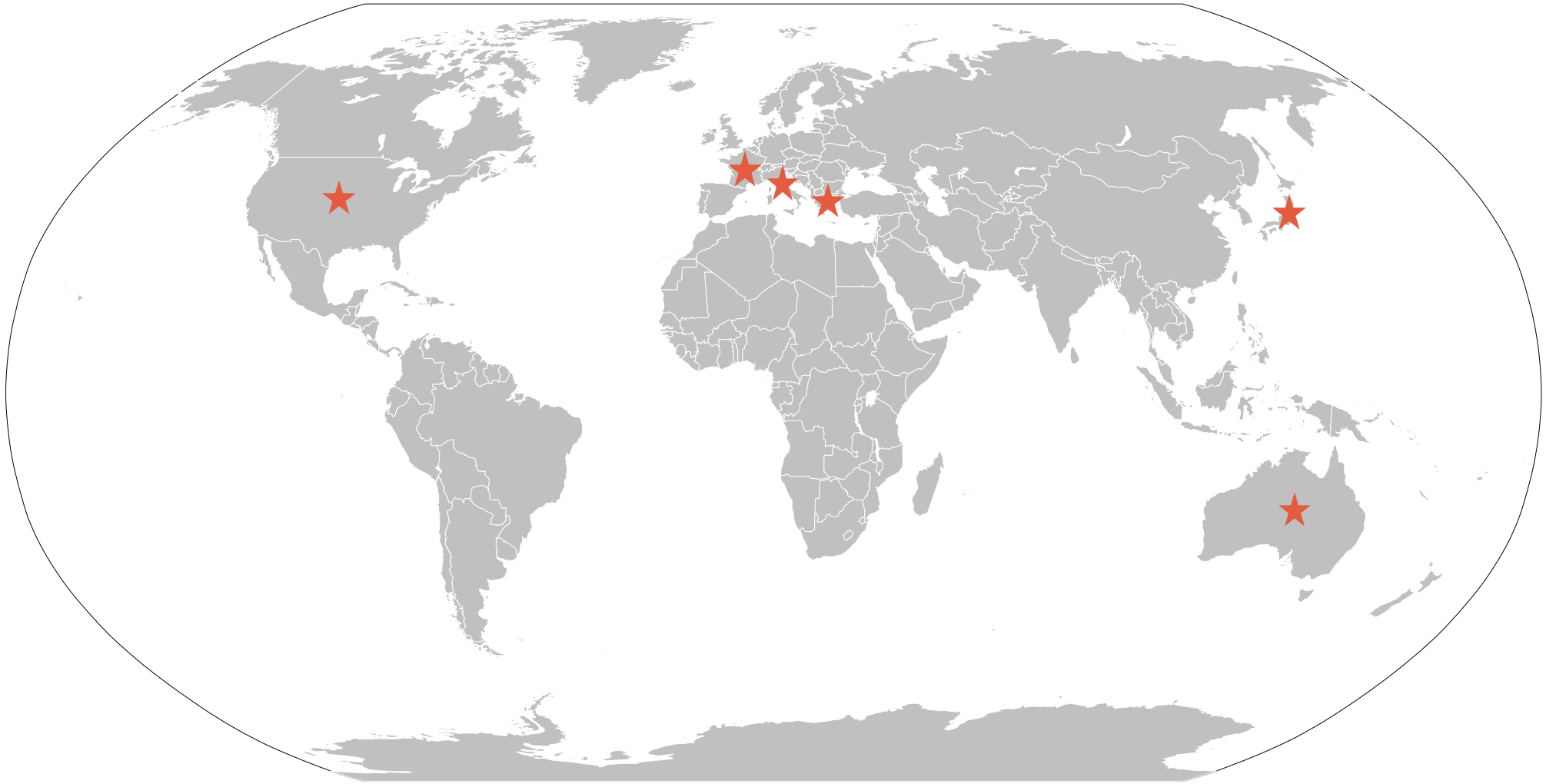

Recruiting Etentamig Centers (as of 4/14/25)

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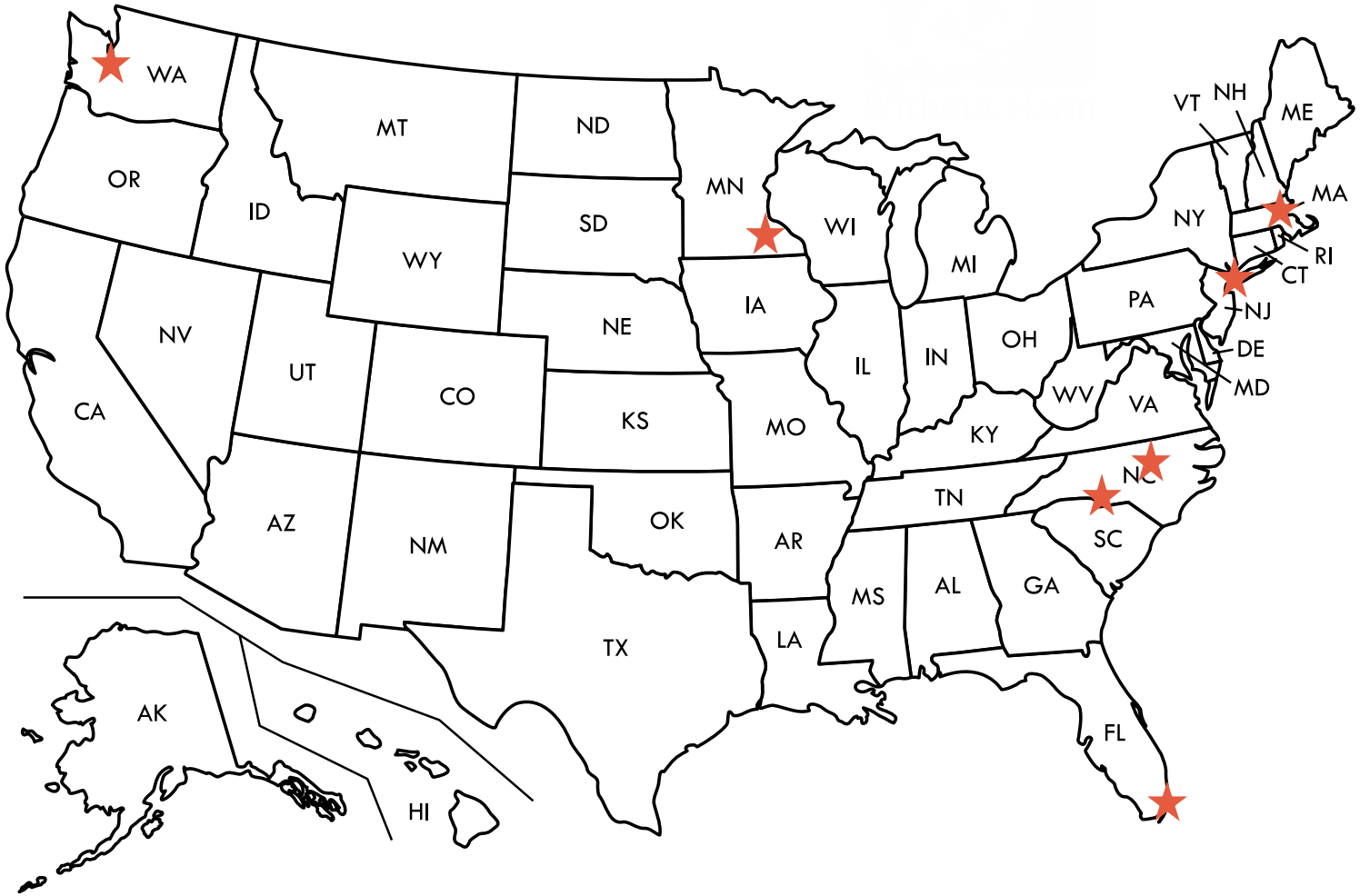

Recruiting Centers:

- **Florida-** Miami
- **Massachusetts-** Boston
- **Minnesota-** Rochester
- **New York-** New York (2 centers)
- **North Carolina-** Charlotte, Winston-Salem
- **Washington-** Seattle

NEXICART-2 (NXC-201; BCMA-targeted investigational chimeric antigen receptor T (CAR-T) cell therapy)

Relapsed or refractory AL amyloidosis

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Study Phase	Phase 1b
Purpose of the study	Measure the safety and efficacy NXC-201
Primary endpoint	- Number of patients with adverse events - Confirm the maximum tolerated dose and recommended phase 2 dose
Key eligibility criteria	- ≥1 line of therapy with a CD38 monoclonal antibody and a proteosome inhibitor and not be in VGPR or CR at the time of inclusion. - Measurable disease (difference between involved and uninvolved free light chains (dFLC)) >20 mg/L with an abnormal kappa:lambda ratio - Symptomatic organ involvement (heart, kidney, liver/GI tract, peripheral nervous system)
Number of patients	40
Study Drug	Single infusion following leukopharesis and lymphodepletion
Chance of receiving study drug?	All patients will receive NXC-201
How long?	2 years

Recruiting NEXICART-2 Centers (as of 4/14/25)

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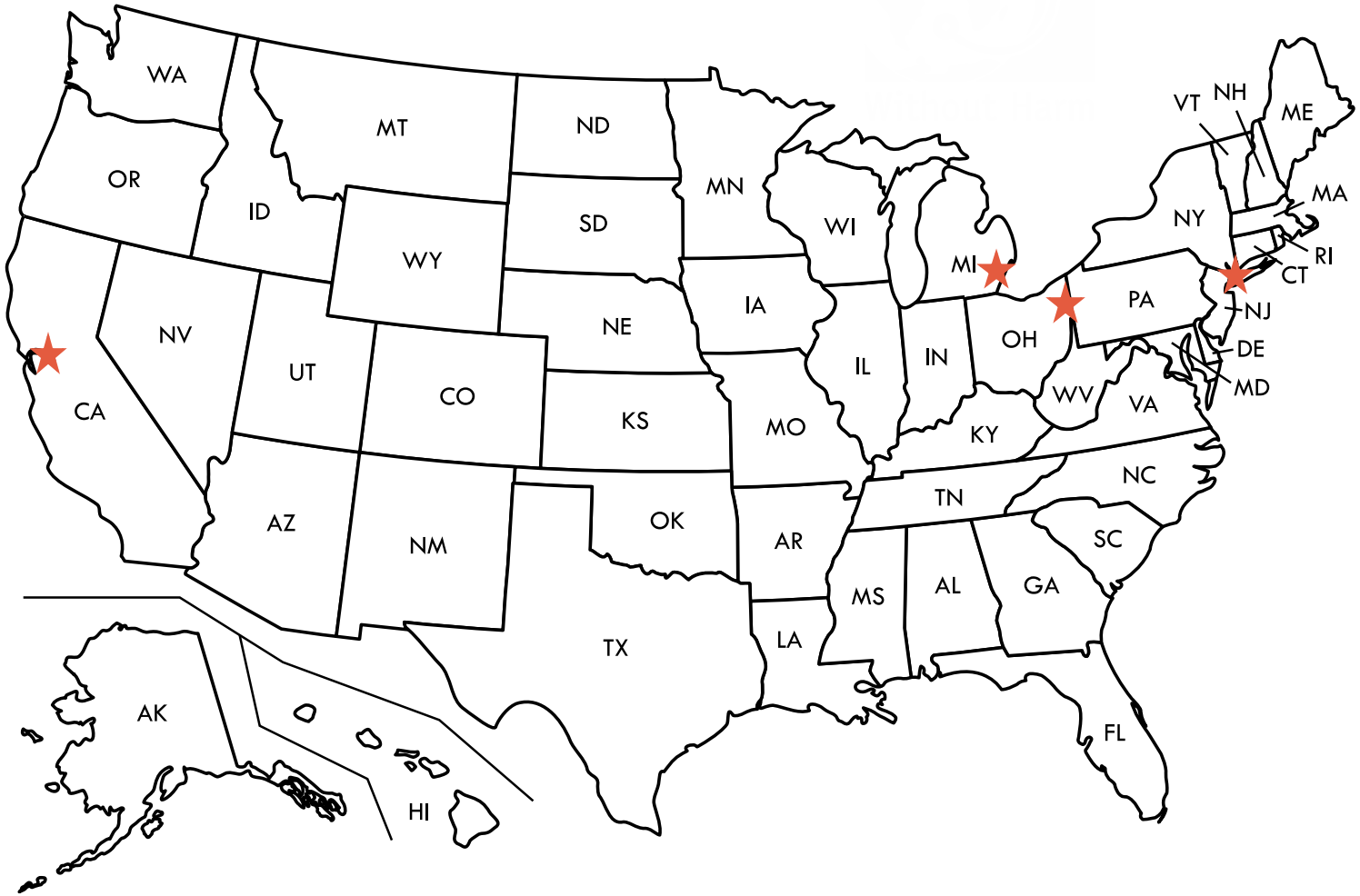

Recruiting Centers:

- **California-** Sacramento
- **Michigan-** Detroit
- **New York-** New York
- **Ohio**- Cleveland

AFFIRM-AL (birtamimab; anti-amyloid antibody)

Newly diagnosed AL amyloidosis

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Study Phase	Phase 3
Purpose of the study	Measure the efficacy and safety of birtamimab plus chemotherapy in adult patients with AL amyloidosis
Primary endpoint	Assess whether treatment with birtamimab reduces the risk of death
Key eligibility criteria	- Newly diagnosed (no prior treatment) - Mayo Stage IV
Number of patients	220
Study Drug	Infusions of birtamimab every 4 weeks
Chance of receiving study drug?	2/3 (67% chance) will receive birtamimab and standard of care 1/3 (33% chance) will receive placebo and standard of care
How long?	2.5-3 years

Recruiting AFFIRM-AL Countries (as of 4/14/25)

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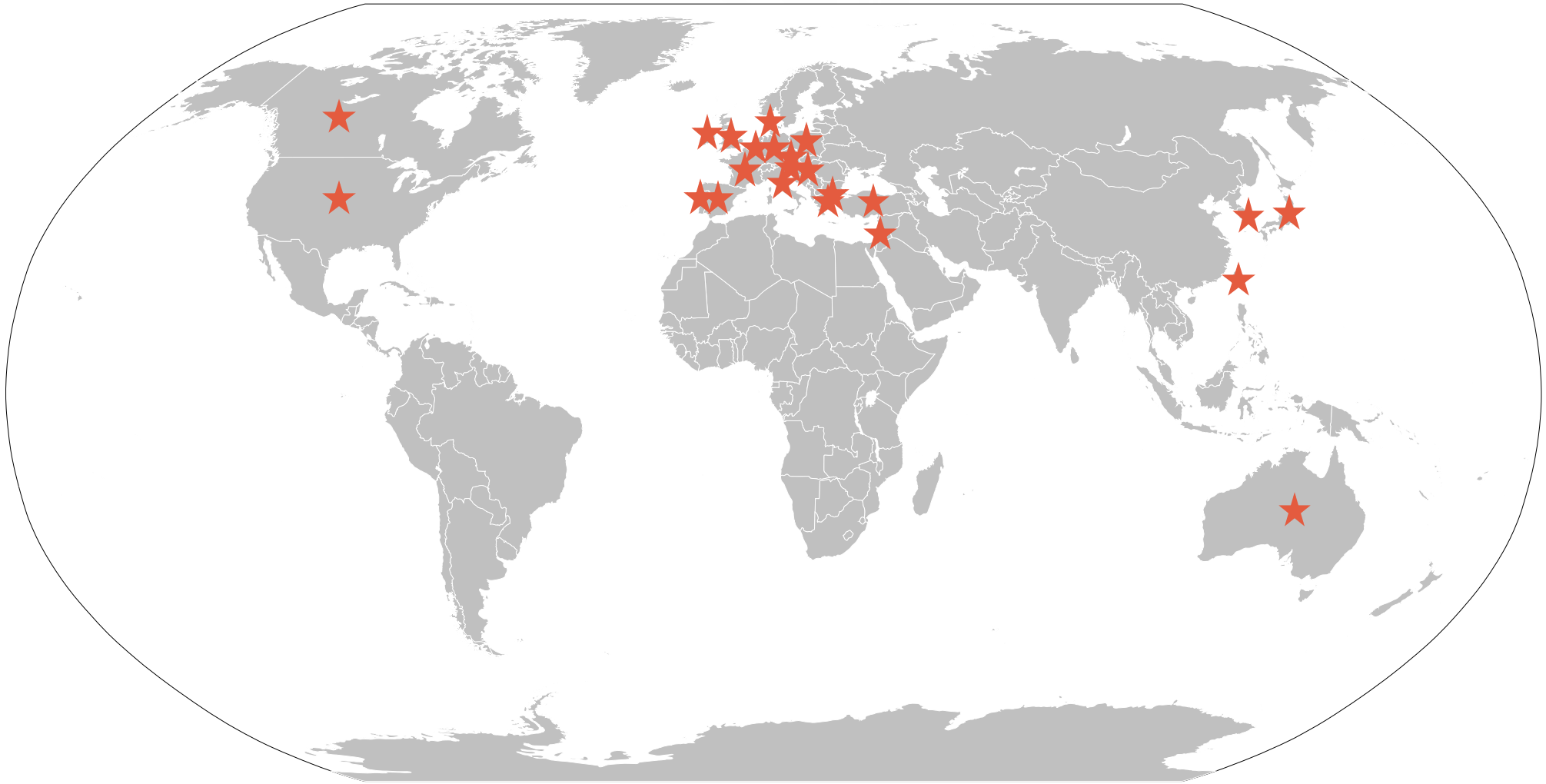

Recruiting AFFIRM-AL Centers (as of 4/14/25)

Amyloidosis Research Consortium

Recruiting Centers:

- **California-** San Francisco
- **Connecticut-** Hartford, North Haven, Trumbull
- **District of Columbia**
- **Florida-** Weston
- **Indiana-** Goshen
- **Maryland-** Bethesda
- **Massachusetts-** Boston (2 centers)
- **Michigan-** Detroit
- **Minnestoa-** Rochester
- **Nebraska-** Omaha
- **New Jersy-** Hackensack
- **New York-** Buffalo, New York (3 centers)
- **North Carolina-** Durham
- **Ohio-** Cleveland, Columbus
- **Tennessee-** Knoxville, Nashville
- **Texas-** Dallas
- **Washington-** Seattle
- **Wisconsin-** Milwaukee

Upcoming Milestones for Novel AL Therapies in 2025

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				Pre-clinical	Phase I	Phase II	Phase III	Commercial
Monoclonal Antibodies	Janssen	Daratumumab (Darzalex)	Approved (accelerated)					
	Sanofi	Isatuximab	Phase 2 IST recruiting					
	BMS	Elotuzumab	Phase 2 IST ongoing					
	GSK	Belantamab mafodotin	Phase 1/2 IST recruiting					
Bispecific Antibodies and Cellular Therapies	Janssen	Teclistimab	ISTs planned					
		JNJ-79635322 (trispecific)	Phase 1 planned					
	Regeneron	Linvoseltamab	Phase 1 recruiting					
	AbbVie	Etentamig (ABBV-383)	Phase 1 recruiting					
	Pfizer	Elrantumab	Phase 1/2 IST recruiting					
	Nexcella	NXC-201	Phase 1 recruiting					
BCL2 Inhibitors	AbbVie	Venetoclax	Phase 1/2 ISTs recruiting					
LC Stabilizer	Protego	TBD	Preclinical					
Anti-Fibril Agents	Prothena	**Birtamimab**	**Phase 3 recruiting, results Q2 2025**					
	Alexion/AZ	**Anselamimab (CAEL-101)**	**Phase 3 results Q2/Q3 2025**					
	Attralus	**AT-02 (pan-amyloid)**	**Phase 1 ongoing**					

Future Development for Novel AL Therapies in 2025

Amyloidosis Research Consortium

				Pre-clinical	Phase I	Phase II	Phase III	Commercial
Monoclonal Antibodies	Janssen	Daratumumab (Darzalex)	Approved (accelerated)					
	Sanofi	Isatuximab	Phase 2 IST recruiting					
	BMS	Elotuzumab	Phase 2 IST ongoing					
	GSK	Belantamab mafodotin	Phase 1/2 IST recruiting					
Bispecific Antibodies and Cellular Therapies	Janssen	Teclistimab	ISTs planned					
		JNJ-79635322 (trispecific)	Phase 1 planned					
	Regeneron	Linvoseltamab	Phase 1 recruiting					
	AbbVie	Etentamig (ABBV-383)	Phase 1 recruiting					
	Pfizer	Elrantumab	Phase 1/2 IST recruiting					
	Nexcella	NXC-201	Phase 1 recruiting					
BCL2 Inhibitors	AbbVie	Venetoclax	Phase 1/2 ISTs recruiting					
LC Stabilizer	Protego	TBD	Preclinical					
Anti-Fibril Agents	Prothena	Birtamimab	Phase 3 recruiting, results Q2 2025					
	Alexion/AZ	Anselamimab (CAEL-101)	Phase 3 results Q2/Q3 2025					
	Attralus	AT-02 (pan-amyloid)	Phase 1 ongoing					

Other Recruiting and Planned Clinical Trials

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	Investigational Product	Study Name/Description	Clinicaltrials.gov link
Investigator Sponsored and Single Center Trials	Venetoclax	Phase 1 Trial of Venetoclax, MLN9708 (Ixazomib Citrate) and Dexamethasone for the Treatment of Relapsed or Refractory AL Amyloidosis (24 patients, 15 locations)	https://clinicaltrials.gov/study/NCT04847453
		Open-label Phase I/II Trial of Venetoclax-Dexamethasone in Relapsed and/or Refractory t(11;14) AL Amyloidosis (53 patients, MN, NY, WI)	https://clinicaltrials.gov/study/NCT05451771
	Daratumumab	Phase 3 Trial Comparing Dara-VCD Chemotherapy Plus Stem Cell Transplant to Dara-VCD Chemotherapy Alone for People Who Have Newly Diagnosed AL Amyloidosis (338 patients, 35 centers in the US)	https://clinicaltrials.gov/study/NCT06022939
		Phase 2 Trial of Daratumumab, Pomalidomide, and Dexamethasone (DPd) in Relapsed/Refractory AL Amyloidosis Patients Previously Exposed to Daratumumab (21 patients, CA, NY, MA, WI)	https://clinicaltrials.gov/study/NCT04270175
		EMILIA: Phase 2 Trial of Daratumumab Maintenance Therapy for Improving Survival in Patients With AL Amyloidosis (96 patients, MN, AZ, FL)	https://clinicaltrials.gov/study/NCT05898646
	Belantamab Mafodotin	Phase 1/2a Study of Belantamab Mafodotin in Relapsed or Refractory AL Amyloidosis (37 patients, TX, CA, MA, MN)	https://clinicaltrials.gov/study/NCT05145816
	Elranatamab	A Phase I/II, Open Label, Study of Elranatamab in Patients With Relapsed or Refractory AL Amyloidosis (49 patients, MA)	https://clinicaltrials.gov/study/NCT06569147
Imaging Trials	I-124 Evuzamitide	REVEAL: Research With I-124 Evuzamitide to Elucidate Cardiac AmyLoidosis	https://clinicaltrials.gov/study/NCT06788535
	[18F]Florbetaben	CArdiag: Efficacy of [18F]Florbetaben PET for Diagnosis of Cardiac AL Amyloidosis	https://clinicaltrials.gov/study/NCT05184088

REVEAL (I-124 Evuzamitide; diagnostic radiotracer)

Suspected cardiac amyloidosis: All types (AL, ATTR, ApoA4, etc.)

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Study Phase	Phase 3
Purpose of the study	To evaluate the effectiveness of I-124 Evuzamitide to diagnose cardiac amyloidosis
Primary endpoint	Sensitivity and specificity of I-124 Evuzamitide to detect cardiac amyloidosis
Key eligibility criteria	Inclusion: Patients with suspected cardiac amyloidosis, including those with positive amyloid from carpal tunnel surgery or spinal laminectomy as long as no other organs have been identified Exclusion: Previously diagnosed with systemic amyloidosis; EGFR <15
Number of patients	Up to 200
Study Drug	Single intravenous (into a vein) infusion
Chance of receiving study drug?	100%; All participants will receive I-124 Evuzamitide
How long?	60 days, 3 in-person visits required

REVEAL Centers (as of 4/14/25)

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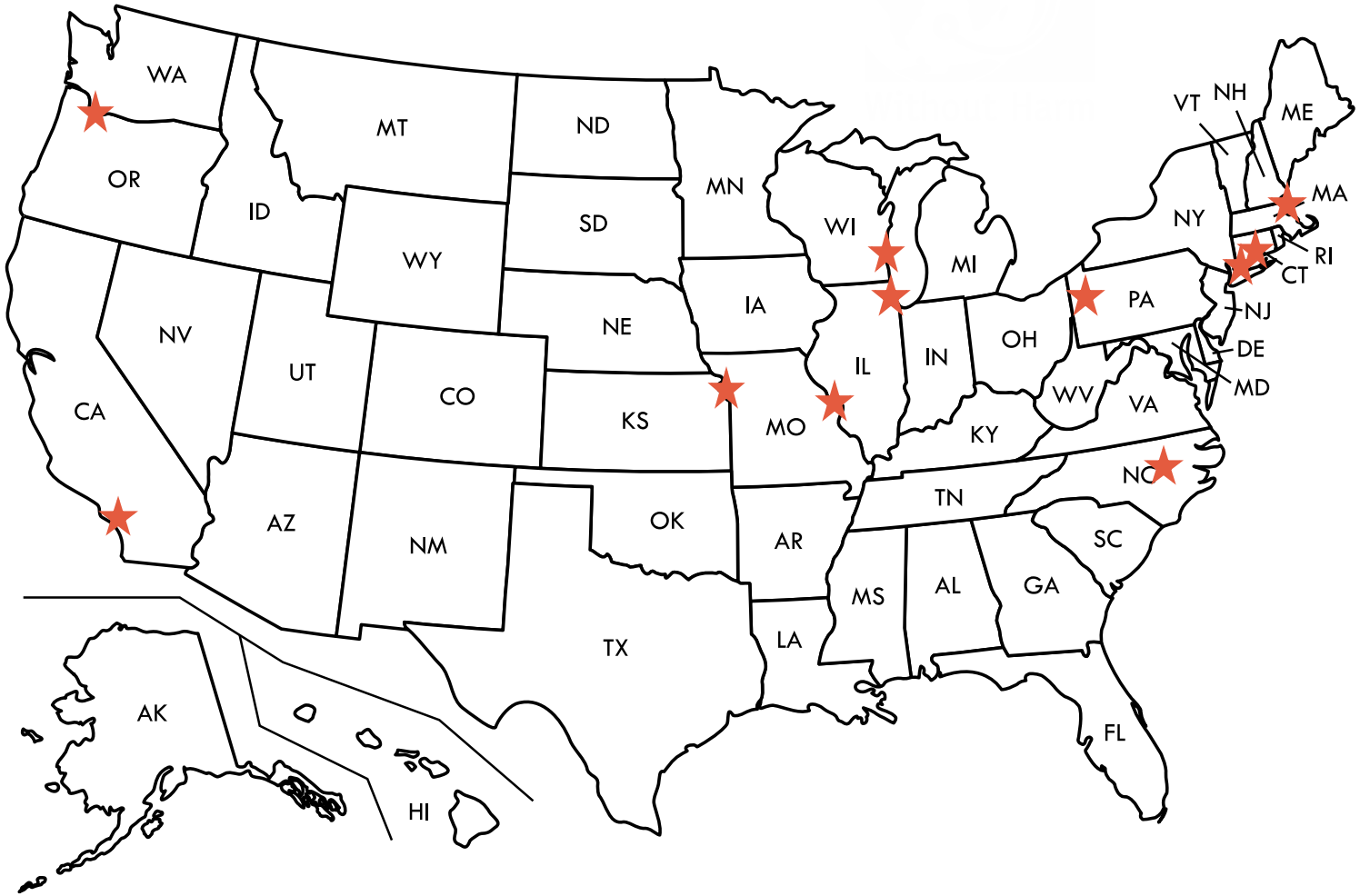

Planned Centers:

- California- Duarte
- Connecticut- New Haven
- Illinois- Chicago (2 centers)
- **Massachusetts- Boston**
- Missouri- Kansas City, St. Louis
- New York- New York
- North Carolina- Durham
- Oregon- Portland
- Pennsylvania- Pittsburgh
- Wisconsin- Milwaukee

CArdiag ([18F]Florbetaben; diagnostic radiotracer)

Suspected cardiac amyloidosis: AL and ATTR amyloidosis)

Amyloidosis Research Consortium

Study Phase	Phase 3
Purpose of the study	To evaluate the efficacy and safety of [18F]Florbetaben positron emission tomography (PET) imaging to diagnose cardiac AL amyloidosis - Additional goals of the study are the differentiation between AL and ATTR cardiac disease
Primary endpoint	Sensitivity and specificity of [18F]Florbetaben to detect cardiac amyloidosis
Key eligibility criteria	Patients being considered for a possible diagnosis of cardiac amyloidosis with a planned diagnostic procedure to establish diagnosis and cardiac involvement
Number of patients	200
Study Drug	Single intravenous (into a vein) infusion
Chance of receiving study drug?	100%; All participants will receive [18F]Florbetaben
How long?	12 weeks

Recruiting Global CArdiag Countries (as of 4/14/25)

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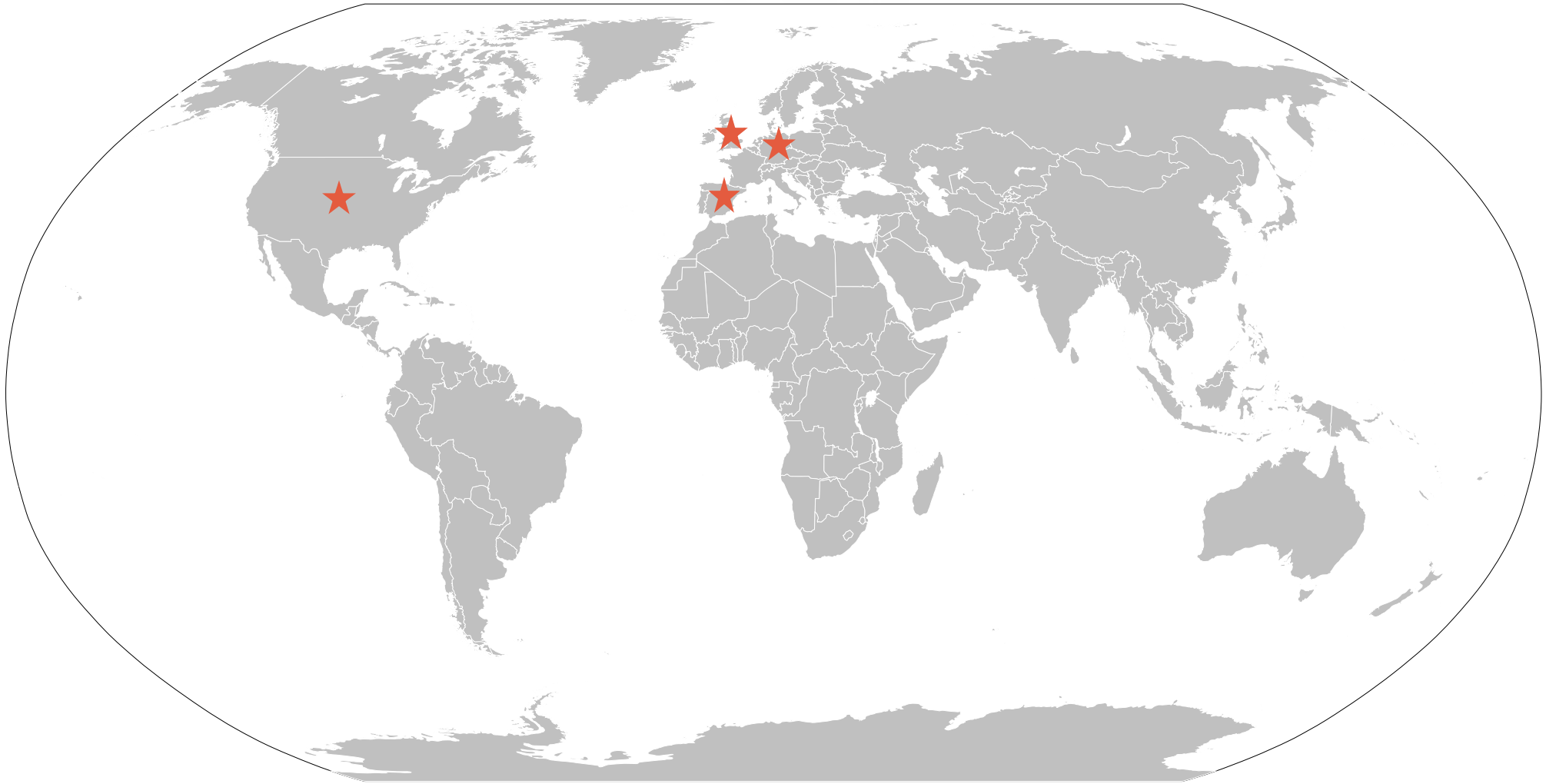

Recruiting CArdiag US Centers (as of 1/15/25)

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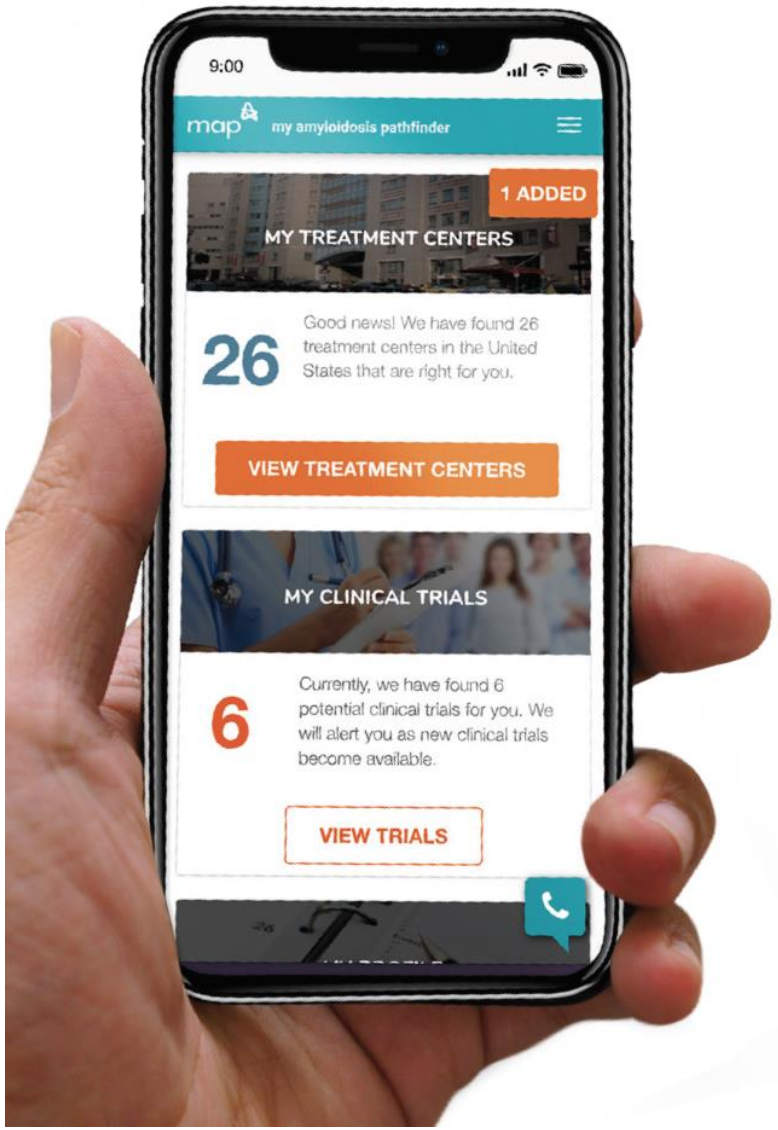
Recruiting Centers:

- **Kansas-** Kansas City
- **Pennsylvania-** Philadelphia

How to find clinical trials

- You can find and stay informed of clinical trials a few different ways:
  - Clinicaltrials.gov
  - Talk to your healthcare provider
  - Follow patient organizations like ARC, ASG, country specific groups, etc.
  - Sign up for My Amyloidosis Pathfinder (MAP)



Discover Personalized Treatment Centers & Clinical Trials for Your Amyloidosis

myamyloidosispathfinder.org

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