ARC TALKS
WEBINAR SERIES

AL Amyloidosis Clinical Trials

November 5 | 12pm - 1pm ET

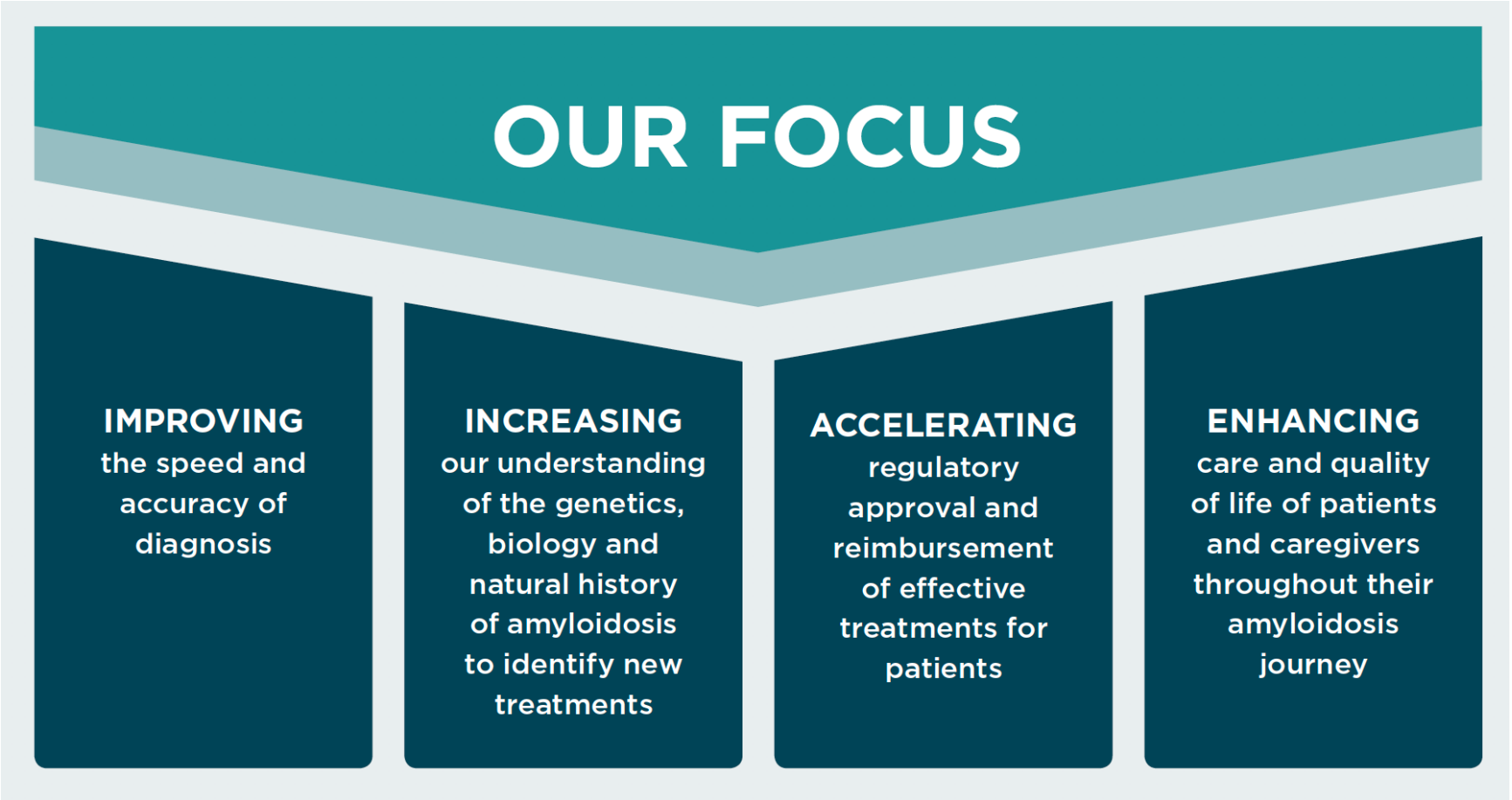
Kristen Hsu

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



ARC Talks Supported By

Amyloidosis Research Consortium

Before We Begin

Amyloidosis Research Consortium

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).

AL Amyloidosis Booklets

arci.org/booklets

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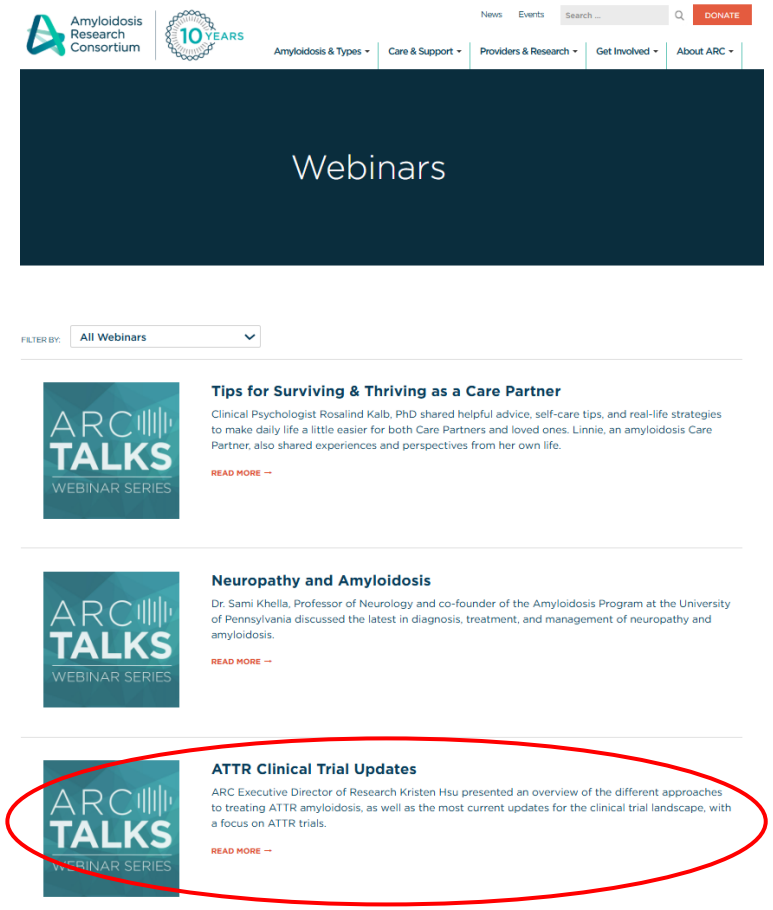
Clinical Trial Updates for the AL Amyloidosis Community

Kristen Hsu, Executive Director of Research

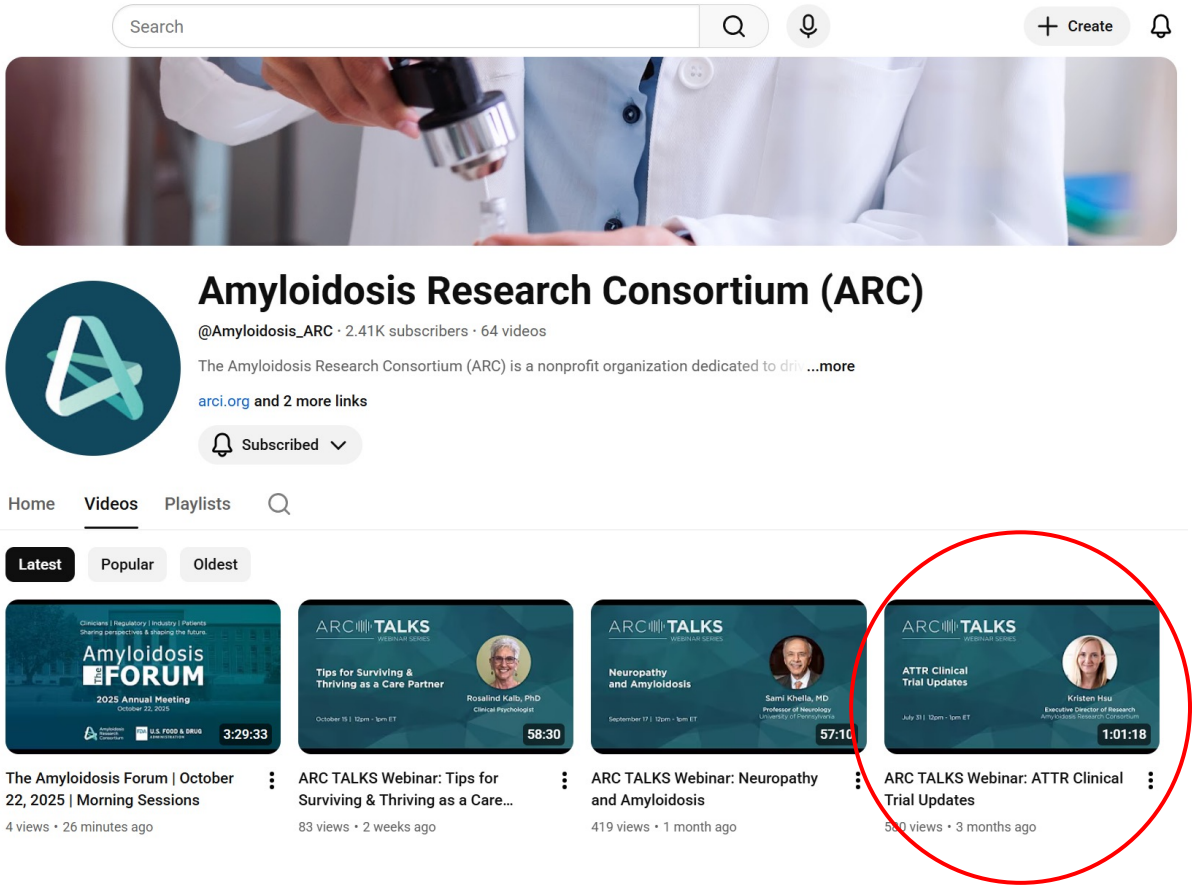
If you are here to learn about ATTR clinical trials…

…check out our July webinar focusing on ATTR amyloidosis clinical trials on our website or YouTube channel.
Our next ATTR amyloidosis clinical trials webinar is planned for early 2026

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



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



What is a Clinical Trial?

- 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

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

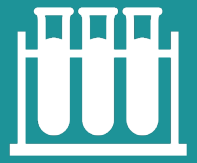
Phase 1	Phase 2	Phase 3	Phase 4
Determines a safe dose of the treatment under study (study drug) and monitors how the new treatment affects the human body (i.e. how the drug is broken down and excreted by the body).	Gather preliminary data on whether the new treatment works in people wohave a certain 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?

- 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?

- 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

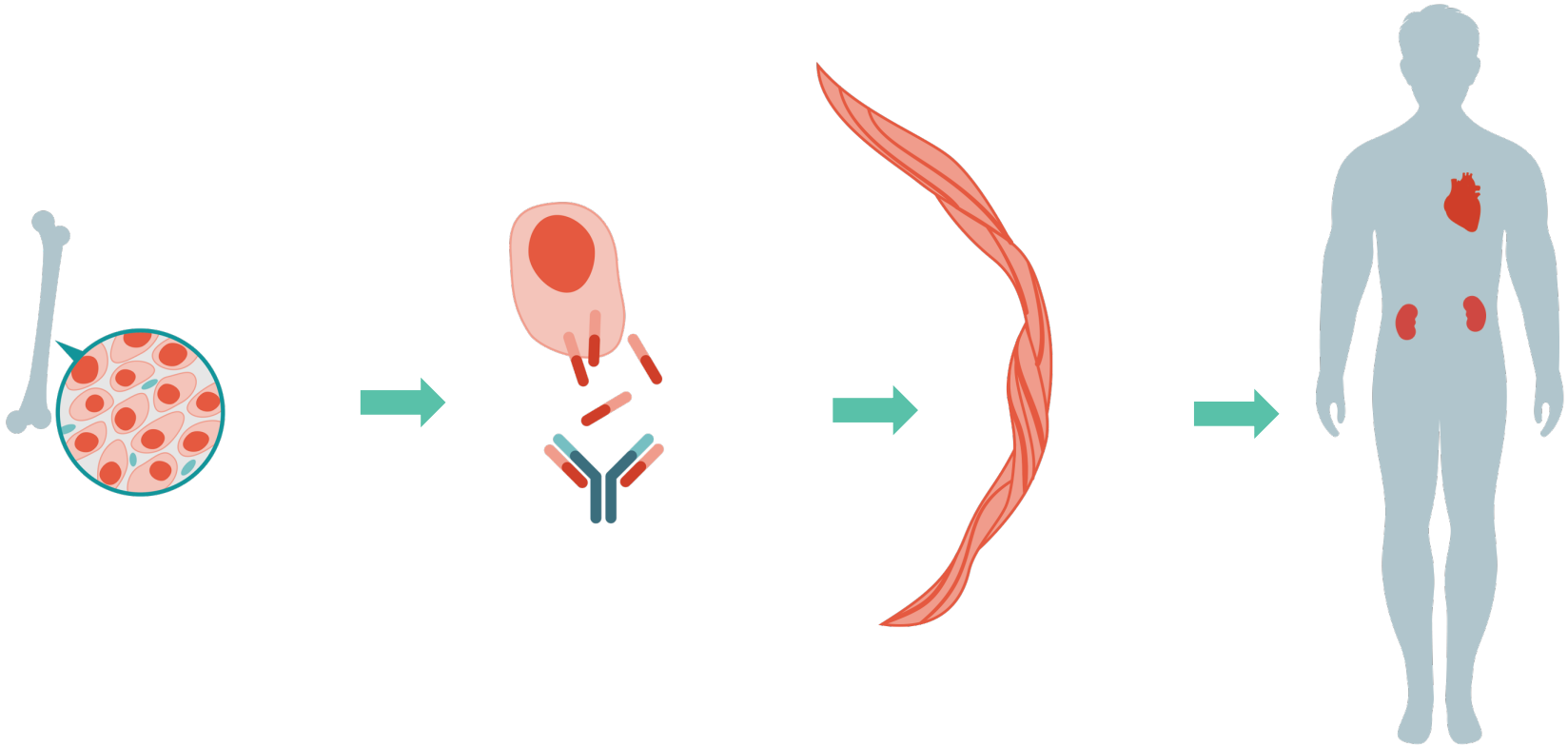
Potential Risks

- 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

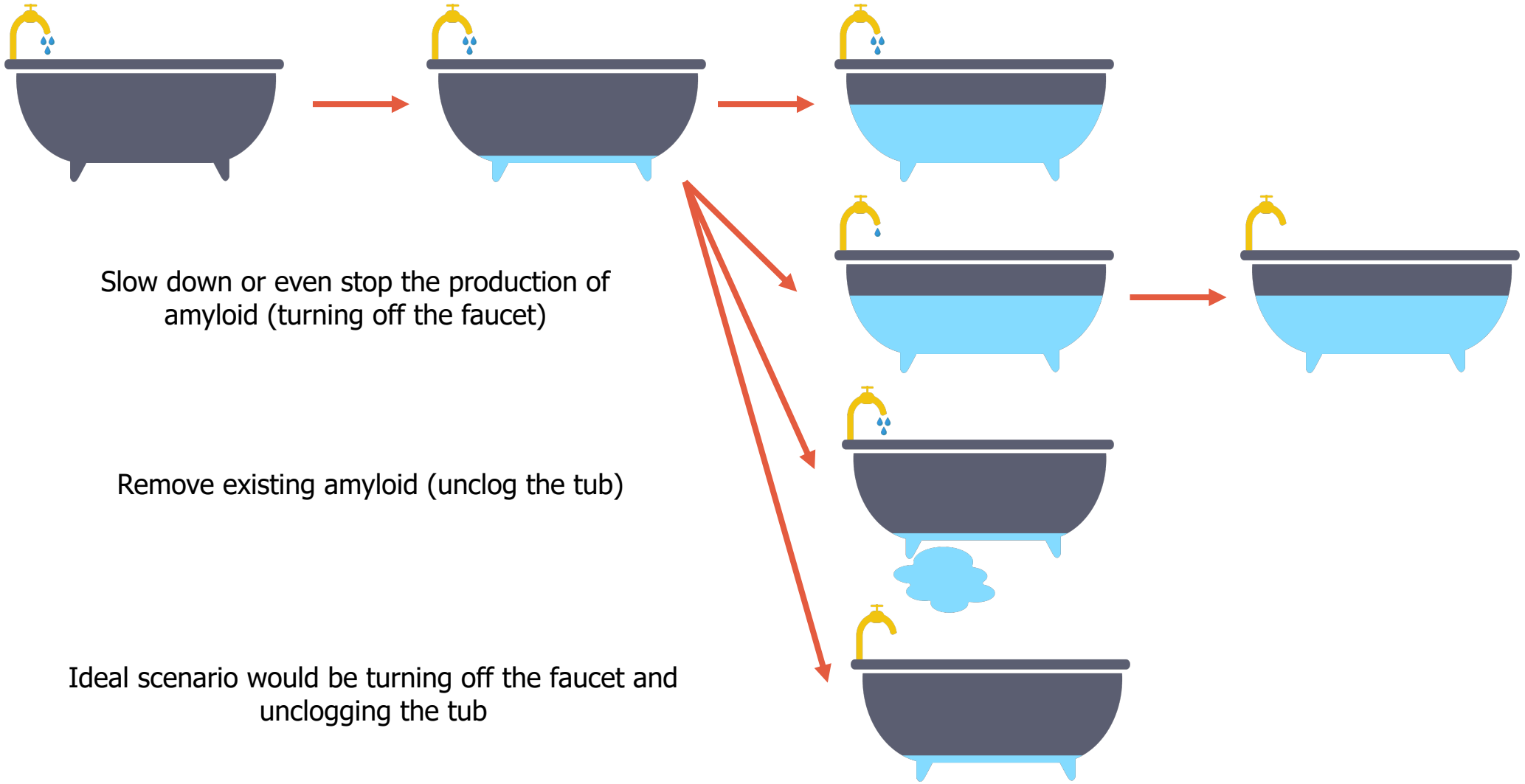
- Potential benefits and risks should be discussed carefully with study doctors and their teams.

AL Amyloidosis Clinical trials

Investigative approaches to treating AL Amyloidosis….



...are like treating a clogged bathtub



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

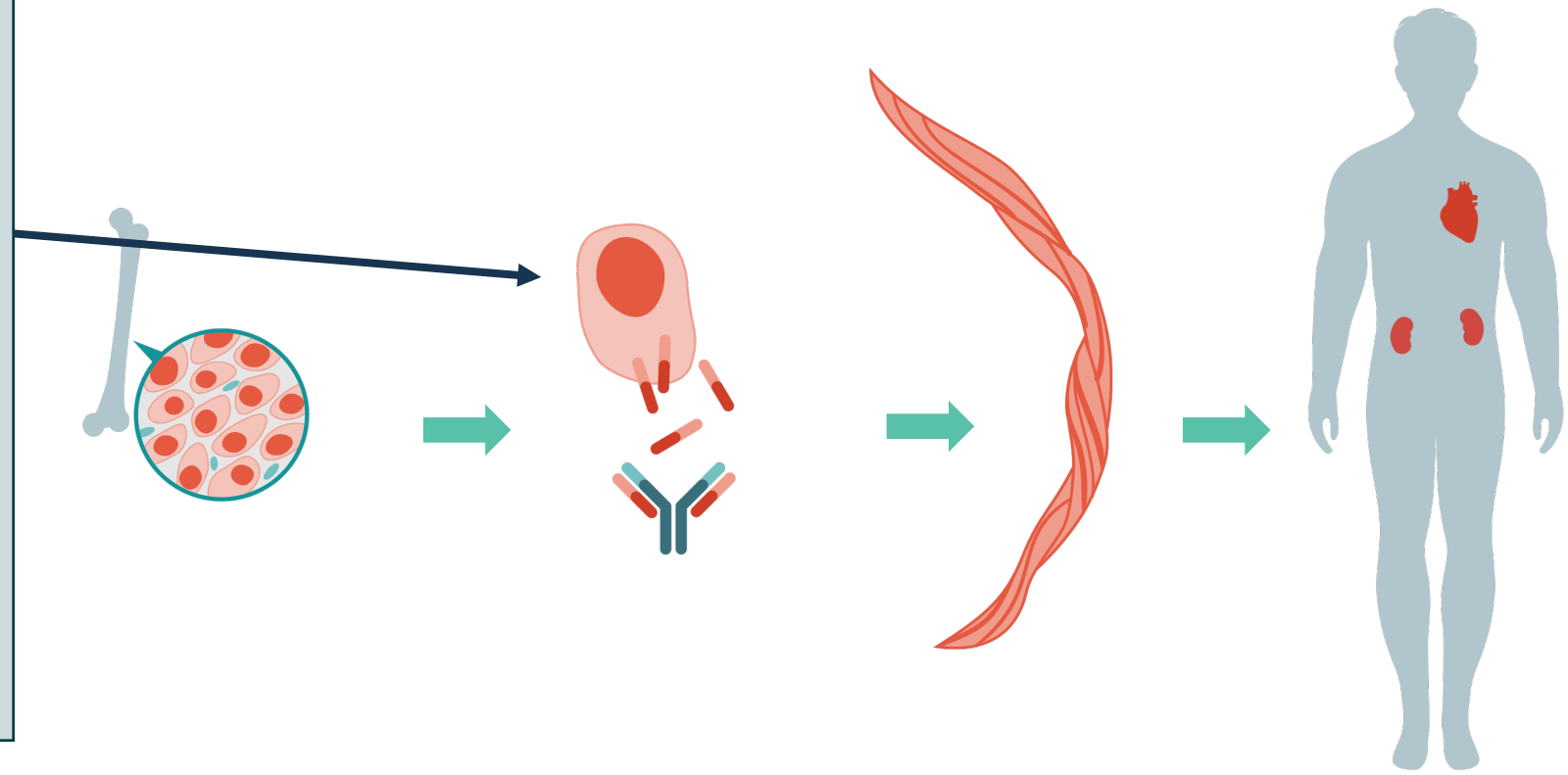
Remove existing amyloid (unclog the tub)

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

Investigative Approaches to Treat AL Amyloidosis

Amyloidosis Research Consortium

Anti-plasma cell therapies



Investigative Approaches to Treat AL Amyloidosis

Anti-plasma cell therapies

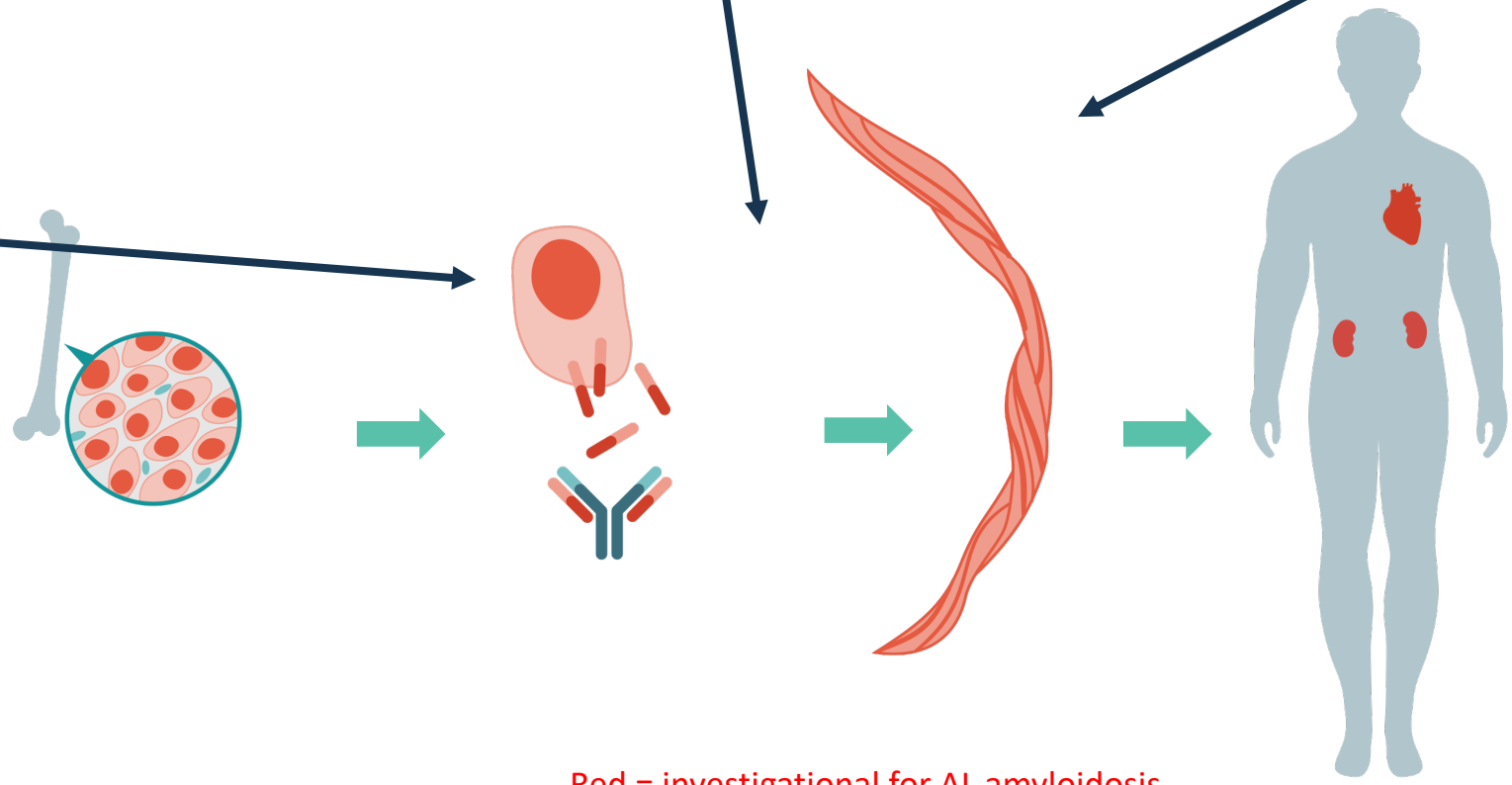
- Monoclonal antibodies
  - Daratumumab (DARZALEX)
  - Isatuximab (SARCLISA)
  - Elotuzumab (EMPLICITI)
  - Belantamab mafodotin (BLENREP)
- BCL-2 Inhibitors
  - Venetoclax (VENCLEXTA)
- Bispecific/Trispecific
  - Teclistamab (TECVAYLI)
  - Ramantamig (JNJ-79635322)
  - Linvoseltamab (LYNOZYFIC)
  - Etentamig (ABBV-383)
  - Elrantamab (ELREXFIO)
- Cellular Therapies
  - AZD0120
  - NXC-201

Light chain Stabilizers

- PROT-001

Anti-Fibril Agents

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



Red = investigational for AL amyloidosis

Recruiting Trials 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 status unk					
	GSK	Belantamab mafodotin	Phase 1/2a IST recruiting					
Bispecific/ Trispecific Antibodies	Janssen	Teclistamab	Phase 2 planned					
		Ramantamig (JNJ-79635322)	Phase 1 planned					
	Regeneron	Linvoseltamab	Phase 1/2 recruiting					
	AbbVie	Etentamig (ABBV-383)	Phase 1b recruiting					
	Pfizer	Elrantamab	Phase 1/2 IST recruiting					
Cellular Therapies	Nexcella	NXC-201	Phase 1b/2 recruiting					
	Alexion/AZ	AZD0120	Phase 1b/2 recruiting					
BCL2 Inhibitors	AbbVie	Venetoclax	Phase 1/2 ISTs recruiting					
LC Stabilizer	Protego	PROT-001	Phase 2/3 planned 2026					
Anti-Fibril Agents	~~Prothena~~	~~Birtamimab~~	~~Discontinued~~					
	Alexion/AZ	Anselamimab (CAEL-101)	P3 primary endpoints not met					
	Attralus	AT-02	Phase 2 (renal) recruiting					

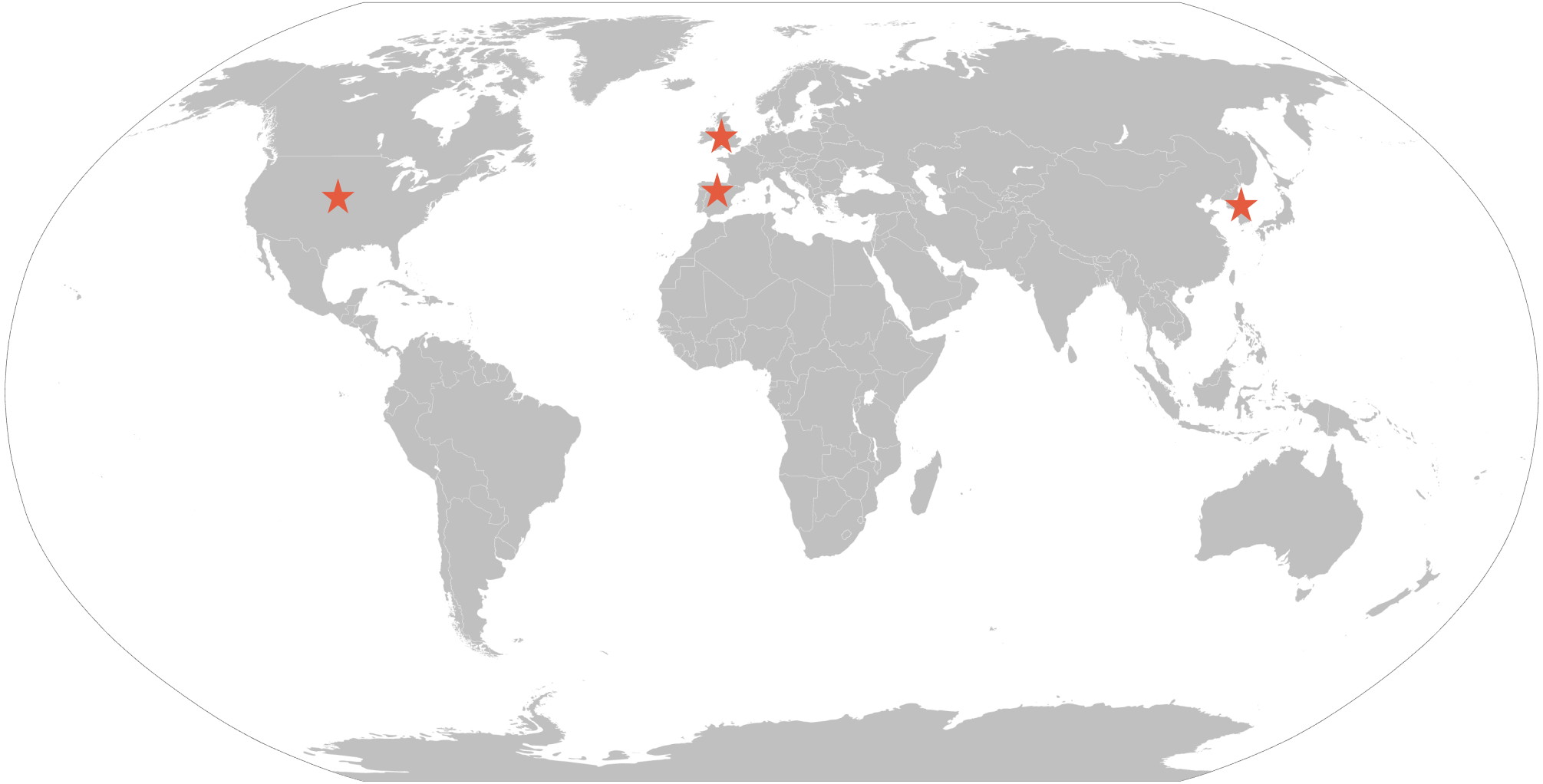
LINKER-AL2 (linvoseltamab; BCMA-CD3 bispecific antibody)

Relapsed/refractory AL amyloidosis

Amyloidosis Research Consortium

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 11/05/25)



Recruiting LINKER-AL2 Centers (as of 11/05/25)

Recruiting Centers:

- **California-** Duarte
- **Colorado**- Denver
- **Michigan**- Detroit
- **New York-** Buffalo
- **Texas**- Houston
- **Tennessee**- Nashville

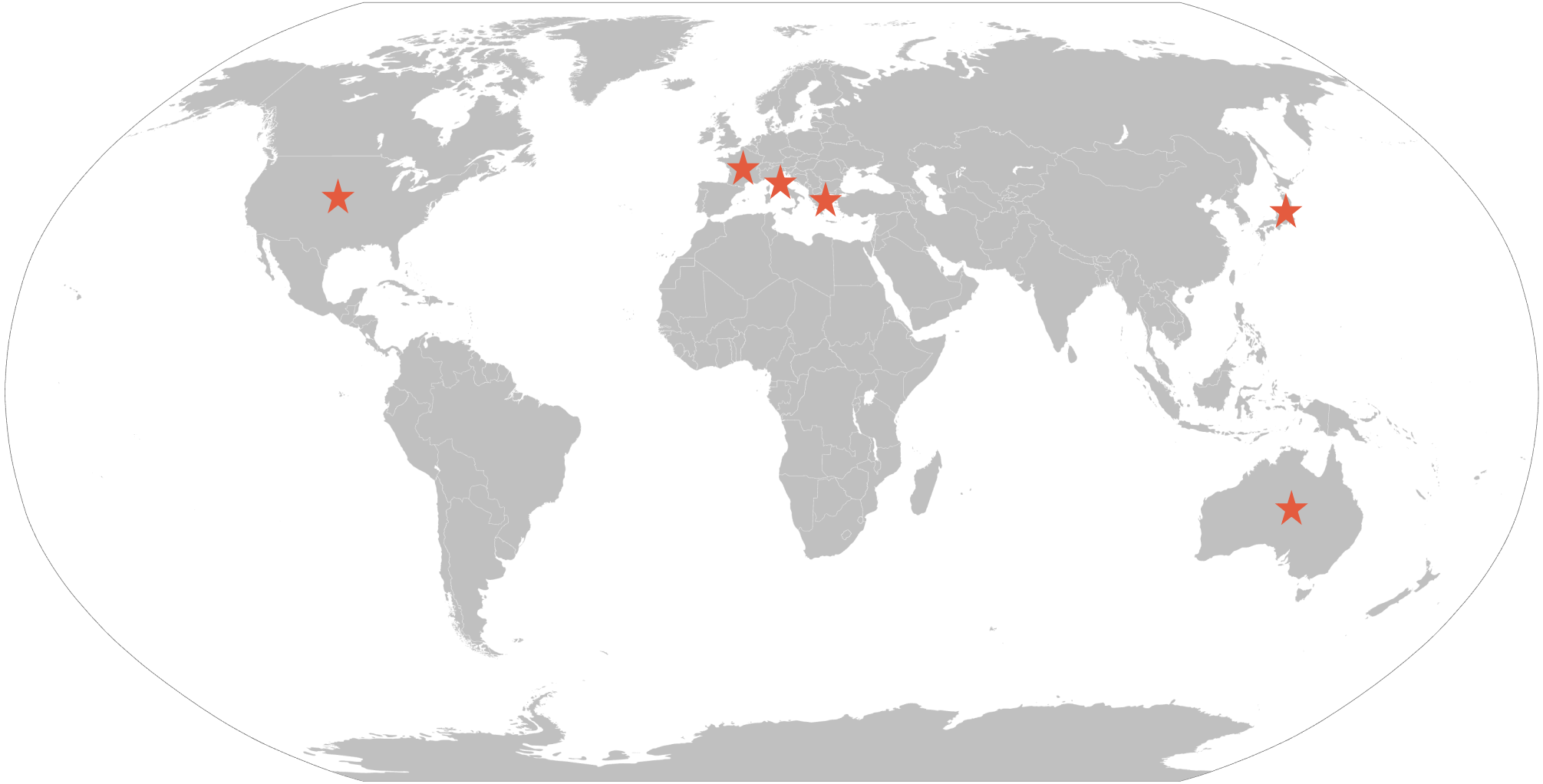
ETENTAMIG (ABBV-383) study (BCMA-CD3 bispecific antibody)

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 11/05/25)



Recruiting Etentamig Centers (as of 11/05/25)

Recruiting Centers:

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

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

Relapsed or refractory AL amyloidosis

Amyloidosis Research Consortium

Study Phase	Phase 1b/ Phase 2 Expansion
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 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. - No prior CAR-T therapy or BCMA targeted therapy - Measurable disease (difference between involved and uninvolved free light chains (dFLC) >20 mg/L with an abnormal kappa:lambda ratio) - ECOG performance status: 0-2 (up and about more than half the day but not fully able to carry out normal activities) - Symptomatic organ involvement
Number of patients	40
Study Drug	NXC-201; 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 11/05/25)

Recruiting Centers:

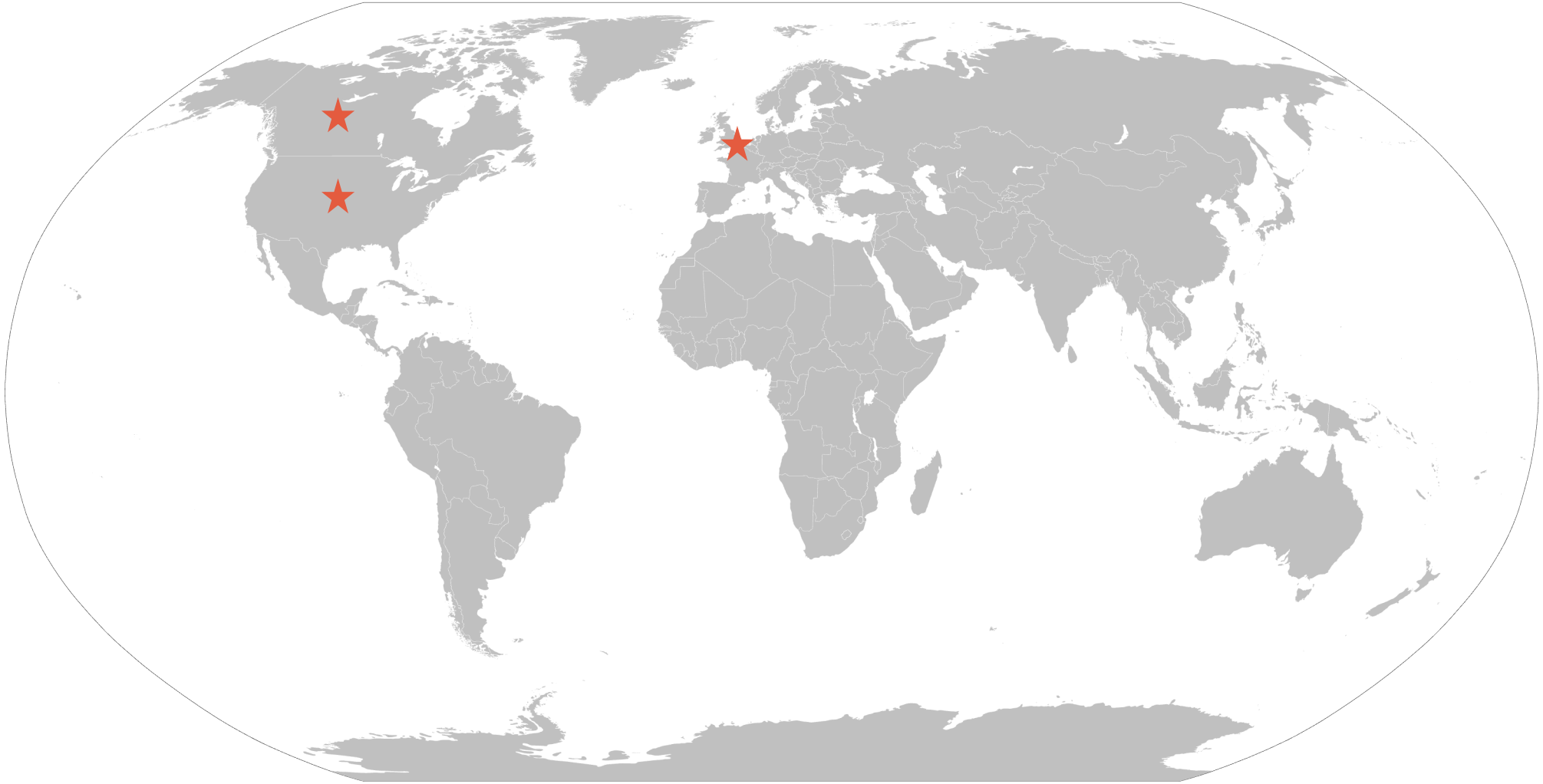
- **California-** Berkeley
  Duarte
  Los Angeles
  Sacremento
  Stanford
- **Georgia-** Atlanta
- **Kansas-** Fairway
- **Massachusetts-** Boston
- **Michigan**- Detroit
- **Minnesota**- Minneapolis
- **Missouri**-St. Louis
- **New York-** New York
- **Ohio**- Cleveland
  Cincinnati
- **Tennessee**- Memphis
- **Utah**- Salt Lake City
- **Washington**- Seattle

ALACRITY (AZD0120; CD19/BCMA chimeric antigen receptor T (CAR-T) cell therapy)

Relapsed/refractory AL amyloidosis

Study Phase	Phase 1b/2
Purpose of the study	Evaluate the Safety and Tolerability of AZD0120
Primary endpoint	Phase 1b: Number of participants with incidence and severity or treatment emergent adverse events Phase 2: Proportion of participants experiencing a complete response
Key eligibility criteria	• At least 1 line of anti-plasma cell-directed therapy with need for additional therapy. • At least 1 organ currently or previously affected • Measurable hematological disease (difference between involved and uninvolved free light chains (dFLC)> 20mg/L or serum M-protein > 5g/L) • ECOG performance status: 0-1 (relatively active and healthy) • No prior CAR-T, no prior BCMA-targeting therapy, no prior treatment within last 6 months with bispecific or trispecifics
Number of patients	91
Study Drug	AZD0120; Single infusion following leukopharesis and lymphodepletion
Chance of receiving study drug?	All patients will receive AZD0120
How long?	Minimum of 6 months

Recruiting ALACRITY Countries (as of 11/05/25)



Recruiting ALACRITY Centers (as of 11/05/25)

Recruiting Centers:

- **New York-** New York

AT-02 (anti-fibril depleter)
AL amyloidosis with kidney disease

Study Phase	Phase 2
Purpose of the study	Evaluate the Long-term Safety and Tolerability of AT-02
Primary endpoint	Incidence, frequency, and severity or treatment emergent adverse events Safety and tolerability of AT-02 through lab results

Key eligibility criteria	• Must have already received plasma cell directed therapy achieved a very good partial response (VGPR) or complete response (CR); may be on daratumumab maintenance therapy
	• At least 6 months from that hematologic response.
	• Must meet one or both of these:
	  • Kidney function test (eGFR) between 20 and 75 mL/min/1.73m^2.
	  • Ongoing protein in the urine that has not improved (urine protein/creatinine ratio not reduced by at least 25% in the past year or since treatment response)

Number of patients	12
Study Drug	AT-02, given as an IV infusion once every 2 weeks, for up to 24 weeks (6 months)
Chance of receiving study drug?	All patients will receive study drug
How long?	At least 6 months

Recruiting AT-02 Centers (as of 11/05/25)

Recruiting Centers:

- **Missouri-** Kansas City
- **Ohio-** Cleveland
- **Oregon-** Portland
- **Pennsylvania-** Philadelphia

Future Development for Novel AL Therapies in 2025

				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 status unk					
	GSK	Belantamab mafodotin	Phase 1/2a IST recruiting					
Bispecific/ Trispecific Antibodies	Janssen	**Teclistamab**	**Phase 2 planned**					
		Ramantamig (JNJ-79635322)	**Phase 1 planned**					
	Regeneron	Linvoseltamab	Phase 1/2 recruiting					
	AbbVie	Etentamig (ABBV-383)	Phase 1b recruiting					
	Pfizer	Elrantamab	Phase 1/2 IST recruiting					
Cellular Therapies	Nexcella	NXC-201	Phase 1b/2 recruiting					
	Alexion/AZ	AZD0120	Phase 1b/2 recruiting					
BCL2 Inhibitors	AbbVie	Venetoclax	Phase 1/2 ISTs recruiting					
LC Stabilizer	Protego	**PROT-001**	**Phase 2/3 planned 2026**					
Anti-Fibril Agents	~~Prothena~~	~~Birtamimab~~	~~Discontinued~~					
	Alexion/AZ	Anselamimab (CAEL-101)	P3 primary endpoints not met					
	Attralus	AT-02	Phase 2 (renal) recruiting					

TECLISTAMAB study (BCMA-CD3 bispecific antibody)

Newly diagnosed AL amyloidosis

Study Phase	Phase 2
Purpose of the study	Assess the effectiveness and safety of teclistamab-daratumumab combination; evaluate whether this combination is able to effectively decrease the level light chains, avoiding organ damage, improving organ function, and prolonging life
Primary endpoint	Hematologic Complete Response (Heme-CR)
Key eligibility criteria	• No prior plasma cell directed therapy • Measurable hematologic disease defined as dFLC≥ 50mg/L or serum M-protein ≥ 5g/L • 1 of more organs involved
Number of patients	25
Study Drug	Teclistamab and Daratumumab (given as subcutaneous (under the skin) injections) - Teclistimab: Step up dosing for 1st week, weekly dosing until Month 1, then monthly dosing through Month 6 - Daratumumab: Weekly for 1st 2 months, then biweekly (every 2 weeks) through Month 6
Chance of receiving study drug?	All patients will receive study drug
How long?	6 months

RAMANTAMIG study (JNJ-79635322; BCMA-GPRC5D-CD3 trispecific antibody)

Previously treated AL amyloidosis

Study Phase	Phase 1
Purpose of the study	Part 1 (dose escalation): identify the recommended phase 2 dose and schedule(s) to be safe for Ramantamig Part 2 (dose expansion): characterize the safety and tolerability of Ramantamig at the selected doses and in disease subgroups
Primary endpoint	Dose limiting toxicities, adverse events, and abnormal lab values
Key eligibility criteria (AL amyloidosis)	• at least 3 cycles of 1 prior line of therapy or a total of at least 2 cycles of 2 or more prior lines of therapy for AL amyloidosis • Measurable hematologic disease defined as dFLC≥ 50mg/L or serum M-protein ≥ 5g/L • 1 of more organs involved • Left ventricular ejection fraction (LVEF) >=45%
Number of patients	180 (mostly multiple myeloma, with smaller group of AL amyloidosis patients)
Study Drug	Ramantamig, given as given as subcutaneous (under the skin) injections
Chance of receiving study drug?	All patients will receive study drug
How long?	Up to 2 Years 5 months

Future Development for Novel AL Therapies in 2025

				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 status unk					
	GSK	Belantamab mafodotin	Phase 1/2a IST recruiting					
Bispecific/ Trispecific Antibodies	Janssen	**Teclistamab**	**Phase 2 planned**					
		Ramantamig (JNJ-79635322)	**Phase 1 planned**					
	Regeneron	Linvoseltamab	Phase 1/2 recruiting					
	AbbVie	Etentamig (ABBV-383)	Phase 1b recruiting					
	Pfizer	Elrantamab	Phase 1/2 IST recruiting					
Cellular Therapies	Nexcella	NXC-201	Phase 1b/2 recruiting					
	Alexion/AZ	AZD0120	Phase 1b/2 recruiting					
BCL2 Inhibitors	AbbVie	Venetoclax	Phase 1/2 ISTs recruiting					
LC Stabilizer	Protego	**PROT-001**	**Phase 2/3 planned 2026**					
Anti-Fibril Agents	~~Prothena~~	~~Birtamimab~~	~~Discontinued~~					
	Alexion/AZ	Anselamimab (CAEL-101)	P3 primary endpoints not met					
	Attralus	AT-02	Phase 2 (renal) recruiting					

Summary of recruiting/upcoming studies by disease status

- Newly Diagnosed
  - Bispecifics: Teclistimab-Daratumuab

- Previously treated or relapsed/refractory
  - Bispecifics/trspecifics: linvoseltamab, ententamig, ramantamig
  - CAR-T: NXC-201, AZD0120
  - Anti-fibrils: AT-02

- Disease status to be confirmed:
  - PROT-001

News and Upcoming Milestones 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 status unk					
	GSK	Belantamab mafodotin	Phase 1/2a IST recruiting					
Bispecific/ Trispecific Antibodies	Janssen	Teclistamab	Phase 2 planned					
		Ramantamig (JNJ-79635322)	Phase 1 planned					
	Regeneron	Linvoseltamab	Phase 1/2 recruiting					
	AbbVie	Etentamig (ABBV-383)	Phase 1b recruiting					
	Pfizer	Elrantamab	Phase 1/2 IST recruiting					
Cellular Therapies	Nexcella	NXC-201	Phase 1b/2 recruiting					
	Alexion/AZ	AZD0120	Phase 1b/2 recruiting					
BCL2 Inhibitors	AbbVie	Venetoclax	Phase 1/2 ISTs recruiting					
LC Stabilizer	Protego	PROT-001	Phase 2/3 planned 2026					
Anti-Fibril Agents	~~Prothena~~	~~Birtamimab~~	~~Discontinued~~					
	Alexion/AZ	Anselamimab (CAEL-101)	P3 primary endpoints not met					
	Attralus	AT-02	Phase 2 (renal) recruiting					

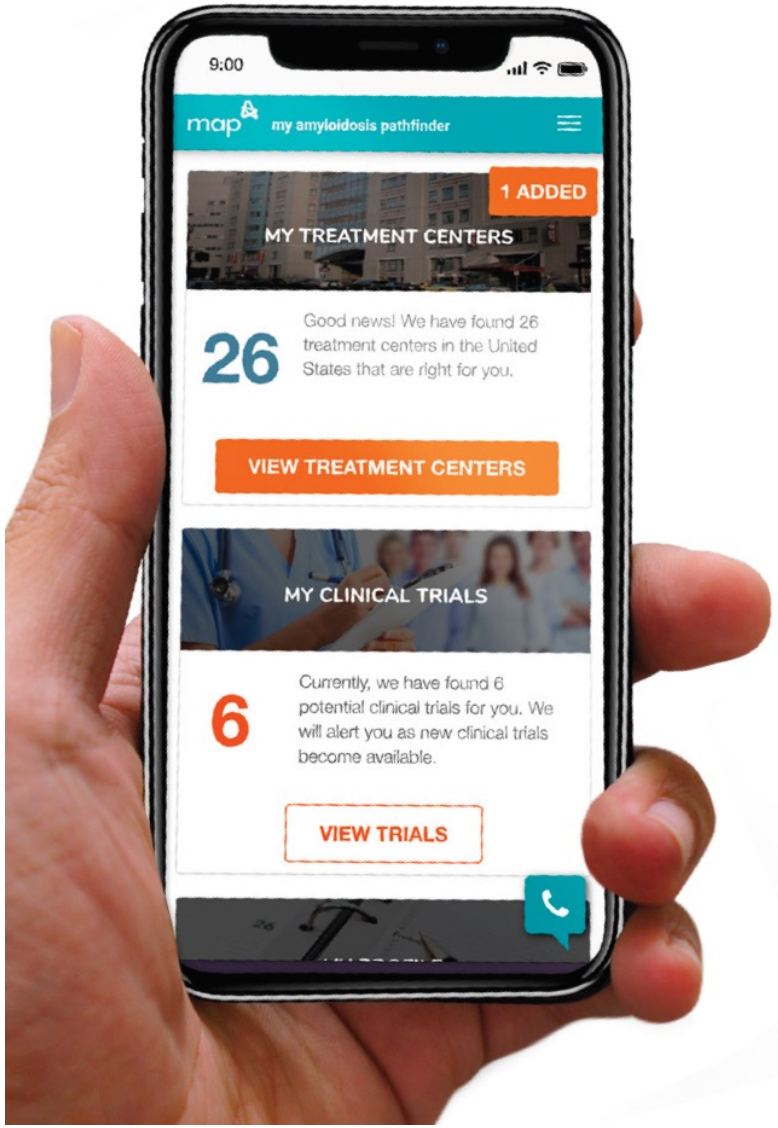
Other Recruiting and Planned Clinical Trials

	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); Dose expansion phase will open soon	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, MA 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
		EMILIA: Phase 2 Trial of Daratumumab Maintenance Therapy for Improving Survival in Patients With AL Amyloidosis (96 patients, MN, AZ)	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

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)

Amyloidosis Research Consortium



Discover Personalized Treatment Centers & Clinical Trials for Your Amyloidosis

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