

Lipoprotein(a) after HORIZON

What the registry shows about the five lead Lp(a)-lowering agents one month after pelacarsen missed its outcome endpoint, and what has to happen before the next hard evidence arrives.

Prepared 6 October 2026 Scope pelacarsen, olpasiran, lepodisiran, zerlasiran, muvalaplin

Registry pull ClinicalTrials.gov, 18 interventional records

SUMMARY

18	4	46,047	Mar 2028
registered interventional trials of the five agents	large cardiovascular outcome trials still running	participants enrolled or planned across those four trials	registry primary completion of the next outcome trial, OCEAN(a)-Outcomes

- On 4 September 2026 Novartis reported that pelacarsen lowered Lp(a) as expected but did not reduce the primary composite of cardiovascular events in Lp(a)HORIZON, a trial of 8,323 patients with established cardiovascular disease and Lp(a) ≥ 70 mg/dL.¹² Full results are expected at the AHA Scientific Sessions in November 2026.⁴
- The hypothesis is now carried by three agents in large outcome trials: olpasiran (Amgen, two trials), lepodisiran (Lilly) and the oral agent muvalaplin (Lilly). By registry dates none completes before March 2028.⁶⁸⁹
- These trials differ from HORIZON in ways that matter when reading the pelacarsen result across: the siRNAs lowered Lp(a) more deeply in phase 2 (roughly 90–100% at top doses versus about 80% for pelacarsen); two trials enrol a primary-prevention population; OCEAN(a)-Outcomes uses a coronary composite that excludes stroke.¹¹¹²¹³

- Zerlasiran (Silence Therapeutics) completed phase 2 in January 2024. No phase 3 trial was registered at the time of this search.¹⁰

CATALYST

Lp(a)HORIZON: what was reported and what is still unknown

Lp(a)HORIZON (NCT04023552) randomised 8,323 patients with established cardiovascular disease to pelacarsen 80 mg monthly or placebo. The registry lists a primary completion date of 16 July 2026; the topline came seven weeks later. The two primary analyses were time to first expanded MACE (cardiovascular death, non-fatal MI, non-fatal stroke, urgent coronary revascularisation requiring hospitalisation) in patients with Lp(a) ≥ 70 mg/dL and, separately, in those with Lp(a) ≥ 90 mg/dL.⁵

Novartis's statement says the trial did not meet its primary endpoint while confirming Lp(a) lowering.¹ Ionis, the originator, disclosed the same outcome in a Form 8-K.³ No effect sizes, confidence intervals or subgroup results have been published.

OPEN QUESTION

Whether the ≥ 90 mg/dL population, the stroke component or the on-treatment Lp(a) reduction show any signal. These determine how much of the miss is read as a drug effect versus a hypothesis effect, and they are not public until the AHA presentation.

OPEN QUESTION

Whether the open-label extension (NCT07517263, 5,700 participants, recruiting since May 2026) continues. Its status in the registry is the earliest public signal of Novartis's intent.⁵

All registered interventional trials of the five agents

TRIAL	PHASE	POPULATION AND DESIGN	N	STATUS	PRIMARY COMPLET
Pelacarsen Novartis / Ionis · antisense oligonucleotide					
NCT04023552 Lp(a)HORIZON	3	Established CVD, Lp(a) ≥70 mg/dL; MACE outcomes	8,323	Completed	16 Jul 202
NCT07517263 HORIZON open-label extension	3	Long-term safety in HORIZON completers	5,700	Recruiting	9 Jan 2030
NCT06813911	3	ASCVD with elevated LDL-C and Lp(a); pelacarsen on background inclisiran	340	Recruiting	3 Feb 202
NCT07625306	3	Recent ACS, US; early initiation, coronary plaque	240	Not yet recruiting	7 Dec 202
NCT05646381 Lp(a)FRONTIERS CAVS	2	Calcific aortic valve stenosis progression	502	Recruiting	12 Mar 20
NCT05305664	3	Weekly lipoprotein apheresis, Germany; apheresis rate	51	Completed	28 Jan 20:
NCT05900141	3	Open-label extension of the apheresis study	41	Active, not recruiting	24 Aug 20
NCT03070782	2	Dose-ranging in established CVD (as ISIS 681257)	286	Completed	26 Jul 201

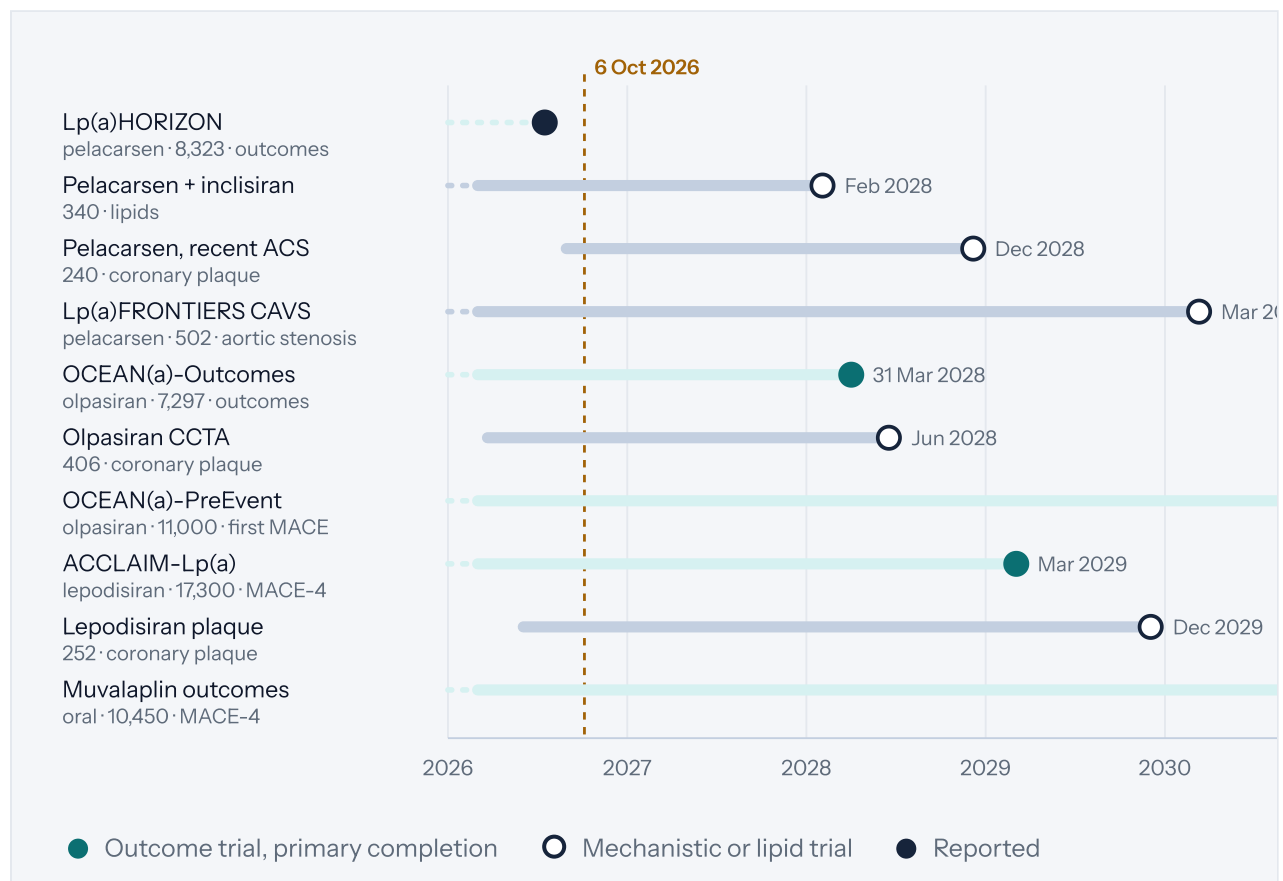
TRIAL	PHASE	POPULATION AND DESIGN	N	STATUS	PRIMARY COMPLET
NCT04993664	n/a	Arterial wall properties after MI (Ljubljana)	0	Withdrawn	—
Olpasiran Amgen · siRNA					
NCT05581303 OCEAN(a)-Outcomes	3	ASCVD with elevated Lp(a); coronary outcomes	7,297	Active, not recruiting	31 Mar 20
NCT07136012 OCEAN(a)-PreEvent	3	Elevated Lp(a), no prior event; first MACE	11,000	Recruiting	20 Oct 20
NCT07293260	3	Stable ASCVD; coronary plaque by CCTA	406	Recruiting	15 Jun 20
NCT04270760 OCEAN(a)-DOSE	2	Dose-ranging, ASCVD	281	Completed	27 Dec 20
NCT04987320	1	Single dose, Chinese participants	24	Completed	12 Nov 20
Lepodisiran Eli Lilly · siRNA					
NCT06292013 ACCLAIM-Lp(a)	3	ASCVD or at risk of first event; MACE-4	17,300	Active, not recruiting	Mar 2029
NCT07613294	3	ASCVD or at risk; coronary plaque	252	Recruiting	Dec 2029
Muvalaplin Eli Lilly · oral small molecule					
NCT07157774	3	ASCVD or at risk of first event; MACE-4	10,450	Recruiting	Mar 2031
Zerlasiran (SLN360) Silence Therapeutics · siRNA					
NCT05537571 ALPACAR-360	2	Elevated Lp(a) at high ASCVD risk	180	Completed	11 Jan 20

Source: ClinicalTrials.gov, searched 6 October 2026 for the five intervention names.⁵ Teal dates mark cardiovascular outcome trials. "n" is enrolment as registered (actual for completed trials, planned for others).

READOUT CALENDAR

When the next evidence can arrive

Primary completion dates are the registry's own and move. HORIZON's topline followed its primary completion by seven weeks, which is a useful lower bound for how quickly a sponsor can report once the last primary-endpoint event is adjudicated. Bars show the registered study period inside the window; a dashed start means the trial began before 2026.



OPEN QUESTION

Some commentary has anticipated an OCEAN(a)-Outcomes readout in late 2026, well ahead of the registry's March 2028 primary completion. The trial is event-driven, so an earlier readout is possible, but this brief could not verify the timing against a primary Amgen source. Confirm against Amgen's next pipeline update before relying on it.

ENDPOINTS

How the four outcome trials define success

All four use a time-to-first-event composite, but the components and populations differ. The table is built from the registered primary endpoints.⁵⁶⁸⁹

TRIAL	CV DEATH	NON-FATAL MI	STROKE	URGENT CORONARY REVASC.	POPULATION
Lp(a)HORIZON pelacarsen · reported	●	●	●	● requiring hospitalisation	Established CVD; Lp(a) ≥70 mg/dL, with a co-primary analysis at ≥90 mg/dL
OCEAN(a)-Outcomes olpasiran	● CHD death only	●	—	●	ASCVD with elevated Lp(a) (secondary prevention)
ACCLAIM-Lp(a) lepodisiran	●	●	● ischaemic	●	Established ASCVD, or at risk of a first event (mixed)
Muvalaplin phase 3 oral	●	●	● ischaemic	●	Prior ASCVD event, or at risk of a first event (mixed)
Primary composite components as registered. Stroke in HORIZON is non-fatal stroke of any type; the Lilly trial ischaemic stroke. OCEAN(a)-Outcomes counts coronary heart disease death rather than all cardiovascular de					

Three points follow. First, OCEAN(a)-Outcomes is the only one of the four that will not be judged on stroke, which removes one source of noise if Lp(a) lowering acts mainly on coronary events. Second, ACCLAIM-Lp(a) pre-specifies a secondary analysis in participants with Lp(a) ≥200 nmol/L, so a threshold effect can be read directly rather than inferred. Third, the two Lilly trials and OCEAN(a)-PreEvent extend the question to people who have not yet had an event, where the event rate is lower and the follow-up correspondingly longer.

AGENTS

The five agents at a glance

NOVARTIS / IONIS Pelacarsen Modality Antisense oligonucleotide, GalNAc Dosing 80 mg s.c. monthly Phase 2 Lp(a) ≈80% reduction at 20 mg weekly / 80 mg monthly¹¹ Stage Outcome trial reported, missed primary endpoint	AMGEN Olpasiran Modality siRNA, GalNAc Dosing s.c. every 12 weeks (phase 3) Phase 2 Lp(a) ≈95–101% placebo-adjusted at ≥75 mg q12w¹² Stage Two outcome trials running
ELI LILLY Lepodisiran Modality siRNA, GalNAc, extended duration Dosing s.c.; once- or twice-yearly regimens tested Phase 2 Lp(a) ≈94% time-averaged reduction at 400 mg¹³ Stage Outcome trial fully enrolled	ELI LILLY Muvalaplin Modality Oral small molecule, apo(a)–apoB binding inhibitor Dosing Once daily Phase 2 Lp(a) ≈70–86% reduction at 240 mg, assay-dependent¹⁴ Stage Outcome trial recruiting
SILENCE THERAPEUTICS Zerlasiran Modality siRNA, GalNAc Dosing s.c. every 16–24 weeks tested Phase 2 Lp(a) ≈80–85% time-averaged reduction at 300 mg¹⁰ Stage No phase 3 registered; partnering status unconfirmed	

Phase 2 figures are approximate top-dose values from the cited publications and use different assays and time windows; they are not directly comparable to one decimal place.

IMPLICATIONS

What this means for a business development or diligence reader

The Lp(a) hypothesis is under test, not resolved. HORIZON tested roughly 80% lowering in a secondary-prevention population. The running trials test deeper lowering, longer follow-up and broader populations. A negative HORIZON narrows the hypothesis; it does not close it. Expect sponsors and commentators to argue the result on residual Lp(a) and achieved reduction once the AHA data are out.

Lp(a) as a surrogate is weaker today than it was in August. Any asset whose value case rests on Lp(a) lowering alone, including diagnostics positioned on treatment eligibility, should assume that regulators and payers will want outcome evidence. The first chance of that evidence is OCEAN(a)-Outcomes.

There is an evidence gap of at least 18 months by registry dates. Partnering and valuation conversations for Lp(a)-adjacent assets will take place without new outcome data until 2028 at the earliest. This favours buyers with patience and sellers who can point to mechanism-level differentiation (depth of lowering, dosing interval, oral route).

Watch items, in order of expected timing. The AHA presentation of HORIZON (November 2026); Amgen's guidance on OCEAN(a)-Outcomes timing; any change to the HORIZON open-label extension; Silence Therapeutics' phase 3 and partnering announcements; regulatory statements on Lp(a) as an accepted surrogate.

OPEN QUESTION

Whether the field consolidates around the two Lilly agents and olpasiran, or whether the HORIZON result reduces appetite for the class as a whole. The first visible signal will be the pace of enrolment in OCEAN(a)-PreEvent and the muvalaplin trial over the next two registry updates.

SOURCES

Every claim above rests on one of these

- [1] Novartis AG. Form 6-K, 4 September 2026 (Lp(a)HORIZON topline). [sec.gov](https://www.sec.gov)
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