

OnKure Therapeutics: how fast to advance two programs?

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OnKure Therapeutics was preparing two preclinical programs for planned Investigational New Drug (IND) submissions in the first half of 2027. At June 30, it reported \$176.4 million in cash, cash equivalents and marketable securities, and management expected that balance to fund operations into 2029. The company was also candid that it had no product revenue, expected development costs to rise, and would need additional capital before completing development. What should guide the next commitments across the two programs? [P1, pp. 22-27; P2]

For this exercise, assume you are on a strategy team preparing an options memo for senior management. The decision is constructed for classroom discussion; public disclosures do not establish a scheduled board vote, binding budget cap, or candidate preference.

A clinical-stage portfolio

OnKure describes itself as a clinical-stage biopharmaceutical company focused on precision medicines. Its stated design objective is to develop small-molecule inhibitors that selectively target mutant PI3K α while sparing wild-type PI3K α . The company says this selectivity could improve the therapeutic index; neither candidate had entered clinical testing by the cutoff, so the design objective was not human efficacy or safety evidence. [P1, pp. 22-23; P2]

The disclosed lead programs were:

Program	Indication named by OnKure	Cutoff stage and company target	Evidence boundary
OKI-345	Breast cancer	IND-enabling work; IND submission planned for 1H 2027	The filing did not provide candidate-specific human data, trial design, probability of success, or program cost.
OKI-355	Vascular anomalies	IND-enabling work; IND submission planned for 1H 2027	The public description did not define a narrower target population or provide candidate-specific human data, trial design, probability of success, or program cost.

The August 4 release also described a discovery research program intended to expand the vascular-anomalies pipeline beyond PI3K α . Its scope, budget and staffing were not quantified. [P2]

Both IND dates were company targets, not completed submissions. The 10-Q said success, timing and completion costs are uncertain; the company expects to revisit program funding in light of scientific and clinical results, commercial potential and possible alliances. Employees and infrastructure are shared, and research-and-development expenses are not tracked by program. Later-stage development is generally more expensive. [P1, pp. 23-24]

What the balance sheet can-and cannot-say

At June 30, 2026, the company reported the following consolidated amounts:

Exhibit 1. Liquidity and reported spending

Measure	Amount	Period / basis
Cash and cash equivalents	\$166.502m	Balance at 30 June 2026
Available-for-sale marketable securities	\$9.884m	Balance at 30 June 2026
Cash plus marketable securities	\$176.386m	Derived sum; reported rounded as \$176.4m
Total current assets	\$177.677m	Balance at 30 June 2026; includes other current assets
Research and development expense	\$12.611m	Q2 2026; versus \$12.613m in Q2 2025
Research and development expense	\$24.318m	H1 2026; versus \$25.625m in H1 2025
Net loss	\$15.346m	Q2 2026
Net loss	\$30.503m	H1 2026
Net cash used in operating activities	\$23.292m	H1 2026

Source: Q2 2026 Form 10-Q, balance sheet, cash-flow statement and MD&A; USD millions. R&D is consolidated, not allocated by candidate. Net loss and operating cash use are different measures. [P1, pp. 8, 20, 24-25]

The Q2 release said management expected the June liquidity balance to fund operations into 2029. The 10-Q separately said resources were expected to support the current operating plan for at least 12 months from issuance. Both are management forecasts under a plan, not guarantees, program-level budgets, or proof that accelerated parallel development fits the same runway. The filing also says substantial additional funding will be needed before product development is complete. [P1, pp. 9-10, 25-27; P2]

In March, OnKure closed a private placement for approximately \$150 million gross, before about \$9.6 million in fees and expenses. The stated uses included R&D for the breast-cancer and vascular-anomalies programs, working capital and general corporate purposes; proceeds could not fund R&D for former lead OKI-219. Separately, the company had an effective shelf and an ATM program with up to \$100 million in stated sales capacity; it reported no ATM shares offered or sold as of August 4. Capacity is not cash proceeds. [P1, pp. 9, 26-27; P3; P5]

Exhibit 2. What the financing disclosures do not allocate

Disclosure	What it establishes	What it leaves open
March placement, ~\$150m gross	Financing closed; use includes the two new programs and corporate needs, while excluding OKI-219 R&D	No OKI-345/OKI-355 split or program-level spending ceiling
June liquidity, \$176.386m	Consolidated cash and marketable securities at quarter-end	Cash available under a faster or different development schedule
Runway into 2029	Management's forecast under its current operating plan	A guarantee, or proof that every alternative has the same runway
Up to \$100m ATM capacity	Potential equity-raising channel; no sales by Aug. 4	Cash raised, share price, dilution or availability on later terms

Disease and competitive context

The breast-cancer pathway includes several approved treatments, but they differ in target, biomarker, combination and treatment setting. OnKure's 2025 Form 10-K identifies alpelisib (Piqray), capivasertib (Truqap) and inavolisib (Itovebi) in the landscape it discussed; capivasertib acts on AKT rather than PI3K α . The filing also names clinical-stage pathway programs. These issuer-identified examples do not establish market share or comparative efficacy, and they do not show that OKI-345 would enter a particular biomarker-defined or treatment-line setting. [C1]

For vascular anomalies, the treatment context is heterogeneous. FDA-approved alpelisib (Vijoice) is labeled for adults and children age two and older with severe manifestations of PIK3CA-Related Overgrowth Spectrum (PROS) who require systemic therapy. PROS is a defined subset, not a synonym for all vascular anomalies. Relay Therapeutics reported in August 2026 that its investigational zovogalisib (RLY-2608) was being studied in PIK3CA-driven vascular anomalies; the ClinicalTrials.gov record identifies RelInspire as NCT06789913. Relay's reported early clinical observations are not head-to-head evidence. [C2-C4]

Relay's earlier SEC-filed presentation describes watch-and-wait/compression, local procedures and systemic approaches including alpelisib and sirolimus. That is an issuer-authored landscape description, not an independent treatment guideline. A completed Phase 2 sirolimus trial record covers a complicated, heterogeneous vascular-anomaly population; it does not establish broad approval or comparative standard-of-care status. No source provides a like-for-like comparison with OKI-355. [C5-C6]

The choice

Two policy paths are available for analysis. Both are constructed alternatives; neither is disclosed as a pending management decision.

1. **Preserve parallel progress.** Continue supporting both disclosed IND-enabling paths toward the company's 1H 2027 targets. This is consistent with the public plan, the March financing's stated uses, and management's June liquidity/runway disclosures. It preserves breadth but leaves the team to monitor rising later-stage costs, shared capacity and the possibility that the runway forecast changes.

2. **Use candidate-specific evidence gates.** Continue work on both candidates, but defer major next-stage commitments until each clears defined scientific, toxicology, CMC/manufacturing and regulatory-readiness milestones. If a candidate falls behind or a suitable alliance becomes available, consider a slower path or partnership for that program. Gates and thresholds would be proposed by the team, not taken from company guidance. This can preserve optionality and flexibility, but may change one or both IND timelines and may require giving up rights if partnered.

The public record does not provide a program cost split, candidate-level comparative data, partner offer or term sheet, or a binding funding limit. It cannot establish which program should go first or calculate the return from either path. Those are questions for the team's recommendation and for further diligence.

Discussion questions

1. Which policy path would you recommend for the next planning period, and what evidence supports it?
2. If you recommend gates, what candidate-specific milestones should release or defer the next commitment? Which are measurable from the current record, and which would require new information?
3. How should the June liquidity balance and management's runway statements affect your recommendation? What do they not tell you?
4. What competitive or treatment context is relevant to each indication, and where does the available evidence stop being comparable?
5. What additional company-specific information would you request before changing pace, deferring a program or negotiating an alliance?

Source notes

Company filing and issuer disclosures

- **P1.** Q2 2026 Form 10-Q, accession 0001193125-26-332773, SEC accepted 4 Aug. 2026 at 16:05:37 ET: [SEC filing index](#); [filing HTML](#). Relevant printed pages/locators: pp. 8-9, Note 1 (merger and accounting history); pp. 9-10, liquidity and placement; pp. 22-24, pipeline, R&D allocation and decisions; pp. 24-27, results, funding and liquidity; pp. 33-35, risk factors.
- **P2.** Q2 2026 results release, furnished as Form 8-K Exhibit 99.1, accession 0001193125-26-332809, SEC accepted 4 Aug. 2026 at 16:10:16 ET: [SEC index](#); [Exhibit 99.1](#). Pipeline claims and 1H 2027 targets: lines 12-38; financial results and management runway statement: lines 34-64, 70-118.
- **P3.** Form 424B5 ATM prospectus supplement, accession 0001193125-26-332839, SEC accepted 4 Aug. 2026 at 16:15:11 ET: [SEC index](#); [supplement](#), lines 7-24. No ATM shares had been offered or sold as of Aug. 4.
- **P5.** Mar. 27, 2026 private-placement release and agreement, SEC accession 0001193125-26-130283: [issuer release](#); [SEC index](#). Final closing, fees and proceeds-use controls are in P1 Note 9 and MD&A.
- **P7.** Aug. 31, 2026 conference notice: [issuer release](#). Notice only; the September event falls after cutoff.

Competitive / treatment sources

- **C1.** OnKure 2025 Form 10-K, Item 1 "Competition," printed pp. 18-19: [SEC filing](#). Issuer-identified competitors and factors; not market-share or efficacy evidence.
- **C2.** FDA orphan-drug approval record for alpelisib (Vijoice), marketing approval date 5 Apr. 2022 and labeled indication: [FDA record](#). C3. Relay Therapeutics Q2 2026 release, 6 Aug., "Vascular Anomalies": [issuer release](#), lines 93-97, 127. C4. Relnspire trial record NCT06789913: [ClinicalTrials.gov](#).
- **C5.** Relay SEC-filed June 2024 presentation, slides 34-35: [SEC-filed Exhibit 99.3](#). Issuer-described treatment journey, not a guideline. C6. Sirolimus Phase 2 study NCT00975819, completed Oct. 2020, results first posted 6 Jan. 2026: [ClinicalTrials.gov record/history](#).