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Competing interests

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In the interest of transparency and to help readers form their own judgements of potential bias, Nature Portfolio journals require authors to declare any competing financial and/or non-financial interest in relation to the work described in the submitted manuscript.

Competing interests declaration

- ☐ We declare that none of the authors have competing financial or non-financial interests as defined by Nature Portfolio.
- ☒ We declare that one or more of the authors have a competing interest as defined by Nature Portfolio.

Gerald Watts (corresponding author) reports personal fees for lectures from Amgen, Novartis and Sanofi; Research grants from Amgen and Arrowhead Pharmaceuticals; honoraria for serving on advisory boards from Amgen, AstraZeneca, Esperion, Novartis, Pfizer, and Arrowhead.

James Hamilton, Bruce Given, Stacey Melquist, Javier San Martin, Ting Chang, and Rong Zhou are, or were recently, Arrowhead Pharmaceuticals employees and shareholders.

Ira Goldberg reports being on advisory boards for Arrowhead Pharmaceuticals and IONIS.

Christie Ballantyne reports Grant/Research Support (all significant [$> \$10,000$] and all paid to institution, not individual): Akcea, Amgen, Arrowhead, Esperion, Ionis, Merck, Novartis, Novo Nordisk, Regeneron, NIH; consultant for 89Bio, Alnylam Pharmaceuticals, Althera, Amarin, Amgen, Arrowhead, Astra Zeneca, Denka Seiken*, Esperion, Genentech, Gilead, Illumina, Matinas BioPharma Inc, Merck, New Amsterdam*, Novartis, Novo Nordisk, Pfizer, Regeneron, and Sanofi-Synthelabo (*significant where noted).

Patrick Gladding reports being principal investigator for Verve101 and receiving consulting fees from Verve Therapeutics.

Robert Hegele reports consulting fees from Acasti, Akcea/Ionis, Amgen, Amryt, Arrowhead, Boston Heart, HLS Therapeutics, Pfizer, Novartis, Regeneron, Sanofi and Ultragenyx.

Daniel Gaudet reports grants and/or personal fees from Arrowhead, Acasti, Amgen, Kowa, Regeneron, Unique, Akcea, Allergan, Amryt, CRISPR Therapeutics, Eli Lilly, Ionis, Novartis, aliogen, Sanofi, Novonordisk, Pfizer, Verve therapeutics, Aegerion, Applied therapeutics, Astra Zeneca, Boehringer-Ingelheim, Ceapro, Dalcor, Esperion, and The Medicine Company.

David Sullivan reports personal fees from Regeneron, personal fees from Amgen, personal fees from AstraZeneca, personal fees from Amarin, personal fees from Esperion, personal fees from Novartis, personal fees from Sanofi, outside the submitted work.

No competing interests were reported by Christian Schwabe, Peter Clifton, Russell Scott, John Baker, and Joshua Knowles.

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- ☐ We have provided an "Inclusion & Ethics" statement.

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Data availability statement

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
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- ☒ We have provided a full data availability statement in the manuscript.

Mandated accession codes ([where applicable](#))

Confirm that all relevant data are deposited into a public repository and that accession codes are provided.

☐ All relevant accession codes are provided ☐ Accession codes will be available before publication ☒ No data with mandated deposition

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Code availability statement

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n/a | Confirmed

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- ☐ ☒ The format shows data distribution clearly (e.g. dot plots, box-and-whisker plots)
- ☒ ☐ Box-plot elements are defined (e.g. center line, median; box limits, upper and lower quartiles; whiskers, 1.5x interquartile range; points, outliers)
- ☐ ☒ Clearly defined error bars are present and what they represent (SD, SE, CI) is noted

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☒ We have complied with all relevant ethical regulations and include a statement affirming this in the manuscript.

Ethics committee

Confirm that the manuscript states the name(s) of the board and/or institution that:

☒ Approved the study protocol -OR- ☐ Provided guidelines for study procedures (if protocol approval is not required)

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Authors must ensure that consent meets the conditions set out in the [Nature Portfolio participant release form](#).

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Phase 2 and 3 randomized controlled trials

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☐ Yes ☐ No ☒ Not a phase 2/3 randomized controlled trial

Tumor marker prognostic studies

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I certify that all the above information is complete and correct.

Typed signature James Hamilton MD

Date Sep 29, 2022