Unlocking Opportunities: Exploring Strategies for Lp(a) therapy in ASCVD Market

Kristy Ma

2024/1/19

ASCVD Market

AtheroSclerotic CardioVascular Disease:

- Plaques built up in blood vessels[1]

- US prevalence: 8% (2020[2]) with CVD high death rate (1/3) [3]

- Risk factors[3]: smoking, age, obesity*, high LDL, diabetes*

++[5]

Projected CAGR **2.8%** from 2023-33[4]

Aging population [6]

Continued* $ [7]

Current therapies target anti-platelet and anti-cholesterol with low adherence [8,9]

Unmet Needs:

High-cost therapies [10]   Limited coverage on diagnosis [11]

UNC | RESEARCH

ASCVD & Lp(a): Niche Market

About:

- Independent, genetic risk factor [12]

- Prevalence ~20% but ~1% tested [13,14]

- Race-based susceptibility [15]

- + ASCVD risk by 2.5 fold [16]

- *No approved therapy on the market*

Testing:

- Blood test ($39- $595, not covered by Medicare) [17,18]

- 23AndMe screening test [19]

Restraints stem from lack of attention → Educational outreach

Competitive Landscape

Competition	Phase	Valuable Assets ━ clinical ━ non-clinical	Diagnostic Pathway/ Target
Pelacarsen[20] (Novartis)	III (80% ↓)	- No side effect/ tolerability concerns[20] - Maybe first in-line	ASO: inhibits Apo(a) synthesis to lower Lp(a) [21]
Lepodisiran[25] (Eli Lilly)	II (94% ↓)	- Long lasting efficacy (336 days) [22] - Collaboration with Verve Therapeutics, Inc. [23]	siRNA: same as above[24]
Muvalaplin[26] (Eli Lilly)	II (65% ↓)	- Oral - No side effect/ tolerability concerns[26]	Small molecule: inhibits Lp(a) formation[26]
Zerlasiran[28] (Silence Therapeutics)	II (99% ↓)	- "Best" mechanism with 2-month efficacy	siRNA: silence LPA gene[27]
Olpasiran[30] (Amgen)	III (96% ↓)	?	siRNA: degrades Apo(a) product[29]

Insight: Stent manufacturers (e.g. Boston Scientific, Abbott)

Be Visionary: Our Opportunities

Previous Unmet Needs/ Problem:

- High-cost with low adherence

- Lack of awareness on Lp(a) test

Attributes (ranked):

1. Long-lasting efficacy/ dosage advantage (adherence)

2. Novel drug mechanism

3. (Non-clinical) Target slogan "lowering ASCVD risk by x%"

Lp(a): Beyond ASCVD
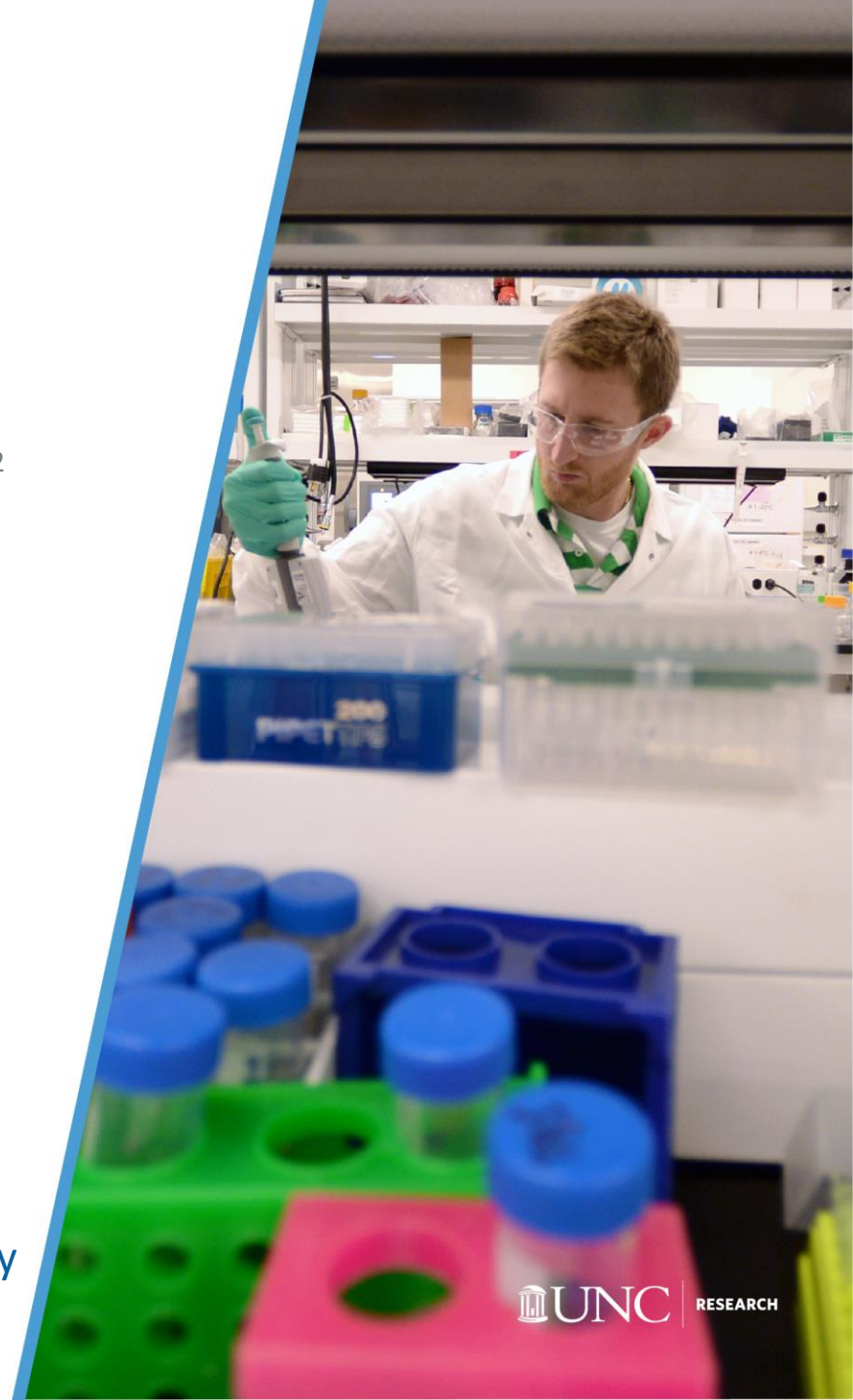
ACS, MI (Acute Coronary Syndrome, Myocardial Infarction):

- High mortality rate ~23%[31] within 1 year of initial MI

- Aggressive treatment then pharmacotherapy: Statin → Lp(a) + + [32]

- Suboptimal adherence to current therapies [33]

- Huge economic burden: room for innovation

Heart Failure:

- US Prevalence 2.6%[34] with greater risk in African descent[35]

- No association with elevated Lp(a) if excluding MI cases[36]

Consider:
1. Survival rate after MI attack   2. Acute/ chronic
3. If there is expectation on new drug target   4. Regulation risk of gene therapy

UNC | RESEARCH

References

1. American Heart Association. Atherosclerotic cardiovascular disease (ASCVD). [Webpage]. https://www.heart.org/en/professional/quality-improvement/ascvd#:~:text=Atherosclerotic%20cardiovascular%20disease%2C%20otherwise%20known,angina%2C%20and%20coronary%20artery%20stenosis

2. ScienceDirect. (2020). Prevalence of atherosclerotic cardiovascular disease is 18.3 million (8.0%). [Journal Article]. https://www.sciencedirect.com/science/article/pii/S2666667720300106#:~:text=Highlights&text=The%20prevalence%20of%20atherosclerotic%20cardiovascular,is%2018.3%20million%20(8.0%25)

3. Centers for Disease Control and Prevention. Heart disease and stroke prevention. [Webpage]. https://www.cdc.gov/chronicdisease/resources/publications/factsheets/heart-disease-stroke.htm

4. Future Market Insights. Atherosclerosis Market. [Webpage]. https://www.futuremarketinsights.com/reports/atherosclerosis-market

5. PubMed. (2022). Cardiovascular Disease Projections in the United States Based on the 2020 Census Estimates [Journal Article]. https://pubmed.ncbi.nlm.nih.gov/35926929/

6. Population Reference Bureau. Fact Sheet: Aging in the United States. [Webpage]. https://www.prb.org/resources/fact-sheet-aging-in-the-united-states/

7. Medicare 365. Medicare Coverage for Calcium Score Tests. [Webpage]. https://medicare-365.com/medicare-coverage-for-calcium-score-tests/

8. Acumen Research and Consulting. Atherosclerosis Drugs Market. [Webpage]. https://www.acumenresearchandconsulting.com/atherosclerosis-drugs-market#:~:text=The%20Global%20Atherosclerosis%20Drugs%20Market,2.8%25%20from%202023%20to%202032

9. US Pharmacist. Overcoming Barriers to Statin Adherence. [Webpage]. https://www.uspharmacist.com/article/overcoming-barriers-to-statin-adherence#:~:text=Predictors%20of%20Statin%20Nonadherence&text=In%20contrast%2C%20factors%20such%20as,been%20linked%20to%20statin%20nonadherence

10. Market Research. Atherosclerotic Cardiovascular Disease (ASCVD) Insight. [Webpage]. https://www.marketresearch.com/DelveInsight-v4028/Atherosclerotic-Cardiovascular-Disease-ASCVD-Insight-35357708/

11. Centers for Medicare & Medicaid Services. Title not available. [Webpage]. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=33423&ver=48&

12. ScienceDirect. (2023). Lipoprotein(a): An important piece of the ASCVD risk factor puzzle across diverse populations. [Journal Article]. https://www.sciencedirect.com/science/article/pii/S2666602223001039

13. PubMed Central. (2021). Characteristics and lipid lowering treatment patterns in patients tested for lipoprotein(a): A real-world US study. [Journal Article]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10015179/#:~:text=It%20is%20estimated%20that%2020,of%20the%20ACC%2FAHA%20guideline

14. GlobeNewswire. Characteristics and lipid lowering treatment patterns in patients tested for lipoprotein(a): A real-world US study. [Webpage]. https://www.globenewswire.com/Tracker?data=DMKKFS8vohU4Qf_hjdPYlOc5D-4HVyetL_K7jGuvNtue7r6t8zPm81z-9NVO8Wa955xtc2TKdVL0ll0HN3A1hfHJw8533zeIpVXruT3LX6uXVXeU0u1nkGVhW4ampaz5-uVo9Kq-zoQ7Shv4bAD7BNlAmuD1Bv2uMFPYd_1cpLEkfYq4hA6rs_0paCJeatRh4vJvGieVu9wu0HrTT6ZhajIxHuCJQWPa3I5HG29xwtMV_vgvNncNtdR0lyHF9T272YH70lcDQCo1XtmOLLDEScbsIJYWvMiEaI2Pj-583VY=

15. Guan, W., et al. (2015). Race is a key variable in assigning lipoprotein(a) cutoff values for coronary heart disease risk assessment. Arteriosclerosis, Thrombosis, and Vascular Biology, 35(4), 996–1001. [Journal Article]. https://doi.org/10.1161/atvbaha.114.304785.

16. American College of Cardiology. (2022). Lipoproteina in ASCVD: ESC 2022. [Webpage]. https://www.acc.org/Latest-in-Cardiology/ten-points-to-remember/2022/09/07/14/43/Lipoproteina-in-ASCVD-ESC-2022#:~:text=An%20Lp(a)%20level%20of,5%2D10%25%20risk

17. FindLabTest.com. Lipoprotein(a) LabCorp. [Webpage]. https://www.findlabtest.com/lab-test/blood-tests-for-heart-disease/lipoprotein-a-labcorp-120188#:~:text=Lipoprotein(a)%20test%20cost%20is,Blood%20Test)%20with%20price%20%2439.00

18. Centers for Medicare & Medicaid Services. [Webpage]. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=102#:~:text=While%20lipid%20screening%20may%20be,history%2C%20tobacco%20use%2C%20etc

19. HMP Global Learning Network. 23andMe Aims to Raise Awareness of Lipoprotein(a) as a Little-Known Genetic Risk Factor. [Webpage]. https://www.hmpglobllearningnetwork.com/site/cathlab/news/23andme-aims-raise-awareness-lipoproteina-little-known-genetic-risk-factor

References

20. PubMed. (2019). Lipoprotein(a) Reduction in Persons with Cardiovascular Disease. [Journal Article]. https://pubmed.ncbi.nlm.nih.gov/31893580

21. Journal of the American College of Cardiology. (2022). Effect of Pelacarsen on Lipoprotein(a) Cholesterol and Corrected Low-Density Lipoprotein Cholesterol. [Journal Article]. https://www.jacc.org/doi/10.1016/j.jacc.2021.12.032

22. JAMA Network. (2023). Lepodisiran, an Extended-Duration Short Interfering RNA Targeting Lipoprotein(a)

A Randomized Dose-Ascending Clinical Trial. [Journal Article]. https://jamanetwork.com/journals/jama/fullarticle/2811935

23. Verve Therapeutics. Verve Establishes Global Collaboration with Lilly to Advance Verve's Vivo. [Webpage]. https://ir.vervetx.com/news-releases/news-release-details/verve-establishes-global-collaboration-lilly-advance-verves-vivo

24. TCTMD. Large Sustained Reductions in Lp(a) Observed in Phase I Study of Lepodisiran. [Webpage]. https://www.tctmd.com/news/large-sustained-reductions-lpa-lepodisiran-phase-i-study

25. American Heart Association News. One Dose of Experimental Therapy Reduced Lipoprotein(a) More Than 94% for Nearly a Year. [Webpage]. https://newsroom.heart.org/news/one-dose-of-experimental-therapy-reduced-lipoprotein-a-more-than-94-for-nearly-a-year

26. PubMed. (2021). Muvalaplin, an Oral Small Molecule Inhibitor of Lipoprotein(a) Formation: A Randomized Clinical Trial. [Journal Article]. https://pubmed.ncbi.nlm.nih.gov/37638695/

27. Silence Therapeutics. Zerlasiran. [Webpage]. https://silence-therapeutics.com/our-pipeline/zerlasiran/default.aspx

28. Clinical Trials Arena. Silence Therapeutics Announces Cardiovascular Disease Trial. [Webpage]. https://www.clinicaltrialsarena.com/news/silence-therapeutics-cardiovascular-disease-trial/?cf-view

29. ScienceDirect. (2022). Study design and rationale for the Olpasiran trials of Cardiovascular Events And lipoproteiN(a) reduction-DOSE finding study (OCEAN(a)-DOSE). [Journal Article]. https://www.sciencedirect.com/science/article/pii/S0002870322000862

30. Amgen. (2023). Amgen Presents Late-Breaking Phase 2 Olpasiran Data at ESC 2023. [Webpage]. https://www.amgen.com/newsroom/press-releases/2023/08/amgen-presents-late-breaking-phase-2-olpasiran-data-at-esc-2023

31. DM;, K. Acute coronary syndromes: Morbidity, mortality, and pharmacoeconomic burden. The American journal of managed care. https://pubmed.ncbi.nlm.nih.gov/19355807/

32. Zhu, L., Fang, Y., Gao, B., Jin, X., Zheng, J., He, Y., & Huang, J. (2022, December 30). Effect of an increase in LP(a) following statin therapy on cardiovascular prognosis in secondary prevention population of coronary artery disease - BMC cardiovascular disorders. BioMed Central. https://bmccardiovascdisord.biomedcentral.com/articles/10.1186/s12872-022-02932-y

33. Bots, S. H., Inia, J. A., & Peters, S. A. E. (2021). Medication Adherence After Acute Coronary Syndrome in Women Compared With Men: A Systematic Review and Meta-Analysis. Frontiers in Global Women's Health, 2. https://doi.org/10.3389/fgwh.2021.637398

34. Bozkurt, B., Ahmad, T., Alexander, K. M., Baker, W. L., Bosak, K., Breathett, K., Fonarow, G. C., Heidenreich, P. A., Ho, J. E., Hsich, E., Ibrahim, N. E., Jones, L. M., Khan, S. S., Prateeti Khazanie, Koelling, T. M., Krumholz, H. M., Khush, K. K., Lee, C. S., Morris, A. A., & Page, R. L. (2023). Heart Failure Epidemiology and Outcomes Statistics A Report of the Heart Failure Society of America. Journal of Cardiac Failure, 29(10). https://doi.org/10.1016/j.cardfail.2023.07.006

35. Lewsey, S. C., & Breathett, K. (2021). Racial and ethnic disparities in heart failure: current state and future directions. Current Opinion in Cardiology, 36(3), 320–328. https://doi.org/10.1097/hco.0000000000000855

36. Agarwala, A., Pokharel, Y., Saeed, A., Sun, W., Virani, S. S., Nambi, V., Ndumele, C., Shahar, E., Heiss, G., Boerwinkle, E., Konety, S., Hoogeveen, R. C., & Ballantyne, C. M. (2017). The association of lipoprotein(a) with incident heart failure hospitalization: Atherosclerosis Risk in Communities study. Atherosclerosis, 262, 131–137. https://doi.org/10.1016/j.atherosclerosis.2017.05.014

Words from Kristy

Dear Mr. Rocha, Mr. Lewis, and Ms. Hadi:

First, I'd like to thank you, not just for the interview, but for witnessing my growth. As a student with little business background, I have learned a great deal about commercial insights knowledge that is entirely new to me (such as how to assess drug targets, what aspects to consider when estimating market potential, understanding the healthcare ecosystem, etc.). I am FASCINATED by this case challenge - I find solving such problems very interesting and enjoyable! While there is definitely a lot of room for improvement, I'd like to take on opportunities to learn and continually develop my acumen and knowledge at Amgen.

Personally speaking, today actually marks an important milestone in my life: I walked through this stage by being bold and proactive about the changes I want to make (transitioning from a career in statistics). I am not sure how well I did today, so regarding the internship, I can only secretly pray that my problem-solving potentials were recognized by you. But life is not a test. Looking beyond the internship, personal exploration goes a long way. Therefore, I am already thankful for this opportunity that I have earned for myself, so that I can walk towards my goals. I will keep fighting on no matter what.

Thank you again for the time reading my inner thoughts and personal story. Fingers crossed for some good news!

Regards,

Kristy

UNC | RESEARCH