Seeking Alpha

Verve: Potential To Advance Gene Based Editing Drugs For ASCVD

Dec. 11, 2023 2:27 PM ET | **Verve Therapeutics, Inc. (VERV) Stock** | LLY

Terry Chrisomalis

Investing Group Leader

About this article

Ticker	Analyst rating	Price at publication	Last price	Change since publication	S&P 500 change since publication
VERV	STRONG BUY	$12.41	$15.14	22.00%	9.87%

Days since publication
86

Summary

Verve Therapeutics, Inc. released positive interim data from its phase 1b heart-1 study using VERVE-101 for treating HeFH patients; LDL-C reduced by as much as 55% after a single dose.

IND clearance for VERVE-101 in the U.S. opens up the inclusion of U.S. trial sites to the phase 1b heart-1 study, along with a possible pathway for FDA approval.

The company has additional candidates in its pipeline being used to treat patients with elevated levels of LDL-C, which are VERVE-102 and VERVE-201, respectively.

Verve has been able to establish a partnership with Eli Lilly which brought an upfront payment of $60 million and then potential for it to earn up to $460 million in milestone payments.

I am Terry Chrisomalis, a long term Biotech investor with a degree in Applied Science. I am the leader of the investing group Biotech Analysis Central, where I analyze high risk/high reward ideas.

ArLawKa AungTun/iStock via Getty Images

Verve Therapeutics, Inc. (NASDAQ:VERV) has been making great progress in being able to advance its pipeline, that's because it has done well to advance its main clinical candidate in the pipeline known as VERVE-101 [based editor targeting PCSK9 protein] for the treatment of patients with heterozygous familial hypercholesterolemia [HeFH]. Matter of fact, VERV has already been able to report positive interim data from its ongoing phase 1b heart-1 study, which used this gene-based editing treatment for this patient population.

One thing to note is that such interim data was released with respect to the testing of patients in the United Kingdom and New Zealand only. It was able to just receive IND clearance of VERVE-101 for the treatment of HeFH patient population for the United States as well. The significance of this is that it may ultimately add an additional regulatory pathway for this drug.

That's because trial sites in the United States can now be added to this phase 1b heart-1 study. Two important trial initiations may also be underway in 2024 as well. That's because it is advancing another based editor drug known as VERVE-102, which is also targeting the PCSK9 protein. However, this particular drug is using a different delivery method, which is the use of the GalNAc-LNP delivery technology. A phase 1b study using VERVE-102 for the treatment of patients with HeFH is expected to be initiated in the 1st half of 2024. Another trial initiation would be the use of VERVE-201, however the protein being targeted here is ANGPTL3. A phase 1b study using this gene base editing drug to target homozygous familial hypercholesterolemia [HoFH]/refractory hypercholesterolemia is expected to begin in the 2nd half of 2024.

VERVE-101 For The Treatment Of Patients With High Levels Of Bad Cholesterol

The main clinical program in Verve Therapeutics' pipeline would be the use of VERVE-101, which is being advanced for the treatment of patients with heterozygous familial hypercholesterolemia [HeFH]. The thing is that this base editing drug was developed to target the PCSK9 protein, which is important for controlling LDL-C levels through an LDL-C receptor. The use of VERV-101 is being explored in the phase 1b heart-1 study treating this specific patient population. As I highlighted above, the study started off only with sites in the United Kingdom and New Zealand. This is great for advancing the use of this drug for this indication only in these territories, but if the biotech wants to make headway in being able to target patients in the United States, then it would need to find a way to get clearance to do so.

That's exactly what it did, in that it **received U.S. FDA clearance of its IND for VERVE-101** to treat patients with HeFH. Such a clearance from the agency will allow it to add U.S. trial sites for this phase 1b heart-1 study. One major issue with HeFH is that it can lead to atherosclerotic cardiovascular disease [ASCVD]. As such, patients recruited not only had HeFH, but also had ASCVD as well. The global heterozygous familial hypercholesterolemia market is **expected to be valued at $58.54 billion by the end of 2033**. This early-stage study is going to first and foremost evaluate safety in this patient population, but other early data aspects to be looked at will also be the pharmacodynamic and pharmacokinetic profile of VERVE-101.

There is an ability to have another shot on goal with respect to a base editing drug being applied towards the targeting of the PCSK9 protein. What do I mean by this? Well, that's because there is another clinical product being advanced in the pipeline known as VERVE-102. This gene based editing drug is the same as VERVE-101, however it is being delivered using its proprietary GalNAc-LNP delivery technology. Should Verve Therapeutics receive clearance from regulatory authorities for this drug, then it believes that a phase 1b study targeting Heterozygous familial hypercholesterolemia [HeFH could be initiated by the 1st half of 2024.

Expansion Opportunities For Atherosclerotic Cardiovascular Disease Using Another Target

A good thing about this biotech is that it is not just highly focused on either using VERVE-101 or VERVE-102 to go after such patients who may have issue with atherosclerotic cardiovascular disease [ASCVD]. That's because it is advancing another candidate known as VERVE-201, which is a base editor also targeting subtypes of ASCVD. However, this time around it is important to note that the protein being targeted is ANGPTL3. Why is this protein critical to the control of LDL-C levels in a person's blood? That's because this gene is critical for driving the reduction of disease-driving LDL-C and triglyceride levels in the blood. Thus, with this alternate targeting approach, it provides another shot-on goal for these patients with ASCVD.

There is one way whereby VERVE-201 is similar to VERVE-102 and that would be based on their delivery methods. Both are being delivered to these patients using the company's proprietary GalNAc-LNP delivery system. It remains to be seen if such a delivery system can yield superior data when given to these ASCVD patients, but it is a good type of delivery technology to test upon nonetheless. One major aspect to consider, though, is that VERVE-201 is being advanced towards the treatment of other subtypes of ASCVD, which are homozygous familial hypercholesterolemia [HoFH] and refractory hypercholesterolemia. The HoFH population is not as large, in that the global market for this segment of ASCVD is **expected to grow** **to $101.8 million by 2030**. On the other hand, when looking at the refractory hypercholesterolemia indication, it is said that about 13% of patients with ASCVD fall into this category. Regardless, these other ASCVD subtypes that are being targeted by Verve Therapeutics that could ultimately yield an increase in shareholder value.

Major Partner On Board To Carry Its Pipeline Towards ASCVD Forward

The targeting of PCSK9 and ANGPTL3 are only the first two proteins being targeted to help patients with atherosclerotic cardiovascular disease [ASCVD]. The other protein being targeted is lipoprotein [a] or Lp[a]. High levels of Lp[a] can lead to ASCVD issues such as a heart attack or stroke and is another good protein to target. Speaking of the advancement of the targeting of Lp[a], Verve Therapeutics was able to bring on board a major pharmaceutical partner. It was able to establish an exclusive collaboration **agreement** whereby it and **Eli Lilly** (LLY) would advance the biotech's preclinical in vivo base gene editing program, which targets Lp[a]. The deal pretty much brought in an upfront payment of $60 million for Verve. Plus, it has the ability to earn up to $465 million in milestone payments as well. This was just the beginning of the collaboration agreement that was established between the two companies. Later on in October of 2023, the initial agreement made by both companies **was expanded upon** to include the targeting of PCSK9, ANGPTL3 and a third undisclosed cardiovascular target.

Financials

According to the **10-Q SEC Filing**, Verve Therapeutics had cash, cash equivalents and marketable securities of $485.2 million as of September 30th 2023. It believed that this cash on hand would be enough to fund its operations into 2026. However, despite having this cash runway, it chose to **raise additional funds regardless**. First, it enacted an underwritten public offering of 12,500,000 shares of its common stock at a public offering price of $10 per share, which is expected to bring in total gross proceeds of approximately $125 million before deducting expenses. In addition, it even granted the underwriters a 30-day option to consider the purchase of up to 1,875,000 additional shares of common stock at the very same public offering price.

Secondly, it has even enacted a concurrent private placement agreement with Eli Lilly to sell 2,296,317 shares of its common stock similar to that of the public offering price. This private placement agreement was to make total gross proceeds of about $23 million. With the public offering of the 12,500,000 shares of common stock, plus the private placement agreement f 2,296,317 shares of common stock to Eli Lilly, it is expected to bring in total gross proceeds of about $148 million before expenses. It is very important to note that this doesn't include the underwriters' option to purchase additional stock at the very same purchase price.

Risks To Business

There are several risks that investors will have to consider before investing in Verve Therapeutics. The **first risk** to consider would be with respect to the advancement of the phase 1b heart-1 study, which is using VERVE-101 for the treatment of patients with heterozygous familial hypercholesterolemia [HeFH]. That's because even though interim results were shown to achieve a 55% reduction in LDL-C, there is no guarantee that similar or superior results will be established later on. Not only that, but two patients taking the higher dose of this treatment had serious adverse events [SAEs].

It was noted that 1 of the SAE was not related to treatment, but that the other one myocardial infraction might have been related to treatment. Thus, it is going to be important to monitor new safety data to be released going forward. There is no assurance that updated data to be released from this very same phase 1b heart-1 study won't have any new safety issues.

A **second risk** to consider would be with respect to VERVE-102 which is being developed to treat HeFH as well. That's because there is no assurance that positive results will ultimately be achieved with this candidate. Not only that, but you have to consider that this gene-based editing drug is also using another form of delivery, which GalNAc-LNP delivery. There is no guarantee that the addition of this proprietary delivery system is going to help Verve Therapeutics yield superior data compared to the other form of delivery.

A **third risk** to consider would then be with respect to the advancement of VERVE-201, which is being advanced to treat patients with both homozygous familial hypercholesterolemia [HoFH] and refractory hypercholesterolemia. The approach for this drug is to target another protein, known as ANGPTL3 and it is not known if this alternate approach is going to yield in substantial clinical data.

A **fourth and final risk** to consider would be with respect to the ongoing collaboration agreement established between Verve and Eli Lilly. There is no assurance that Eli Lilly is going to like the eventual data to be released from the ongoing collaboration studies, nor that such a partnership agreement will remain in place.

Conclusion

Verve Therapeutics has made great progress in being able to advance its pipeline, especially since it has been able to achieve positive interim results with the use of VERVE-101 for the treatment of patients with heterozygous familial hypercholesterolemia [HeFH]. It has several other shots on goal anyways just in case it doesn't continue to achieve positive results in the clinic for its lead candidate VERVE-101. It is gearing up to advance VERVE-102 which also targets PCSK9 that uses GalNAc-LNP delivery system and VERVE-201 which is also using this very same delivery technology but targeting another protein known as ANGPTL3 instead.

There has even been a **collaboration agreement made** between it and Eli Lilly to advance these clinical candidates, along with a preclinical collaboration agreement to target another protein known as lipoprotein[a] or Lp[a]. Such an agreement brought in a lot of upfront cash of about $60 million and then the potential for it to earn up to $465 million as milestone payments as well. The key here is that if the targeting of both HeFH and HoFH ends up paying off, then this biotech would be capable of being able to target a multibillion-dollar market opportunity.

This article was written by

Terry Chrisomalis

12.1K Followers

Terry Chrisomalis is a private investor in the Biotech sector with years of experience utilizing his Applied Science background to generate long term value from Healthcare.

He is the author of the investing group Biotech Analysis Central which contains a library of 600+ Biotech investing articles, a model portfolio of 10+ small and mid-cap stocks with deep analysis for each, live chat, and a range of analysis and news reports to help Healthcare investors make informed decisions. Learn more.

Value Investing
ETF Screener
Big Bank Stocks
Growth vs. Value ETFs
M&A

Comments

Sort by Newest

Tech Stocks
Quantitative Investing

LEARN

Investing Education
Investing Strategies
Retirement Investing
Stock Market Sectors
Stock Market Holidays & Hours
After Hours Trading
Portfolio Management
Cryptocurrency
Dividend Investing
Portfolio Strategy
Fixed Income
Retirement
IPO's

Closed End Funds
Editors' Picks

DIVIDENDS

Dividend Stock News
REITs
Dividend Ideas
Dividend Strategy
Dividend Quick Picks
Editors' Picks

TOP INDEXES

Dow Jones
S&P 500
Nasdaq
Gold
Bitcoin

ETF Strategies
Smart Beta
Themes & Subsectors ETFs
Cryptocurrency

NEWS BY SECTOR

Consumer
Energy
Financials
Healthcare
Tech

EARNINGS

Earnings Calendar
Earnings News
Earnings Analysis
Earnings Calls Transcripts

Podcasts

Editors' Picks