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Verve：推进 ASCVD 基因编辑药物的潜力

美国东部时间 2023 年 12 月 11 日下午 2:27 | **Verve Therapeutics, Inc. (VERV) 股票** | LLY

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概括

Verve Therapeutics, Inc. 发布了使用 VERVE-101 治疗 HeFH 患者的 1b 期 heart-1 研究的积极中期数据；单剂量后 LDL-C 降低多达 55%。

VERVE-101 在美国获得 IND 批准，开启了将美国试验地点纳入 1b 期 heart-1 研究的大门，并为 FDA 批准提供了可能的途径。

该公司还有其他候选药物正在研发中，用于治疗 LDL-C 水平升高的患者，分别是 VERVE-102 和 VERVE-201。

Verve 已与礼来公司建立了合作伙伴关系，获得了 6000 万美元的预付款，然后有可能获得高达 4.6 亿美元的里程碑付款。

我是 Terry Chrisomalis，一位拥有应用科学学位的长期生物技术投资者。我是生物技术分析中心投资集团的领导者，负责分析高风险/高回报的想法。

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Verve Therapeutics, Inc.（纳斯达克股票代码：VERV）在推进其研发管线方面取得了巨大进展，这是因为该公司在推进其主要临床候选药物VERVE-101（针对 PCSK9 蛋白的编辑器）方面做得很好。用于治疗杂合子家族性高胆固醇血症[HeFH]患者。事实上，VERV 已经能够报告其正在进行的 1b 期 heart-1 研究的积极中期数据，该研究对该患者群体使用了这种基于基因的编辑治疗。

需要注意的一件事是，此类临时数据仅针对英国和新西兰的患者测试而发布。它也刚刚获得了 VERVE-101 的 IND 批准，用于治疗美国的 HeFH 患者群体。这样做的意义在于，它最终可能会为该药物增加一条额外的监管途径。

这是因为现在可以将美国的试验地点添加到这项 1b 期 heart-1 研究中。两项重要的试验也可能在 2024 年启动。这是因为它正在开发另一种名为 VERVE-102 的编辑药物，该药物也针对 PCSK9 蛋白。然而，这种特殊的药物使用了不同的递送方法，即使用 GalNAc-LNP 递送技术。使用 VERVE-102 治疗 HeFH 患者的 1b 期研究预计将于 2024 年上半年启动。另一个试验启动将是使用 VERVE-201，但这里的目标蛋白是 ANGPTL3。使用这种基因碱基编辑药物来靶向纯合家族性高胆固醇血症 [HoFH]/难治性高胆固醇血症的 1b 期研究预计将于 2024 年下半年开始。

VERVE-101 用于治疗高水平坏胆固醇患者

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 在推进其产品线方面取得了巨大进展，特别是在使用 VERVE-101 治疗杂合子家族性高胆固醇血症 [HeFH] 患者方面取得了积极的中期结果。不管怎样，它还有其他几次尝试，以防万一它的主要候选药物 VERVE-101 不能继续在临床中取得积极的结果。它正在准备推进 VERVE-102，它也针对使用 GalNAc-LNP 递送系统的 PCSK9 和 VERVE-201，后者也使用这种完全相同的递送技术，但靶向另一种称为 ANGPTL3 的蛋白质。

它与礼来公司甚至达成了一项**合作协议**，以推进这些临床候选药物的发展，同时还达成了一项临床前合作协议，以针对另一种称为脂蛋白[a]或Lp[a]的蛋白质。此类协议带来了约 6000 万美元的大量预付款，并且还有可能赚取高达 4.65 亿美元的里程碑付款。这里的关键是，如果 HeFH 和 HoFH 的目标最终获得回报，那么该生物技术将能够瞄准数十亿美元的市场机会。

这篇文章的作者是

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12.1K 关注者

Terry Chrisomalis 是生物技术领域的私人投资者，拥有多年利用其应用科学背景从医疗保健领域创造长期价值的经验。他是投资小组Biotech Analysis Central的作者，该小组包含 600 多篇生物技术投资文章的库、包含 10 多只中小型股票的模型投资组合，并对每只股票进行深入分析、实时聊天以及一系列分析和新闻报告帮助医疗保健投资者做出明智的决定。了解更多。

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