Seeking Alpha α

引入 Verve 疗法

2024 年 1 月 14 日上午 8:45 美国东部时间 | **Verve Therapeutics, Inc. (VERV) 股票** | AMGN、REGN、NVS

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关于本文

股票行情指示器	分析师评级	出版时的价格	最后价格	自发布以来的变化	标准普尔 500 指数自发布以来发生变化
位置	抓住	**12.50 美元**	**15.14 美元**	**21.12%**	**6.42%**

自发布以来的天数
52

概括

Verve Therapeutics 旨在通过使用碱基编辑技术的体内基因治疗彻底改变心血管疾病的治疗。

他们的主要候选药物 VERVE-101 在临床前研究中显示出在降低 LDL-C 水平方面有希望的结果。

Verve 与 Beam Therapeutics、Eli Lilly 和 Vertex Pharmaceuticals 建立了合作伙伴关系，分析师对该公司前景持乐观态度。

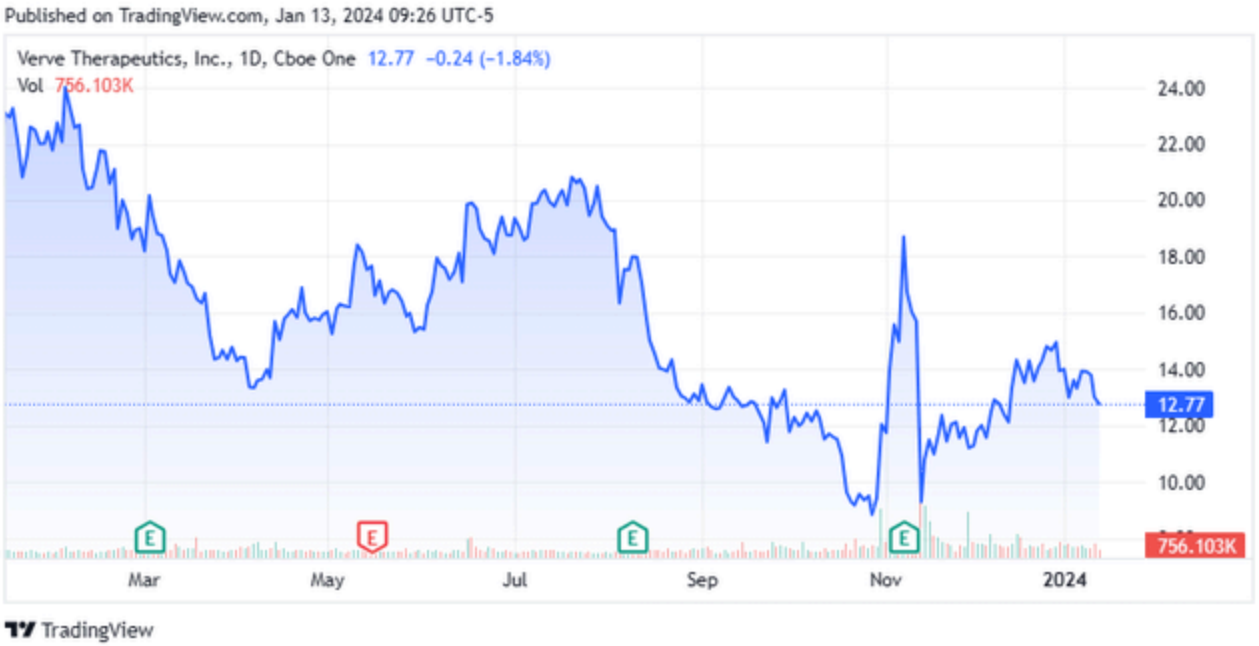
以下段落介绍了有关 Verve Therapeutics 股票的完整投资分析。

我是 Bret Jensen，一位在生物技术领域拥有多年经验的分析师。我领导生物技术论坛投资小组，我们专注于生物技术和生物制药股票的专有、突破性研究。

穆罕默德•哈内法•尼扎穆丁

追求吸引你心的东西，而不是吸引你眼睛的东西。”——罗伊·T·贝内特

今天，我们将**Verve Therapeutics （纳斯达克股票代码：VERV）**置于聚光灯下。Verve 旨在通过使用碱基编辑技术的体内基因治疗彻底改变治疗方法，其主要候选药物 VERVE-101 在降低 LDL-C 水平方面显示出有希望的结果。下面进行分析。



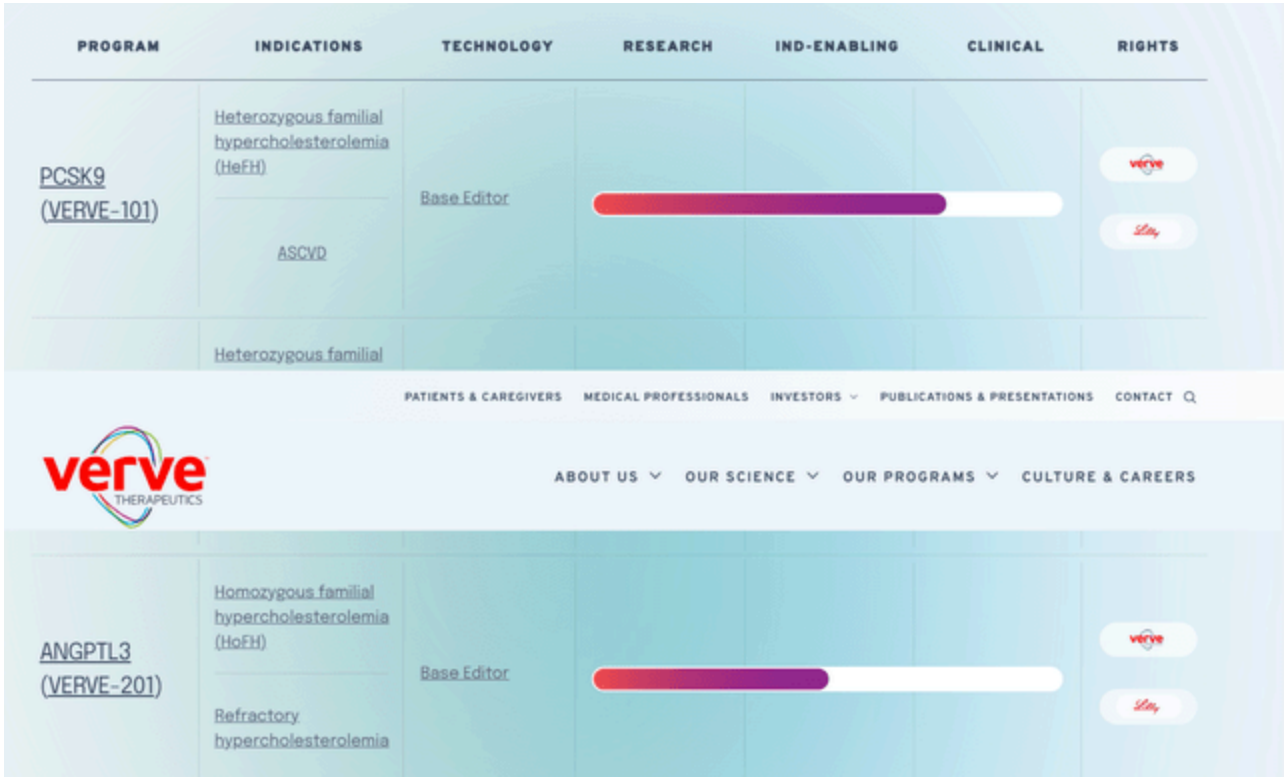
寻找阿尔法

公司简介

Verve Therapeutics, Inc. 是一家位于波士顿的早期临床阶段基因药物公司，专注于开发治疗心血管疾病 [CVD] 的单疗程编辑模式。该公司作为一个临床项目和另外两个正在进行 IND 支持的研究。Verve 于 2018 年开始运营，并于 2021 年 6 月上市，以每股 19 美元的价格筹集净收益 2.816 亿美元。首次公开募股(IPO)火热，开盘价为30美元，九个交易日后达到73.80美元，其股价每股略低于14.00美元，市值为10.5亿美元。

心血管疾病

该公司尝试减少 CVD 的主要目标是低密度脂蛋白胆固醇 (LDL-C)，这种化合物的促进作用很大程度上受到与 PCSK9 蛋白结合的影响。据信，LDL-C 会促进动脉粥样硬化斑块形成，进而发展为动脉硬化，这是动脉粥样硬化性 CVD (ASCVD) 的主要特征，表现为冠心病、缺血性中风和外周血管疾病。研究证实了这种相关性，研究表明，五年内 LDL-C 降低 39mg/dL，且已确诊 ASCVD，可将另一事件的风险降低 21%。在个体一生中，LDL-C 降低同样可以将首次 ASCVD 事件的风险降低 88%。



公司网站

The current paradigm for lowering LDL-C involves (first and foremost) daily ingestion of statin drugs, which according to Dr. Perlmutter in his book *Grain Brain*, ups the risk for Alzheimer's disease by 50%. Two monoclonal antibodies designed to bind to the PSCK9 protein have been approved - **Amgen's (AMGN)** Repatha (evolocumab) and **Regeneron's (REGN)** Praluent (alirocumab) - but they require twice monthly injections. Also, **Novartis' (NVS)** Leqvio (inclisiran) is a twice yearly small interfering RNA subcutaneous injection that likewise targets PCSK9. Across three studies, Leqvio demonstrated an LDL-C reduction of 47.4% at day 510. Blunt force workarounds include the insertion of stents and bypass surgery. Despite these 'advancements' in care, four out of five patients do not achieve their LDL-C goals and CVD remains the leading cause of death worldwide, with approximately one in three succumbing to the malady. Furthermore, according to the CDC, CVD saps over $350 billion annually out of American wallets (over $1,000 per citizen) in healthcare outlays and lost productivity.

Verve's Solution(s)

Verve aims to turn the current treatment paradigm on its head through single administration (*in vivo*) gene therapy that employs base editing technology. To further illustrate the company's approach, the currently en vouge CRISPR-Cas gene editing technology involves splicing the double-stranded DNA with the consequent self-repair designed to knockout the gene. By contrast, Verve's base editing strategy is akin to a pencil that erases and rewrites one letter in the gene. This is accomplished through a compound consisting of a lipid nanoparticle that encapsulates both the mRNA encoding for the gene (or base) editor and a guide RNA targeting the gene of interest. In theory, this more tailored and precise approach should lead to fewer unwanted DNA modifications or off-target editing effects. Although in its early stage, Verve is the only company advancing an *in vivo* CVD gene therapy in the clinic, giving it potential first-mover advantage.

VERVE-101

That candidate, VERVE-101, is designed to permanently disable the PCSK9 gene in the liver in order to knockout the production of PCSK9 protein. Through its reduction, the liver can more easily clear LDL-C from the blood. VERVE-101 is undergoing evaluation for the treatment of heterozygous familial hypercholesterolemia (HeFH), a genetic disorder characterized by LDL-C levels between 200 and 400mg/dL (normal/good: 70 to 130mg/dL) that afflicts ~1.3 million Americans. This is not to be confused with homozygous familial hypercholesterolemia (HoFH), which is characterized by two mutant alleles of the LDLR gene - HeFH has one mutated allele - and LDL-C levels north of 500mg/dL that afflicts ~1,300 Americans.

In the preclinic, a single one to two hour infusion of VERVE-101 was shown to reduce LDL-C levels by 50% (0.75mg/kg) and 68% (1.5mg/kg) in non-human primates at one-year post-treatment, which set that stage for a Phase 1b clinical trial (heart-1) that dosed its first of ~40 HeFH patients with established ASCVD in July 2022. However, the trial was only given a green light in New Zealand and the UK, as the FDA placed a hold on Verve's IND in December 2022, requesting various information, including available clinical data from heart-1, as well as a request to modify its trial protocol in the U.S. to (amongst other measures) increase the length of the staggering interval between dosing of participants.

The hold was finally lifted in October 2023 with first data from New Zealand and the UK released on November 12, 2023. The good news: the efficacy data was positive with the evaluable patients treated with a therapeutic level of VERVE-101 (0.45mg/kg n=2; 0.60mg/kg n=1) achieving LDL-C reductions of 39%, 48%, and 55% (0.60mg/kg patient) at least one month after infusion.

However, one patient in the low dose cohort (0.30mg/kg n=6) suffered a fatal heart attack (deemed not treatment related) while one patient in the 0.45mg/kg cohort experienced a Grade 3 myocardial infarction that was deemed potentially treatment related due to the proximity to dosing (one day post-treatment). It should be noted that the patient had unstable chest pain symptoms prior to dosing that went unreported to investigators. That same patient also suffered an unrelated Grade 2 non-sustained ventricular tachycardia (rapid heartbeat) four weeks post-treatment. This news sent shares of VERV into a one-day 41% decline to $9.29 a share, immediate squashing potentially positive news regarding its collaboration with **Beam Therapeutics (BEAM)** announced back on October 31, 2023. More on that development shortly.

Pre-Clinical Assets

In addition to VERVE-101, the company has similar functioning assets in the preclinic. One, VERVE-102, is essentially VERVE-101 with a modified delivery vehicle that includes a N-Acetylgalactosamine lipo-nanoparticle that permits introduction through either the LDLR receptor (like VERVE-101) or ASGPR hepatocyte receptor to lower LDL-C. Initiation of a Phase 1b study is expected in 1Q24.

Verve's other asset undergoing IND-enabling studies is VERVE-201, an ANGPTL3 targeting gene therapy for the treatment of HoFH that should enter the clinic in 2H24.

Collaboration News

The base editor technology for VERVE-101, -102, and -201 was in-licensed from Beam under a 2019 agreement that was amended in 2022. For the PCSK9 and ANGPTL3 gene therapies, after the final patient has been dosed in a Phase 1, Beam has the right to opt-in to each program, which constitutes covering 33% of the clinical expenses and a 50/50 share of profits in the U.S. An opt-in to a third gene target by Beam would obligate it to 35% of the development expenses and 35% of the profit share worldwide.

That arrangement was somewhat modified when Eli Lilly entered into an agreement with Beam to obtain certain product rights to all three Verve targets for a consideration of $200 million upfront, a $50 million equity investment in Beam, and potential milestone obligations totaling $350 million.

That news comes on the heels of Verve's own agreement with Lilly in June 2023, under which the latter obtained a license from the former to develop a lipoprotein(a) targeted gene therapy for the treatment of ASCVD for a consideration of $30 million upfront, a $30 million stock investment, potential milestones of $465 million, and high single-digit to low double-digit royalties. Verve has the option to forego the milestones and royalties by opting-in after Phase 1 for an undisclosed fee in return for a 40% of the profit share as well as 40% of the development expenses after Phase 1.

Verve also has a 2022 collaboration agreement with Vertex Pharmaceuticals (VRTX), under which it received a total initial consideration of $60 million ($25 million cash; $35 million equity investment) for one target. Vertex is potentially on the hook for milestones totaling $406 million and single digit royalties.

Balance Sheet & Analyst Commentary

Although the market reacted negatively to the early data on VERVE-101, the company executed secondary offerings on November 28, 2023, raising total net proceeds of $157.7 million at $10 per share, including a private placement purchased by Lilly that accounted for $23.0 million of the total funds raised. That should put cash and investments somewhere in the neighborhood of $610 million with one month remaining in 2023, providing a cash runway into 2026.

Despite the market's unenthusiastic reaction to VERVE-101 data, Street analysts lean positive on Verve. Since third quarter numbers were posted in early November, four analyst firms including RBC Capital and BMO Capital have reissued Buy ratings on the stock. Price targets proffered range from $32 to $56 a share. JP Morgan maintained its Hold rating and $27 price target.

GV 2023 GP, LLC, represented on the board by Krishna Yeshwant, purchased 1.8 million shares on the secondary, raising its ownership interest to 15%.

Verdict:

Net of balance sheet cash, the market values Verve's one-off, *in vivo* eraser-and-pencil approach at ~$450 million. There is little in the way of data, but there is also little in the way of competition for a one-and-done approach. Only **CRISPR Therapeutics (CRSP)** has a one-off *in vivo* asset on the drawing board (CTX330) targeting CVD and that is still in the discovery phase. Although very early in the game, if further safety data on VERVE-101 can validate that the adverse event in the 0.45mg/kg patient was a fluke - meaning higher dose levels are possible - Verve could be off to the races, as the efficacy aspect of its approach does not appear to be much in question.

Admittedly, this is a coin flip. However, a '*heads*' outcome not only produces a significant rise in its share price - shares of VERV traded at $78 shortly after the company's IPO in September 2021 - but also introduces the likelihood of a buyout by Eli Lilly, who is energetically perusing a meaningful stake in the CVD gene therapy arena. A *'tails*' outcome leaves the company with (currently) ~$7.50 a share in cash and two more assets entering the clinic in 2024. As such, for the risk tolerant, Verve is worthy of a small investment pending further developments.

> *When the heart speaks, the mind finds it indecent to object.*"– Milan Kundera

This article was written by

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Bret Jensen has over 13 years as a market analyst, helping investors find big winners in the biotech sector. Bret specializes in high beta sectors with potentially large investor returns.

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评论

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