UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE TO

TENDER OFFER STATEMENT UNDER SECTION 14(D)(1) OR 13(E)(1)
OF THE SECURITIES EXCHANGE ACT OF 1934
(AMENDMENT NO. 1)

ALPINE IMMUNE SCIENCES, INC.
(Name of Subject Company (Issuer))

ADAMS MERGER SUB, INC.
(Offeror)
a wholly owned subsidiary of

VERTEX PHARMACEUTICALS INCORPORATED
(Parent of Offeror)
(Names of Filing Persons (identifying status as offeror, issuer or other person))

Common stock, $0.001 par value per share
(Title of Class of Securities)

02083G100
(CUSIP Number of Class of Securities)

Jonathan Biller
Executive Vice President, Chief Legal Officer
Vertex Pharmaceuticals Incorporated
50 Northern Avenue
Boston, Massachusetts 02210
Telephone: (617) 341-6100
(Name, address and telephone number of person authorized to receive notices and communications on behalf of filing persons)

Copies to:

Graham Robinson
Skadden, Arps, Slate, Meagher & Flom LLP
500 Boylston Street
Boston, MA 02116
(617) 573-4850

Faiz Ahmad
Skadden, Arps, Slate, Meagher & Flom LLP
One Rodney Square
920 N. King Street
Wilmington, DE 19801
(302) 651-3250

☐ Check the box if the filing relates solely to preliminary communications made before the commencement of a tender offer.

Check the appropriate boxes below to designate any transactions to which the statement relates:

- ☒ Third-party tender offer subject to Rule 14d-1.
- ☐ Issuer tender offer subject to Rule 13e-4.
- ☐ Going-private transaction subject to Rule 13e-3.
- ☐ Amendment to Schedule 13D under Rule 13d-2.

Check the following box if the filing is a final amendment reporting the results of the tender offer: ☐

If applicable, check the appropriate box(es) below to designate the appropriate rule provision(s) relied upon:

- ☐ Rule 13e-4(i) (Cross-Border Issuer Tender Offer).
- ☐ Rule 14d-1(d) (Cross-Border Third-Party Tender Offer).

This Amendment No. 1 to the Tender Offer Statement on Schedule TO (this "Amendment") amends and supplements the Tender Offer Statement on Schedule TO filed with the Securities and Exchange Commission (the "SEC") on April 22, 2024 (as it may be further amended and supplemented from time to time, the "Schedule TO") and relates to the offer by Adams Merger Sub, Inc., a Delaware corporation and a wholly owned subsidiary of Vertex Pharmaceuticals Incorporated ("Vertex"), a Massachusetts corporation, to purchase all of the issued and outstanding shares of common stock, par value $0.001 per share (the "Shares"), of Alpine Immune Sciences, Inc., a Delaware corporation, at a purchase price of $65.00 per Share, net to the seller in cash, without interest thereon and subject to any applicable tax withholding, upon the terms and subject to the conditions described in the Offer to Purchase dated April 22, 2024 (together with any amendments or supplements thereto, the "Offer to Purchase") and in the accompanying Letter of Transmittal (together with the Offer to Purchase, as each may be amended or supplemented from time to time, collectively constitute the "Offer"), which are annexed to and filed with the Schedule TO as Exhibits (a)(1)(A) and (a)(1)(B), respectively.

The Offer will expire at one minute past 11:59 p.m., Eastern Time, on May 17, 2024, unless the expiration of the Offer is extended to a subsequent date in accordance with the terms of the Merger Agreement (such date and time or such subsequent time on such subsequent date, the "Expiration Time"). In the case of an extension of the Expiration Time, a public announcement of such extension will be made no later than 9:00 a.m., Eastern Time, on the business day after the previously scheduled Expiration Time. The terms and conditions relating to the Offer, including the procedures regarding the extension of the Expiration Time, are described in the Offer to Purchase.

Except as otherwise set forth in this Amendment, the information set forth in the Schedule TO remains unchanged and is incorporated herein by reference to the extent relevant to the items in this Amendment. Capitalized terms used but not defined herein have the respective meanings ascribed to them in the Schedule TO.

Items 1, 4, 6, 7 and 11.

The Offer to Purchase and Items 1, 4, 6, 7 and 11 of the Schedule TO are hereby amended and supplemented as follows:

The information set forth on page 47, in the existing second paragraph under the subheading "Antitrust Compliance" in Section 16 — "Certain Legal Matters; Regulatory Approvals" of the Offer to Purchase is amended and supplemented as follows (new language underlined; deleted language struck through):

Vertex and Alpine ~~expect to~~ filed their respective Premerger Notification and Report Forms pursuant to the HSR Act (the "HSR Notification Forms") with the FTC and the DOJ on ~~or prior to~~ April 24, 2024, which filing ~~will~~ initiated a 15-day waiting period.

Items 4, 5, 9 and 11.

The Offer to Purchase and Items 4, 5, 9 and 11 of the Schedule TO are hereby amended and supplemented as follows:

The information set forth on page 18, in the existing seventh paragraph under the subheading "Background of the Offer" in Section 10 — "Background of the Offer; Past Contacts or Negotiations with Alpine" of the Offer to Purchase is amended and supplemented as follows (new language underlined; deleted language struck through):

On April 4, 2024, the Vertex ~~Transaction Committee~~ Board met to discuss the status and strategy of the potential transaction with Alpine. The Vertex ~~Transaction Committee~~ Board reviewed the ongoing diligence which Vertex had conducted and further considered deal strategy, economic terms, and potential next steps for engagement with Alpine.

Item 12. Exhibits.

Item 12 of the Schedule TO is hereby amended and supplemented by adding the following exhibits:

Exhibit No.	Description
(a)(5)(D)	Press Release dated May 6, 2024 (incorporated herein by reference to Exhibit 99.1 of the Current Report on Form 8-K filed by Vertex Pharmaceuticals Incorporated with the SEC on May 6, 2024).
(a)(5)(E)*	Slide Excerpts from Vertex Q1 Earnings Call Presentation on May 6, 2024.
(a)(5)(F)*	Transcript of Vertex Q1 Earnings Call on May 6, 2024.

* filed herewith

SIGNATURE

After due inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

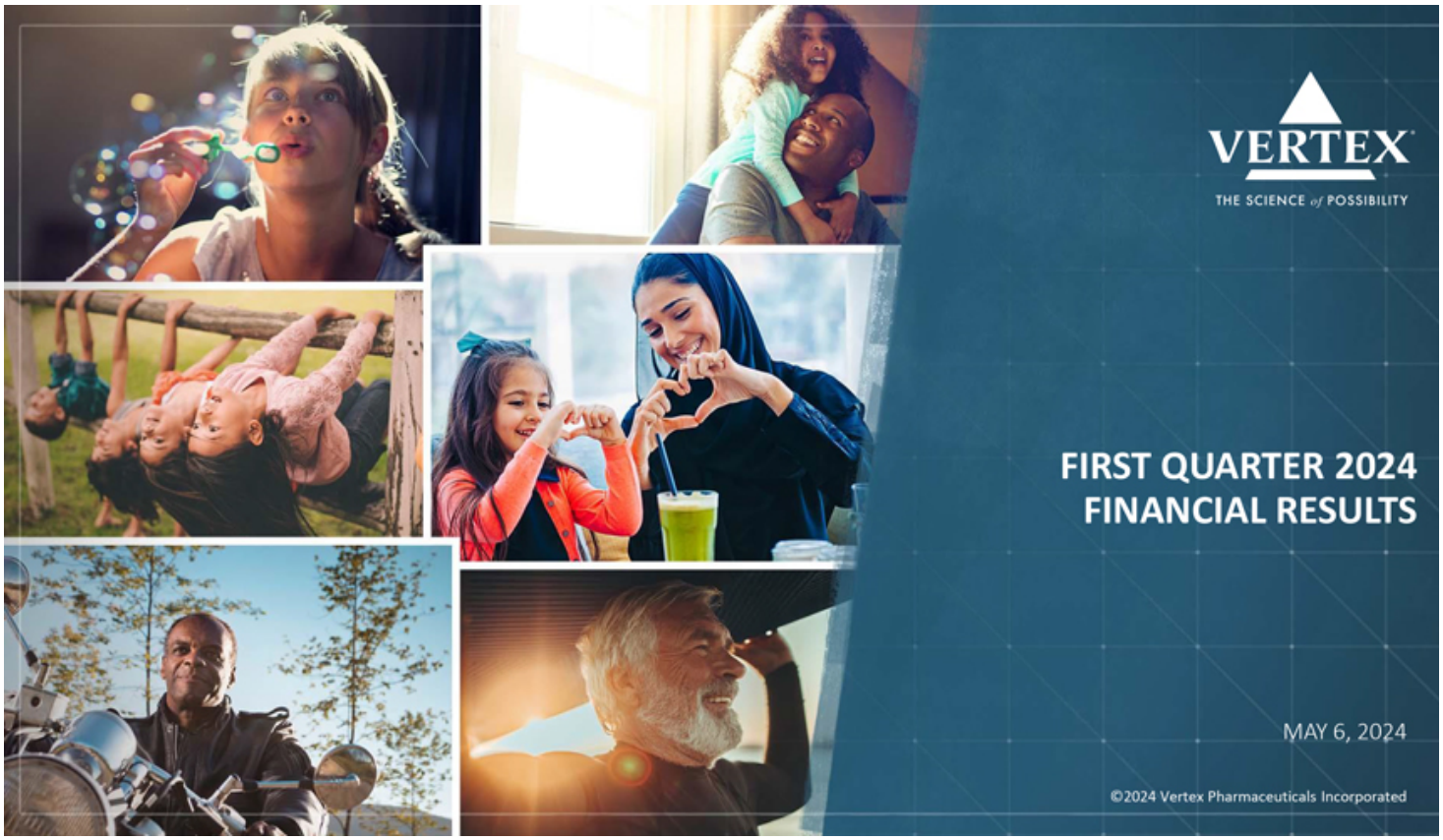
Dated: May 8, 2024.

ADAMS MERGER SUB, INC.

By: /s/ Jonathan Biller
Name: Jonathan Biller
Title: Secretary

VERTEX PHARMACEUTICALS INCORPORATED

By: /s/ Jonathan Biller
Name: Jonathan Biller
Title: Executive Vice President and Chief Legal Officer


VERTEX
THE SCIENCE of POSSIBILITY
FIRST QUARTER 2024
FINANCIAL RESULTS
MAY 6, 2024
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SAFE HARBOR STATEMENT & NON-GAAP FINANCIAL MEASURES

This presentation contains forward-looking statements that are subject to risks, uncertainties and other factors. All statements other than statements of historical fact are statements that could be deemed forward-lookin statements, including all statements regarding the intent, belief, or current expectation of Vertex and members of the Vertex senior management team. Forward-looking statements are not purely historical and may b accompanied by words such as "anticipates," "may," "forecasts," "expects," "intends," "plans," "potentially," "believes," "seeks," "estimates," and other words and terms of similar meaning. Such statements include, witho limitation, the information provided regarding and expectations for future financial and operating performance, the section captioned "Reiterate-Full Year 2024 Financial Guidance," and statements regarding (i) expectation development plans and timelines for the company's products and pipeline programs, including expectations for anticipated near-term commercial launch opportunities in CF and acute pain, anticipated benefits of ne products and relevant patient populations, and plans to broaden and deepen R&D pipeline across modalities, (ii) expectations, plans, and the anticipated timeline for the acquisition of Alpine Immune Sciences, Inc. (Alpine including with respect to the therapeutic scope of Alpine and potential benefits of povetacicept, our beliefs regarding povetacicept's target patient population, and our beliefs regarding the clinical progress and availability clinical data for Alpine's pipeline, (iii) expectations for the vanzacaftor triple, including the anticipated benefits and plans to complete various global regulatory submissions in 2024 and preparations for commercial launch multiple geographies, (iv) expectations regarding VX-522 to reach the >5,000 CF patients who cannot benefit from a CFTR modulator, VX-522 study progress and plans to have VX-522 data in late 2024/early 2025, (expectations for our acute pain program, including plans for near-term launch and commercial potential, beliefs regarding the potential benefits of suzetrigine as a non-opioid treatment option, expectations regarding th target profile for suzetrigine, plans to complete the suzetrigine U.S. regulatory submission in the second quarter of 2024, plans to initiate Phase 2 studies of the oral formulation of VX-993 later this year, plans to enro patients in the Phase 1 study of the intravenous formulation of VX-993, and our expectations, plans, and beliefs regarding the commercial potential of suzetrigine, including as multi-billion dollar opportunity, the treatab patient population, and potential impactful legislation, (vi) expectations for our PNP pain program, including plans to seek a broad PNP label, plans to advance suzetrigine in DPN into Phase 3 pivotal development in th second half of 2024, enrollment and dosing plans for the Phase 2 study of suzetrigine in LSR, plans to advance an oral formulation of VX-993 into a Phase 2 study in PNP in 2024, and plans to advance additional NaV 1.7 an NaV1.8 inhibitors, (vii) expectations for our T1D program, including the potential benefits of VX-880, expectations for completion of dosing in the global VX-880 study, plans for VX-880 data, and beliefs regarding the treatab T1D patient population, (viii) expectations regarding our CF program, (ix) expectations for CASGEVY, including the potential benefits for patients with SCD or TDT, expectations for on-going commercial launch, expectatio with respect to access and reimbursement, expectations for additional approvals, and plans for studies in younger age groups. While Vertex believes the forward-looking statements contained in this presentation ar accurate, these forward-looking statements represent the company's beliefs as of the date of this presentation and there are risks and uncertainties that could cause actual events or results to differ materially from thos expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that data from clinical trials, especially if based on a limited number of patients, may not to be indicative final results, the company may not be able to complete, successfully integrate, or profit from the Alpine acquisition, the company's regulatory submissions may be delayed, actual patient populations eligible for our product may be smaller than anticipated, data from the company's development programs may not be available on expected timelines, or at all, support registration or further development of its potential medicines due to safet efficacy or other reasons, and other risks listed under the heading "Risk Factors" in Vertex's annual report and subsequent quarterly reports filed with the Securities and Exchange Commission at www.sec.gov and availabl through the company's website at www.vrtx.com. You should not place any undue reliance on these statements, or the data presented. Vertex disclaims any obligation to update the information contained in this presentatio as new information becomes available.

In this presentation, Vertex's financial results and financial guidance are provided in accordance with accounting principles generally accepted in the United States (GAAP) and using certain non-GAAP financial measures. In particular, non-GAAP financial results and guidance exclude from Vertex's pre-tax income (i) stock-based compensation expense, (ii) intangible asset amortization expense, (iii) gains or losses related to the fair value of the company's strategic investments, (iv) increases or decreases in the fair value of contingent consideration, (v) acquisition-related costs, and (vi) other adjustments. The company's non-GAAP financial results also exclude from its provision for income taxes the estimated tax impact related to its non-GAAP adjustments to pre-tax income described above and certain discrete items. These results should not be viewed as a substitute for the company' GAAP results and are provided as a complement to results provided in accordance with GAAP. Management believes these non-GAAP financial measures help indicate underlying trends in the company's business, are important in comparing current results with prior period results and provide additional information regarding the company's financial position that the company believes is helpful to an understanding of its ongoing business. Management also uses these non-GAAP financial measures to establish budgets and operational goals that are communicated internally and externally, to manage the company's business and to evaluate its performance. Th company's calculation of non-GAAP financial measures likely differs from the calculations used by other companies. The company provides guidance regarding combined R&D, Acquired IPR&D and SG&A expenses and effective tax rate on a non-GAAP basis. Unless otherwise noted, the guidance regarding combined GAAP and non-GAAP R&D, Acquired IPR&D and SG&A expenses does not include estimates associated with any potential future business development transactions, including collaborations, asset acquisitions and/or licensing of third-party intellectual property rights. The company does not provide guidance regarding its GAAP effective tax rate because it is unable to forecast with reasonable certainty the impact of excess tax benefits related to stock-based compensation and the possibility of certain discrete items, which could be material. Non-GAAP financial measures are presented compared to corresponding GAAP measures in the appendix hereto. A reconciliation of the GAAP financial results to non-GAAP financial results is included in the company's Q1 2024 press release dated May 6, 2024.

ACQUISITON OF ALPINE IMMUNE SCIENCES:
$65/SHARE, ~$4.9B CASH

Announced 4/10/24; expected close Q2:24

- Compelling fit with the Vertex strategy of investing in serial innovation to create transformative medicines that target serious diseases with high unmet need in specialty markets
- Alpine's lead asset, povetacicept ("pove"), is a Phase 3-ready, innovative, and potentially transformative approach to IgAN, a serious, progressive, autoimmune kidney disease
  - Best-in-class potential; Phase 3 trial to begin H2:24
- Povetacicept, given dual BAFF/APRIL inhibition, also offe promise of "pipeline-in-a-product" in multiple other serious diseases, including pMN, LN, and autoimmune cytopenias
- Vertex capabilities expected to accelerate povetacicept development in IgAN and other indications, while Alpine will add protein engineering and immunotherapy expertise to Vertex

BAFF: B-cell activating factor; APRIL: a proliferation-inducing ligand; IgAN: immunoglobulin A nephropathy; pMN: primary membranous nephropathy; LN: lupus nephritis

ALPINE IMMUNE SCIENCES ACQUISITION: POVETACICEPT HAS SHOWN BEST-IN-CLASS POTENTIAL WITH IMPORTANT MILESTONES IN H2:2024

Best-in-class potential

- High affinity and potency against both BAFF and APRIL pathways in pre-clinical assays
- Differentiated efficacy in both human B-cell depletion assays and models of disease
- Strong benefit:risk profile demonstrated through Phase 2

Well-tolerated in clinical studies to date

- Well-tolerated with dose-dependent PK/PD in Phase 1 (healthy volunteers)
- In RUBY3, povetacicept 80 mg was well-tolerated with no severe infections to date[1]

Compelling activity in IgAN

- RUBY-3 data with povetacicept 80 mg reduced UPCR by ~45% at 24 weeks (n=10); >60% at 36 weeks (n=6); and >70% at 48 weeks (n=1)[1]

Convenient delivery

- Once every four weeks, subcutaneous, small volume dosing

Upcoming milestones

- H2:24 milestones include initiation of Phase 3 study in IgAN and potential readouts in multiple indications from ongoing RUBY-3 and RUBY-4 basket studies in autoimmune renal diseases and cytopenias, respectively

[1] "Povetacicept, an Enhanced Dual BAFF/APRIL Antagonist, in Autoantibody-Associated Glomerulonephritis (GN)" poster presentation at ASN Kidney Week, Nov. 2, 2023; Alpine Immune Sciences press release April 10, 2024

Alpine Immune Sciences acquisition is expected to close in Q2:24, subject to majority tender and customary closing conditions.

ADDITIONAL INFORMATION ABOUT THE ACQUISITION AND WHERE TO FIND IT

The tender offer for the outstanding shares of common stock of Alpine Immune Sciences, Inc. referenced in this presentation commenced on April 22, 2024. This presentation is for informational purposes only and is neither an offer to purchase nor a solicitation of an offer to sell shares of Alpine Immune Sciences, Inc., nor is it a substitute for any tender offer materials that Vertex or Alpine Immune Sciences, Inc. have filed with the SEC. On April 22, 2024, when the tender offer commenced, Vertex filed with the SEC a Tender Offer Statement on Schedule TO which included an Offer to Purchase, a related Letter of Transmittal and certain other tender offer documents (together, the "Tender Offer Materials"), and Alpine Immune Sciences, Inc. filed with the SEC a Solicitation/Recommendation Statement on Schedule 14D-9 (the "Solicitation/Recommendation Statement") with respect to the tender offer. ALPINE IMMUNE SCIENCES, INC. SECURITY HOLDERS ARE URGED TO READ THE TENDER OFFER MATERIALS AND THE SOLICITATION/RECOMMENDATION STATEMENT BECAUSE THEY CONTAIN IMPORTANT INFORMATION WHICH SHOULD BE READ CAREFULLY BEFORE ANY DECISION IS MADE WITH RESPECT TO THE TENDER OFFER. The Tender Offer Materials and the Solicitation/Recommendation Statement are available for free at the SEC's website at www.sec.gov. Additional copies of the Tender Offer Materials can be obtained free of charge under the "Investors" section of Vertex's website at https://investors.vrtx.com/financial-information/sec-filings or by contacting Vertex by phone at (617) 341-6108, by email at Investorinfo@VRTX.com, or by directing requests for such materials to the information agent for the offer, which is named in the Tender Offer Materials. In addition to the Tender Offer Materials and the Solicitation/Recommendation Statement, Alpine Immune Sciences, Inc. and Vertex file periodic reports and other information with the SEC. Vertex's and Alpine Immune Sciences, Inc.'s filings with the SEC are also available for free to the public from commercial document-retrieval services, at the website maintained by the SEC at www.sec.gov, and their respective investor relations websites.

● Event Details

Date: 2024-05-06
Company: Vertex Pharmaceuticals, Inc.

Ticker: VRTX-US

● Company Participants

Susie Lisa - Vertex Pharmaceuticals, Inc., Senior Vice President-Investor Relations
Reshma Kewalramani - Vertex Pharmaceuticals, Inc., President, Chief Executive Officer & Director
Stuart A. Arbuckle - Vertex Pharmaceuticals, Inc., Executive Vice President & Chief Operating Officer
Charles F. Wagner - Vertex Pharmaceuticals, Inc., Executive Vice President & Chief Financial Officer

● Other Participants

Geoff Meacham - Analyst
Jessica Fye - Analyst
Salveen Richter - Analyst
Evan David Seigerman - Analyst
Colin Nigel Bristow - Analyst
Terence C. Flynn - Analyst
Philip Nadeau - Analyst
Olivia Brayer - Analyst
Debjit Chattopadhyay - Analyst
Liisa A. Bayko - Analyst

MANAGEMENT DISCUSSION SECTION

Operator

00:00:10 Good day and welcome to the Vertex Pharmaceuticals First Quarter 2024 Earnings Conference Call. All participants will be in a listen-only mode. After today's presentation, there will be an opportunity to ask questions.

00:00:21 I would now like to turn the conference over to Ms. Susie Lisa. Please go ahead.

Susie Lisa

00:00:26 Good evening, all. My name is Susie Lisa, and as the Senior Vice President of Investor Relations, it is my pleasure to welcome you to our first quarter 2024 financial results conference call. On tonight's call, making prepared remarks, we have Dr. Reshma Kewalramani, Vertex's CEO and President; Stuart Arbuckle, Chief Operating Officer; and Charlie Wagner, Chief Financial Officer.

00:00:47 We recommend that you access the webcast slides as you listen to this call. The call is being recorded, and a replay will be available on our website. We will make forward-looking statements on this call that are subject to the risks and uncertainties discussed in detail in today's press release and in our filings with the Securities and Exchange Commission.

00:01:05 These statements including, without limitation, those regarding Vertex's marketed medicines for cystic fibrosis, sickle cell disease and beta thalassemia; our pipeline; Vertex's anticipated acquisition of Alpine Immune Sciences; and Vertex's future financial performance are based on management's current assumptions. Actual outcomes and events could differ materially.

00:01:28 I would also note that select financial results and guidance that we will review on the call this evening are presented on a non-GAAP basis. In addition, the impact of foreign exchange is presented inclusive of our foreign exchange risk management program.

00:01:42 I will now turn the call over to Reshma.

Reshma Kewalramani

00:04:00 Alpine's lead asset, povetacicept or pove, is a potential best-in-class Phase 3-ready molecule for IgA nephropathy or IgAN, a disease with high unmet need. Pove is also a molecule that holds a pipeline-in-a-product potential in a number of other serious autoimmune renal diseases and cytopenias in Phase 2 development. We see the acquisition as just the right fit with just the right assets at just the right phase of development where Vertex's capabilities can accelerate pove's development in IgAN and other indications.

00:04:39 And lastly, Alpine will add protein engineering and immunotherapy expertise to Vertex's capabilities, with particular relevance for our development programs in gentler conditioning for CASGEVY and immune evasion for our type 1 diabetes cell therapies. We are excited to begin working with the Alpine team, and together, advance pove into Phase 3 in IgAN later this year.

00:14:01 I'll conclude with a few comments on povetacicept, the lead asset from our pending acquisition of Alpine Immune Sciences. We are excited about the potential of povetacicept across multiple dimensions including: preclinically with its high affinity and potency against both APRIL and BAFF pathways in preclinical assays, as well as high efficacy in cell and animal models of B cell-driven diseases; clinically, with patient data in IgAN through Phase 2 that look potentially best-in-class in proteinuria, in hematuria, GFR and clinical remission; better drug-like properties with direct patient benefit, including once every four week dosing subcutaneously with low injection volume; a good safety and tolerability profile; the broadest development plan in the field; and a robust IP portfolio. Important upcoming pove milestones in the second half of this year include initiation of the Phase 3 study in IgAN and readouts from the ongoing RUBY-3 and RUBY-4 basket studies in autoimmune renal diseases and cytopenias, respectively.

Charles F. Wagner

00:29:26 First quarter 2024 non-GAAP earnings per share were $4.76, including benefits from revenue and expense phasing, as well as a lower tax rate, compared to $3.05 in the first quarter of 2023. We ended the quarter with $14.6 billion in cash and investments. We will use a portion of this cash on hand to fund the $4.9 billion acquisition of Alpine Immune Sciences, which is expected to close this quarter, subject to certain customary conditions.

00:29:56 Alpine is a prime example of our priority for capital deployment, to invest in innovation, including external innovation via business development. We see multibillion-dollar potential for Phase 3- ready povetacicept, given its transformative and best-in-class potential in IgAN, a disease area with high unmet need. We also look forward to exploring pove's full potential in other serious diseases. Additionally, we deployed over $140 million of cash in the first quarter to repurchase 336,000 shares.

00:30:59 For total Vertex operating expenses, we continue to project $4.3 billion to $4.4 billion in full year 2024 combined non-GAAP SG&A, R&D and acquired IPR&D. This operating expense range continues to include approximately $125 million in currently anticipated IPR&D charges. Upon the close of the Alpine acquisition, we expect Alpine's projected non-GAAP operating expenses for the remainder of 2024 to be absorbed within this guidance range, but note the potential impacts of transaction accounting, including any potential acquired IPR&D charges will be determined at the time of closing.

00:32:10 Importantly, we also announced the anticipated acquisition of Alpine Immune Sciences, a compelling fit with Vertex's strategy. Post-close, we aim to leverage Vertex's clinical, regulatory and commercial capabilities to accelerate development and commercialization of Pove. We are targeting approval in IgAN in 2027 and contribution to Vertex's revenue growth and diversification beginning in 2028, leveraging a specialty market approach with attractive margins.

Operator

00:33:26 We will now begin the question-and-answer session. Go ahead, Ms. Susie.

Operator

00:56:53 The next question will come from Debjit Chattopadhyay with Guggenheim Securities. Please go ahead.

Analyst: Debjit Chattopadhyay

00:57:00 Question – Debjit Chattopadhyay: Hey. Good afternoon. I've got a couple. First, on IgAN, when Vertex is ready to launch in IgAN, it's likely Otsuka will have GFR data. How are you thinking about navigating this commercially? And then, on DM1, with the IND cleared and the Phase 1/2 underway, do you think myotonia is an approvable endpoint or is the agency going to ask for splicing correction with strength or force (00:57:27) measurements? Thanks so much.

Answer – Reshma Kewalramani:

00:58:37 On IgA nephropathy, so the most important things to know about IgA nephropathy is that it's a serious chronic disease, and this is a disease that over time leads to decline in GFR and end-stage renal disease, death, or transplantation. The most important thing that I would be looking at as a nephrologist is efficacy, because proteinuria is known to translate to GFR, and therefore, the decline in renal function. So, if we have a medicine that has high reductions in proteinuria, and as I said in my prepared remarks, everything that we've seen from pove preclinically and clinically through Phase 2 is best-in-class across many dimensions, but certainly including efficacy, I think that's the drug that physicians will choose.

Analyst: Liisa A. Bayko

00:59:53 Question – Liisa A. Bayko: Hi. Thanks for squeezing me in. So, just two from me. Just a follow-up on IgA nephropathy. Have you thought any more about how you might highlight having BLyS, because in addition to APRIL, I think that's one kind of key differentiator of this program? And just wondering how you're thinking about how you could differentiate on that point. I don't know if there's biopsies or some kind of different point that you could really highlight the potential benefits of BLyS. And then, just for CF and TRIKAFTA for the quarter, I noticed you had your price increase, yet sales looked slightly down quarter-over-quarter. Can you kind of just describe in the US what's going on? Was there some higher gross-to-net, inventory changes, whatnot? That'd be great for some color there. Thank you so much.

01:00:46 Answer – Reshma Kewalramani: Thanks, Liisa. Let me take the IgAN question first, and then I'll ask Charlie to comment on CF. On IgAN, you are correct in pointing out that it's a dual inhibitor. It's an inhibitor of BAFF as well as APRIL, and this is one of the most attractive features of povetacicept is this dual inhibition. Yes, preclinically, we can certainly share and we have information, and you'll certainly see all of this with the fullness of time, the inhibition of BAFF and the measurement of that and how we can show that preclinically. We can also do that with APRIL.

01:01:29 However, I think the data that's more interesting is the clinical data which is already available and that is with this dual APRIL, BAFF inhibitor on proteinuria. But I'd encourage you to look at the poster from the WCN Meeting that Alpine showed. It has proteinuria results. It has hematuria results. It has GFR results and it has a composite of remission. And I find those data very, very interesting, particularly the hematuria results clinically, because as you know, hematuria is a hallmark of this disease along with proteinuria. Let me turn it over to Charlie on the question about CF and US.

Operator

01:02:53 This concludes our question-and-answer session, as well as our conference call for today. Thank you for attending today's presentation. A replay of today's event will be available shortly after the call concludes by dialing 1-877-344-7529 or 1-412-317-0088 using replay access code 10186968. Again, that is 10186968. Thank you for your time today. You may now disconnect.

Special Note Regarding Forward-Looking Statements

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(Alpine), including with respect to the therapeutic scope of Alpine and potential benefits of povetacicept, our beliefs regarding povetacicept’s target patient population, and our beliefs regarding the clinical progress and availability of clinical data for Alpine’s pipeline, (iii) expectations for the vanzacaftor triple, including the anticipated benefits and plans to complete various global regulatory submissions in 2024 and preparations for commercial launch in multiple geographies, (iv) expectations regarding VX-522 to reach the >5,000 CF patients who cannot benefit from a CFTR modulator, VX-522 study progress and plans to have VX-522 data in late 2024/early 2025, (v) expectations for our acute pain program, including plans for near-term launch and commercial potential, beliefs regarding the potential benefits of suzetrigine as a non-opioid treatment option, expectations regarding the target profile for suzetrigine, plans to complete the suzetrigine U.S. regulatory submission in the second quarter of 2024, plans to initiate Phase 2 studies of the oral formulation of VX-993 later this year, plans to enroll patients in the Phase 1 study of the intravenous formulation of VX-993, and our expectations, plans, and beliefs regarding the commercial potential of suzetrigine, including as multi-billion dollar opportunity, the treatable patient population, and potential impactful legislation, (vi) expectations for our PNP pain program, including plans to seek a broad PNP label, plans to advance suzetrigine in DPN into Phase 3 pivotal development in the second half of 2024, enrollment and dosing plans for the Phase 2 study of suzetrigine in LSR, plans to advance an oral formulation of VX-993 into a Phase 2 study in PNP in 2024, and plans to advance additional NaV 1.7 and NaV1.8 inhibitors, (vii) expectations for our T1D program, including the potential benefits of VX-880, expectations for completion of dosing in the global VX-880 study, plans for VX-880 data, and beliefs regarding the treatable T1D patient population, (viii) expectations regarding our CF program, (ix) expectations for CASGEVY, including the potential benefits for patients with SCD or TDT, expectations for on-going commercial launch, expectations with respect to access and reimbursement, expectations for additional approvals, and plans for studies in younger age groups. While Vertex believes the forward-looking statements contained in this transcript are accurate, these forward-looking statements represent the company’s beliefs as of the date of this transcript and there are risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that data from clinical trials, especially if based on a limited number of patients, may not to be indicative of final results, the company may not be able to complete, successfully integrate, or profit from the Alpine acquisition, the company’s regulatory submissions may be delayed, actual patient populations eligible for our products may be smaller than anticipated, data from the company’s development programs may not be available on expected timelines, or at all, support registration or further development of its potential medicines due to safety, efficacy or other reasons, and other risks listed under the heading “Risk Factors” in Vertex’s annual report and subsequent quarterly reports filed with the Securities and Exchange Commission at www.sec.gov and available through the company’s website at www.vrtx.com. You should not place any undue reliance on these statements, or the data presented. 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