



THE SCIENCE *of* POSSIBILITY

VERTEX PHARMACEUTICALS ACQUISITION OF ALPINE IMMUNE SCIENCES

APRIL 10, 2024

©2024 Vertex Pharmaceuticals Incorporated

SAFE HARBOR STATEMENT

This presentation contains forward-looking statements related to Vertex, Alpine and the proposed acquisition of Alpine by Vertex (the “Transaction”) that are subject to risks, uncertainties and other factors. While Vertex believes the forward-looking statements contained in this communication are accurate, these forward-looking statements represent Vertex’s belief only as of the date of this communication, and there are a number of risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. All statements other than statements of historical fact are statements that could be deemed forward-looking statements, including all statements regarding the intent, belief or current expectation of the companies’ and members of their senior management teams. Forward-looking statements are not purely historical and may be 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 may relate to: the ability of Vertex to advance Alpine’s platform technology and potential therapies, such as povetacicept, on a timely basis; filings and approvals relating to the Transaction; the expected timing of the completion of the Transaction; the ability to complete the Transaction considering the various closing conditions; difficulties or unanticipated expenses in connection with integrating the companies; and any assumptions underlying any of the foregoing.

Forward-looking statements are subject to certain risks, uncertainties, or other factors that are difficult to predict and could cause actual events or results to differ materially from those indicated in any such statements due to a number of risks and uncertainties. Those risks and uncertainties that could cause the actual results to differ from expectations contemplated by forward-looking statements include, among other things: uncertainties as to the timing of the Transaction; uncertainties as to how many of Alpine’s stockholders will tender their stock in the offer; the possibility that competing offers will be made; the possibility that various closing conditions for the Transaction may not be satisfied or waived, including that a governmental entity may prohibit, delay or refuse to grant approval for the consummation of the Transaction; the effects of the Transaction on relationships with employees, other business partners or governmental entities; the difficulty of predicting the timing or outcome of FDA approvals or actions, if any; the impact of competitive products and pricing; that Vertex may not realize the potential benefits of the Transaction; other business effects, including the effects of industry, economic or political conditions outside of the companies’ control; Transaction costs; and actual or contingent liabilities related to the Transaction. In addition, the product candidates being developed by Alpine are subject to all the risks inherent in the drug development process, and there can be no assurance that the development of these product candidates will be commercially successful. Forward-looking statements in this communication should be evaluated together with the many uncertainties that affect Vertex’s and Alpine’s businesses, particularly those risks listed under the heading “Risk Factors” and the other cautionary factors discussed in the parties’ periodic reports filed with the SEC, including Vertex’s annual report on Form 10-K for the year ended December 31, 2023, and its quarterly reports on Form 10-Q and current reports on Form 8-K, and Alpine’s annual report on Form 10-K for the year ended December 31, 2023, and its quarterly reports on Form 10-Q and current reports on Form 8-K, as well as the Solicitation/Recommendation Statement to be filed by Alpine and the Tender Offer Materials to be filed by Vertex and Adams Merger Sub, Inc., a direct wholly owned subsidiary of Vertex, all of which are available, or will be available when filed, for free on the SEC’s website at www.sec.gov. You should not place undue reliance on these statements. All forward-looking statements are based on information currently available to Vertex, and Vertex disclaims any obligation to update the information contained in this communication as new information becomes available, except as required by law.

ACQUISITION OF ALPINE IMMUNE SCIENCES FOR ~\$4.9B CASH

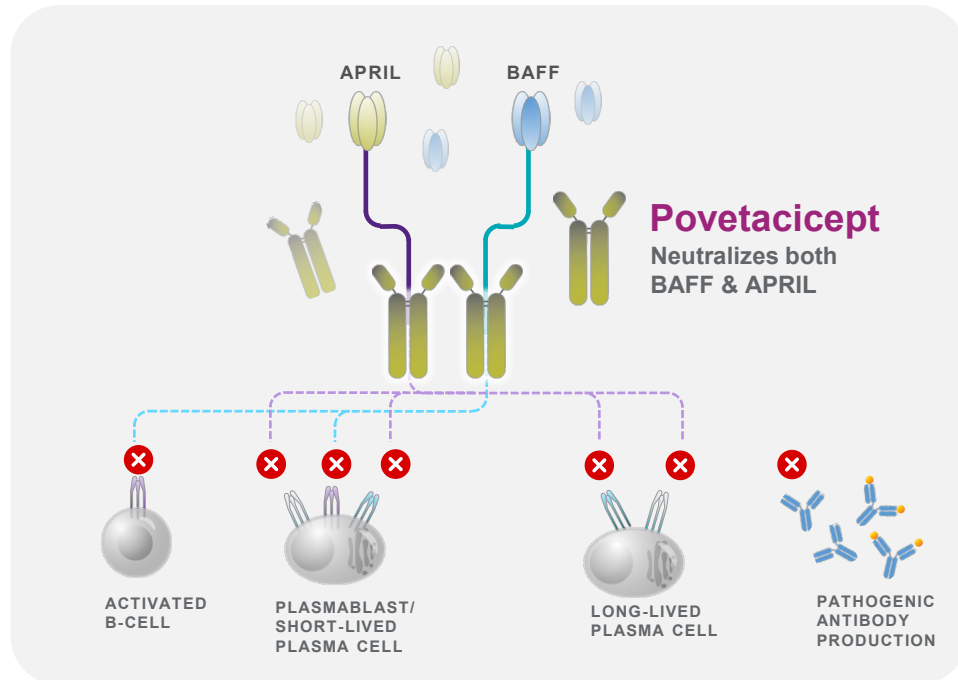
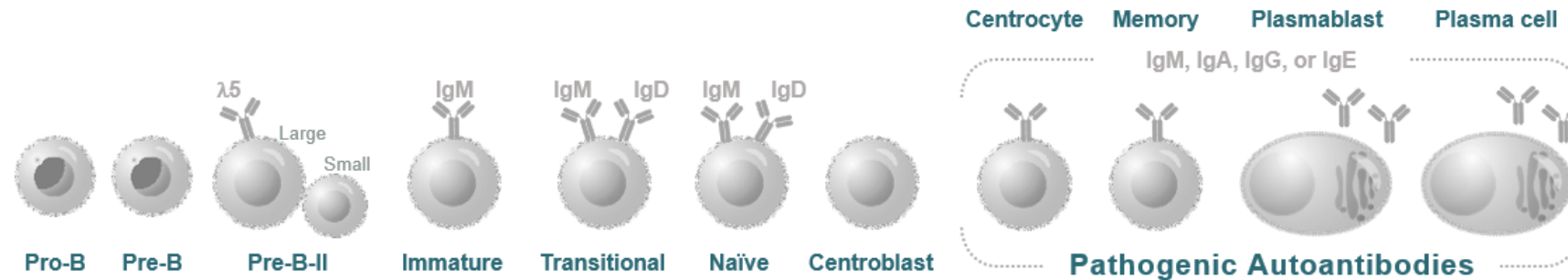


- Vertex to acquire Alpine Immune Sciences for \$65/share in cash; unanimously approved by both Boards of Directors
- Compelling fit with Vertex strategy of investing in serial innovation to create transformative medicines that target serious diseases with high unmet need in specialty markets
- Alpine’s 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 offers 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

©2024 Vertex Pharmaceuticals Incorporated

DUAL BAFF/APRIL INHIBITION HAS POTENTIAL FOR OPTIMAL EFFICACY AND SUPERIOR CLINICAL OUTCOMES ACROSS MULTIPLE AUTOIMMUNE DISEASES



- **BAFF and APRIL play critical roles in B-cell maturation and function**
 - Both genetically validated and pharmacologically validated in IgAN and other autoimmune diseases
- **Povetacicept targets both BAFF and APRIL with best-in-class affinity and potency, providing potential for increased efficacy and broad utility**
 - Clinical data in IgAN has shown potential for transformative benefit (i.e., remission)
 - MOA broadly applicable in other autoimmune diseases such as membranous nephropathy, lupus nephritis and autoimmune cytopenias

BAFF: B-cell activating factor; APRIL: a proliferation-inducing ligand

Image Adapted from Nat Rev Neurol 8:613, 2012

©2024 Vertex Pharmaceuticals Incorporated

ALPINE IMMUNE SCIENCES



**DEVELOPING NOVEL
THERAPIES for AUTOIMMUNE
and INFLAMMATORY DISEASES**

Company Overview

- Clinical-stage biotechnology company founded 2015
- Focused on discovering and developing protein-based immunotherapies for autoimmune and inflammatory diseases
- Protein engineering platform yielded potentially best-in-class dual BAFF/APRIL antagonist, povetacicept
- Povetacicept has achieved proof of concept for IgAN with best-in-class potential

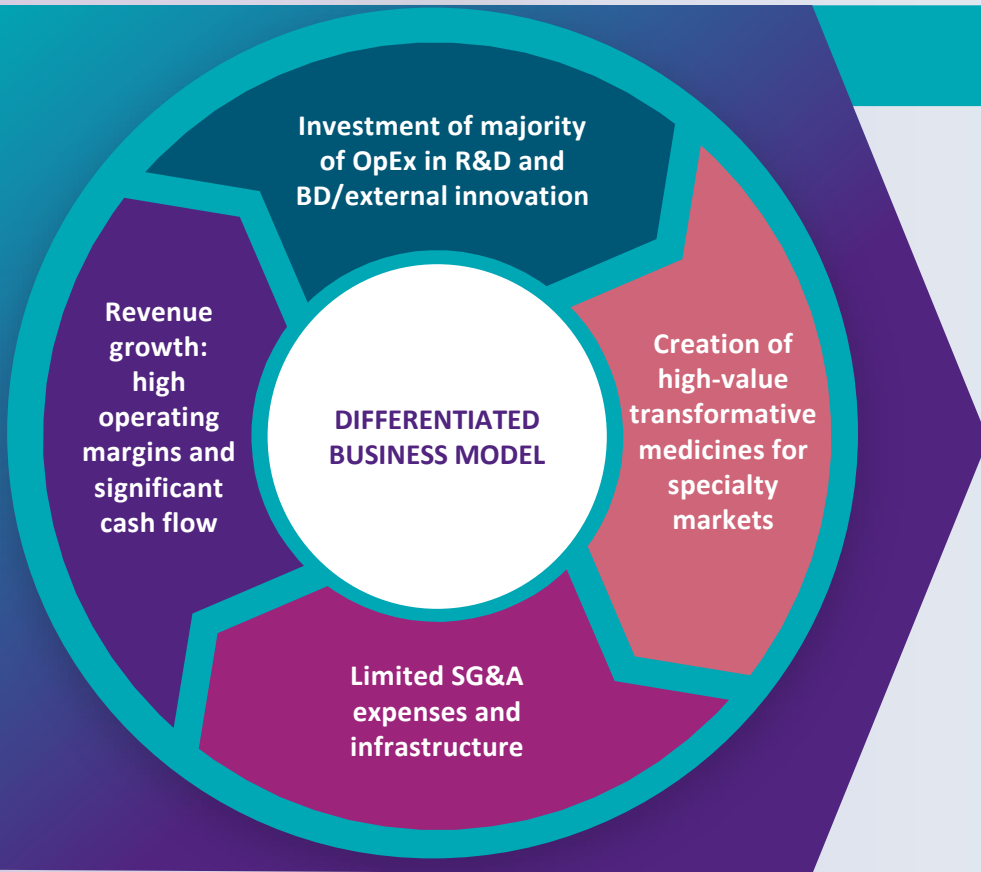


HQ in Seattle,
Washington



~145 Employees
>70% in R&D

ALPINE IMMUNE SCIENCES IS A STRONG STRATEGIC & CULTURAL FIT FOR VERTEX: INNOVATION AND PATIENT CENTRIC, TRANSFORMATIVE MEDICINES, SERIOUS DISEASES, HIGH UNMET NEED, SPECIALTY MARKETS



VERTEX CRITERIA

ALPINE/POVE FIT

<ul style="list-style-type: none"> • Understanding of causal human biology • Validated targets 	<ul style="list-style-type: none"> ✓ BAFF/APRIL pathways play key roles in multiple B-cell-driven diseases ✓ Genetic and pharmacologic validation in IgAN
<ul style="list-style-type: none"> • High unmet need • Transformative effect • Biomarkers that translate from bench to bedside 	<ul style="list-style-type: none"> ✓ No approved therapies address underlying cause of IgAN ✓ Through Phase 2, povetacicept has shown potential best-in-class efficacy in IgAN ✓ Convenient every four week, subcutaneous, small volume dosing regimen ✓ Proteinuria predictive of clinical outcomes
<ul style="list-style-type: none"> • Efficient development & regulatory pathways 	<ul style="list-style-type: none"> ✓ Povetacicept is Phase 3 ready in IgAN ✓ Accelerated approval possible with proteinuria endpoint
<ul style="list-style-type: none"> • Specialty market 	<ul style="list-style-type: none"> ✓ Autoimmune renal diseases and cytopenias treated by specialists and can leverage our expertise in these areas given overlap with AMKD, ADPKD, SCD and TDT

IGA NEPHROPATHY IS A SERIOUS DISEASE WITH LARGE UNMET NEED

U.S. PREVALENCE ~130K



SEVERE DISEASE

- Serious, progressive, autoimmune kidney disease and the most common form (20-30%) of glomerulonephritis^{1,2}; most patients diagnosed before age 40³
- ~30-40% of patients progress to end stage renal disease/kidney failure within 20 years²



UNDERLYING HUMAN BIOLOGY WELL UNDERSTOOD

- Progressive autoimmune disease, in which immunoglobulin A (IgA) aggregates in the kidney, leading to inflammation, protein and blood in urine, and loss of kidney function⁴
- Characterized by the overproduction of aberrantly glycosylated IgA1 (galactose-deficient IgA1, Gd-IgA1) by plasma cells, which binds together with IgA1 autoantibodies and C3 forming an immune complex⁴



VALIDATED TARGETS

- Genetic and pharmacologic validation of APRIL and BAFF^{5,6}



LARGE UNMET NEED

- ~130,000 patients in the U.S.; no current currently approved therapies target the underlying cause of IgAN
- Despite current standard of care (ACEi/ARBs, steroids), most patients' kidney function continues to decline; does not prevent progression to end stage renal disease^{3,7}

Given large numbers of patients, the serious and relentlessly progressive nature of the disease, and the high unmet need, IgAN has multi-billion-dollar market potential

1. Molnár A, et al. *Sci Rep.* 2021; 11(24479). 2. Shirai S, et al. *Clin Exp Nephrol.* 2023; 27(4):340-348. 3. Pitcher et al. *Clin J Am Soc Nephrol.* 2023; 18(6)727-738. 4. Stamellou E, et al. *Nat Rev Dis Primers.* 2023. 5. Barratt J et al. *Kidney Int Rep.* 2022; 7(8):1831-1847. 6. Mohit M et al. *N Eng J Med.* 2024; 390:20-31. 7. KDIGO 2021 *Clinical Practice Guidelines.* 2021; 100(4s):S1-S276. global.vrtx.com

POVETACICEPT HAS SHOWN BEST-IN-CLASS POTENTIAL PRECLINICALLY AND THROUGH PHASE 2 DEVELOPMENT IN IGAN



Best-in-class potential

- Greater affinity and potency versus other BAFF and/or APRIL inhibitors
- 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 date¹



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
- Data will be presented at World Congress of Nephrology 4/15/24



Convenient delivery

- Once every four weeks, subcutaneous, small volume dosing

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








ADDITIONALLY, POVETACICEPT HOLDS “PIPELINE-IN-A-PRODUCT” POTENTIAL



Ongoing Phase 1b/2 basket trial
in autoimmune kidney diseases:
IgAN, pMN, LN, AAV



Ongoing Phase 1b/2 basket trial
in autoimmune cytopenias:
ITP, AIHA, CAD

Pove could deliver patient benefit in multiple serious diseases			U.S. prevalent patient population ¹
	IgAN	Immunoglobulin A nephropathy	~130K
	pMN	Primary membranous nephropathy	
	LN	Lupus nephritis	
	AAV	Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides	
	ITP	Idiopathic thrombocytopenia	~150K
	AIHA	Warm autoimmune hemolytic anemia	
	CAD	Cold agglutinin disease	

1: Vertex Pharmaceuticals and Alpine Immune Sciences corporate estimates
©2024 Vertex Pharmaceuticals Incorporated

TRANSACTION TERMS AND FINANCIAL OVERVIEW

Transaction summary

- Vertex acquiring Alpine Immune Sciences for \$65/share in an all-cash transaction (\$4.9B)
- Unanimously approved by Boards of Directors of both companies
- Expected to close in Q2:24, subject to majority tender and customary closing conditions

Deal rationale

- Povetacicept represents multi-billion-dollar commercial opportunity in IgAN alone
- Upside from potential for povetacicept as “pipeline-in-a-product” across multiple serious diseases
- Vertex disease focus and clinical/regulatory/commercial capabilities accelerate development and commercialization – targeting approval in IgAN in 2027
- Alpine protein engineering/immunology capabilities can be leveraged in other Vertex sandbox diseases

Financial impact

- Transaction consistent with Vertex capital allocation priorities of investing in internal and external innovation; fully funded from cash (reduces 2024 interest income)
- Vertex 2024 non-GAAP OpEx guidance of \$4.3-4.4B is unchanged and can absorb Alpine OpEx for the balance of the year, excluding potential impact of transaction accounting
- With significant revenue potential, povetacicept can contribute to Vertex growth and diversification beginning in 2028; attractive margin and commercial profile adds to profitability thereafter

KEY TAKEAWAYS: VERTEX/ALPINE IMMUNE SCIENCES IS A COMPELLING STRATEGIC FIT



- Povetacicept Phase 3 ready in IgAN; best-in-class potential demonstrated through Phase 2
- Phase 3 trial to begin H2:24
- Ongoing Phase 2 studies in renal and heme conditions



- Povetacicept has “pipeline-in-a-product” potential
- Multiple clinical data read-outs H2:24:
 - pMN, LN, autoimmune cytopenias



- Vertex capabilities can accelerate povetacicept development in IgAN and other indications
- Alpine’s expertise in protein engineering and immunology will add to Vertex toolbox



- Strongly aligned cultures of innovation and commitment to patients



VERTEX PHARMACEUTICALS

APRIL 10, 2024

©2024 Vertex Pharmaceuticals Incorporated

ADDITIONAL INFORMATION AND WHERE TO FIND IT

The tender offer for the outstanding shares of common stock of Alpine Immune Sciences, Inc. ("Alpine") referenced in this communication has not yet commenced. This communication is for informational purposes only and is neither an offer to purchase nor a solicitation of an offer to sell shares of Alpine, nor is it a substitute for any tender offer materials that Vertex Pharmaceuticals Incorporated (together with its subsidiaries, "Vertex"), or Alpine will file with the Securities and Exchange Commission ("SEC"). At the time the tender offer is commenced, Vertex will file with the SEC a Tender Offer Statement on Schedule TO which will include an Offer to Purchase, a related Letter of Transmittal and certain other tender offer documents (together, the "Tender Offer Materials"), and Alpine will file with the SEC a Solicitation/Recommendation Statement on Schedule 14D-9 (the "Solicitation/Recommendation Statement") with respect to the tender offer. ALPINE'S SECURITY HOLDERS ARE URGED TO READ THE TENDER OFFER MATERIALS AND THE SOLICITATION/RECOMMENDATION STATEMENT WHEN THEY BECOME AVAILABLE BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION WHICH SHOULD BE READ CAREFULLY BEFORE ANY DECISION IS MADE WITH RESPECT TO THE TENDER OFFER. The Tender Offer Materials, as well as the Solicitation/Recommendation Statement, will be sent to all stockholders of Alpine at no expense to them. The Tender Offer Materials and the Solicitation/Recommendation Statement will be made available for free at the SEC's website at www.sec.gov. Additional copies may 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 or by email at InvestorInfo@vrtx.com, or by directing requests for such materials to the information agent for the offer, which will be named in the Tender Offer Materials. In addition to the Tender Offer Materials and the Solicitation/Recommendation Statement, Alpine and Vertex file periodic reports and other information with the SEC. Vertex's and Alpine's filings with the SEC are also available for free to the public from commercial document-retrieval services and at the website maintained by the SEC at www.sec.gov and their respective investor relations websites.