VERTEX PHARMACEUTICALS ACQUISITION OF ALPINE IMMUNE SCIENCES

APRIL 10, 2024

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• 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, povetaciceps (“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

• Povetaciceps, 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 povetaciceps development in IgAN and other indications, while Alpine will add protein engineering and immunotherapy expertise to Vertex
**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
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

• Understanding of causal human biology
  ✓ BAFF/APRIL pathways play key roles in multiple B-cell-driven diseases

• Validated targets
  ✓ Genetic and pharmacologic validation in IgAN

• High unmet need
  ✓ No approved therapies address underlying cause of IgAN

• Transformative effect
  ✓ Through Phase 2, povetacicept has shown potential best-in-class efficacy in IgAN

• Biomarkers that translate from bench to bedside
  ✓ Convenient every four week, subcutaneous, small volume dosing regimen

• Efficient development & regulatory pathways
  ✓ Proteinuria predictive of clinical outcomes

• Specialty market
  ✓ Povetacicept is Phase 3 ready in IgAN

ALPINE/POVE FIT

• Investment of majority of OpEx in R&D and BD/external innovation

• Creation of high-value transformative medicines for specialty markets

• Revenue growth: high operating margins and significant cash flow

• Limited SG&A expenses and infrastructure

DIFFERENTIATED BUSINESS MODEL
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 40\(^3\)
- ~30-40% of patients progress to end stage renal disease/kidney failure within 20 years\(^2\)

### 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 function\(^4\)
- 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 complex\(^4\)

### 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\(^4,7\)

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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
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

<table>
<thead>
<tr>
<th>Condition</th>
<th>U.S. prevalent patient population¹</th>
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<tbody>
<tr>
<td>IgAN Immunoglobulin A nephropathy</td>
<td>~130K</td>
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<tr>
<td>pMN Primary membranous nephropathy</td>
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<tr>
<td>LN Lupus nephritis</td>
<td>&gt;150K</td>
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<td>AAV Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides</td>
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<tr>
<td>ITP Idiopathic thrombocytopenia</td>
<td>~150K</td>
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<td>AIHA Warm autoimmune hemolytic anemia</td>
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<td>CAD Cold agglutinin disease</td>
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¹: Vertex Pharmaceuticals and Alpine Immune Sciences corporate estimates
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**TRANSACTION TERMS AND FINANCIAL OVERVIEW**

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<th>Transaction summary</th>
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<td>- Vertex acquiring Alpine Immune Sciences for $65/share in an all-cash transaction ($4.9B)</td>
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<td>- Unanimously approved by Boards of Directors of both companies</td>
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<td>- Expected to close in Q2:24, subject to majority tender and customary closing conditions</td>
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<th>Deal rationale</th>
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<td>- Povetacicept represents multi-billion-dollar commercial opportunity in IgAN alone</td>
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<td>- Upside from potential for povetacicept as “pipeline-in-a-product” across multiple serious diseases</td>
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<td>- Vertex disease focus and clinical/regulatory/commercial capabilities accelerate development and commercialization – targeting approval in IgAN in 2027</td>
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<td>- Alpine protein engineering/immunology capabilities can be leveraged in other Vertex sandbox diseases</td>
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<th>Financial impact</th>
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<td>- Transaction consistent with Vertex capital allocation priorities of investing in internal and external innovation; fully funded from cash (reduces 2024 interest income)</td>
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<td>- 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</td>
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<td>- With significant revenue potential, povetacicept can contribute to Vertex growth and diversification beginning in 2028; attractive margin and commercial profile adds to profitability thereafter</td>
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KEY TAKEAWAYS:
VERTEX/ALPINE IMMUNE SCIENCES IS A COMPPELLING 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
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.