

DEVELOPING NEXT-GENERATION THERAPEUTICS FOR T CELL DRIVEN INFLAMMATORY DISEASES

Biotech Showcase Steve Chan, CFO January 9, 2023 NASDAQ: CNTB

### **Forward-Looking Statements**

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We have not conducted a head-to-head study of CBP-201 versus dupilumab and have not conducted a head-to-head study of CBP-307 versus Etrasimod or Ozanimod. Comparisons of CBP-201 to dupilumab and comparisons of CBP-37 to Etrasimod and Ozanimod contained herein are based on analysis of data from separate studies. Such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or safety of CBP-201 compared to dupilumab or of the relative efficacy or safety of CBP-307 compared to Etrasimod or Ozanimod. The potential benefits of CBP-201 or CBP-307 do not imply an expectation of regulatory approval which is solely within the authority of the FDA (or applicable foreign regulator).



Large Opportunity	Targeting inflammatory diseases (dermatology, gastroenterology, respiratory) with high unmet need representing multi-billion-dollar global market opportunities
Late-Stage Pipeline	<b>CBP-201</b> : Interleukin-4-receptor alpha (IL-4Rα) blocker (ongoing China Pivotal trial) <b>CBP-307</b> : Sphingosine 1-phosphate-1 (S1P) modulator (Phase 3-ready asset) <b>CBP-174</b> : Peripherally acting histamine-3 receptor (H3R) antagonist
Potential Regulatory Approval	<b>CBP-201</b> : Potential first product approval for AD in China as early as 2025*; Asthma trial opens door to additional Type II disease indications
Strong Cash Position	\$181.5 million in Cash and Investments** at September 30, 2022, expected to fund operations into at least 2025
Multiple Catalysts	Three key readouts anticipated by end of 2023 for three disease indications (CBP-307 UC Ph2 maintenance data; CBP-201 AD China Pivotal 52-week data; CBP-201 Asthma Ph2 topline data)



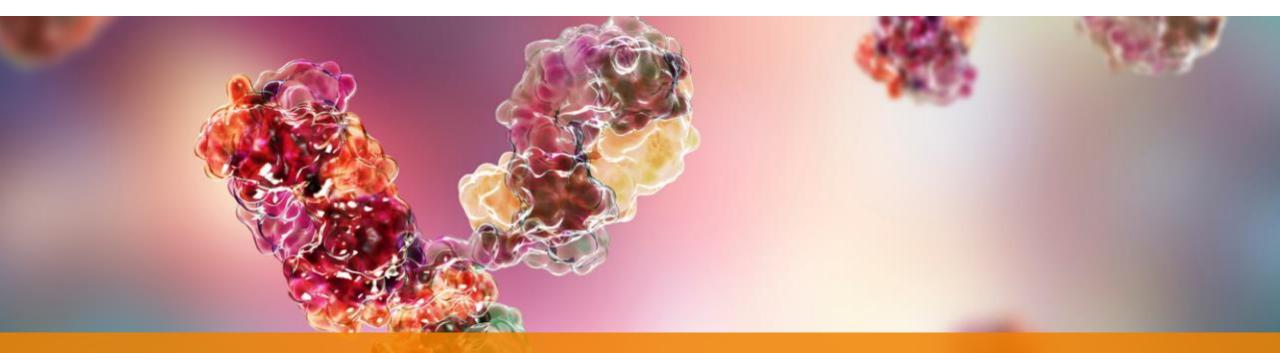
### Connect Biopharma has global development & commercialization rights to all product candidates

	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PIVOTAL OR PHASE 3*	NEXT ANTICIPATED MILESTONE
<b>CBP-201</b> Antibody targeting IL-4Ra cytokine receptor (Th2 cell modulator)	Atopic Dermatitis (AD) in China					Conduct pre-NDA discussions in Q1'23 on Pivotal Trial Stage 1 results***
	Atopic Dermatitis (AD) - Global					Secure partnership to advance Global Ph3 in 2023
	Asthma					Complete full enrollment in 1H2023
<b>CBP-307</b> Small molecule targeting S1P1 (Th1 cell modulator)	Ulcerative Colitis (UC)					Secure partnership to advance into future
	Crohn's Disease (CD)**					trials for UC and CD
<b>CBP-174</b> Peripherally restricted H3 receptor antagonist	Pruritus associated with AD					

\*The Company's clinical trial in China of CBP-201 in patients with AD is included as the Company intends to submit a New Drug Application (NDA) in China based on the results of this trial, pending pre-NDA discussions with the Center for Drug Evaluation (CDE) of China's National Medical Products Administration. \*\*Phase 2 CD trial ended early due to COVID-19-related enrolment challenges.

\*\*\* Represent the primary analysis population of 255 adult patients





CBP-201: A next generation anti-interleukin-4-receptor alpha (IL-4R $\alpha$ ) antibody in development for type 2 inflammatory diseases

### **Atopic Dermatitis (AD)**

### Large Opportunity with High Unmet Need Despite Advent of Biologics

A chronic inflammatory disorder characterized by eczematous skin lesions, itch, localized pain, and sleep disturbances

#### **Current treatment limitations**

- Limited efficacy with topical corticosteroids and immunosuppressants
- Safety concerns with systemic corticosteroids
- Dupilumab is the only approved biologic agent
  - Sales of \$6.2 billion in 2021<sup>1</sup> and expected to grow to  $\sim$ \$15 billion<sup>2</sup>
  - Unmet efficacy needs remain
  - Q2W administration regimen can be inconvenient for patients

# Key opportunities for a new novel treatment

- 1. Improved efficacy and sustained efficacy
- 2. Faster onset of efficacy
- 3. Reduced adverse events
- 4. Reduced injection burden frequency with biologic agents



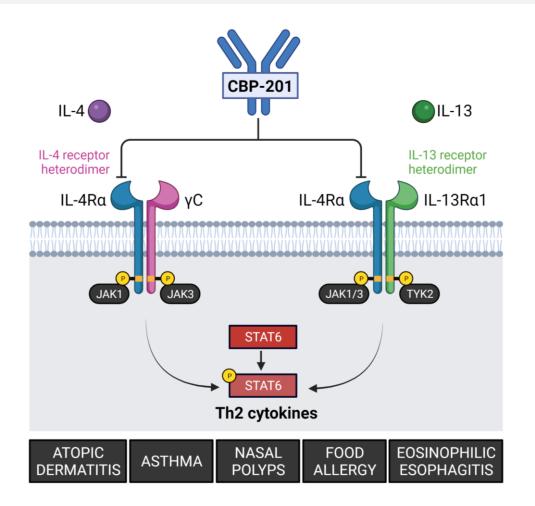
Gould, Carter, Barclays Equity Research Report, "4Q21 Post-Call Thoughts" on Regeneron, February 6, 2022

3. Guo, Y., et al. Prevalence of Atopic Dermatitis in Chinese Children aged 1–7 years. Scientific Reports | 6:29751 | DOI: 10.1038/srep29751

Atopic Dermatitis. National Eczema Association. https://nationaleczema.org/eczema/types-of-ecze

#### Dual inhibition of IL-4 and IL-13 is a validated therapeutic strategy across many Th2-mediated diseases

- CBP-201 is a novel, human monoclonal IgG4 antibody directed against IL-4Rα, a common subunit for IL-4 and IL-13 receptors
- Blockade of IL-4 and IL-13 binding to IL-4Rα results in inhibition of both IL-4 and IL-13 signaling
- Potential for differentiation based on observations of
  - CBP-201 engages with distinct epitopes and binds with higher affinity to the IL-4Rα target than dupilumab<sup>1</sup>
  - 2. CBP-201 inhibits IL-4/IL-13-dependent activation of the JAK-STAT pathway and cell proliferation in a concentration-dependent manner<sup>1</sup>
  - 3. Cytokine-mediated release of TARC, and inflammatory Th2 chemokine, is downregulated in the presence of CBP-201<sup>1</sup>
  - 4. CBP-201 detected longer in plasma than dupilumab<sup>2</sup>
- Potential for clinical results to show
  - Faster onset of action
  - Greater clinical response
  - Less frequent dosing (Q4W)



- Yang et al., Society for Investigative Dermatology, Portland, 2022, poster LB945. Observations were made from our in-house preclinical experiments, including all comparisons to dupilumab
- Not head-to-head trial results. Differences exist between trial designs and subject characteristics and caution should be exercised when comparing data across trials. Results are from CBP-201 Phase 1 study (AU001) and dupilumab Phase 1 study (Li, Z et al 2020):



- Á Randomized, Double-blind, Placebo-controlled, Single Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of CBP-201 Administered to Healthy Adult Subjects (CBP-201AU001)
- Li Z et al Pharmacokinetics Pharmacodynamics Safety and Tolerability of Dunilymph in Healthy Adult Subjects (Linical Pharmacology in Drug Development 2020. 0/6) 7/12–7

## Key Takeaways from CBP-201 Global Phase 2b AD Trial

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#### **Met Primary Endpoint & Key Secondary Endpoints**

- CBP-201 showed significant improvements in skin clearance, disease severity, and itch compared to placebo in adult patients with moderate-to-severe AD<sup>1,2</sup>
- Cross-trial comparisons to SOLO 1,2 are difficult due to CBP-201's less severe AD population and higher patient discontinuations due to the impact of the COVID-19 pandemic
- Additional *a priori* and post-hoc analyses of trial populations showed
  - As baseline disease severity increased, CBP-201 efficacy response further improved<sup>1,2</sup>
  - With baseline severity that more closely matches SOLO1,2, side by side comparisons of CBP-201 300mg Q2W & Q4W appeared at least comparable, with some endpoints numerically better than dupilumab 300mg Q2W<sup>1,2,3,4</sup>
  - CBP-201 300mg has the potential for a differentiated efficacy and safety profile with the convenience of Q4W dosing

Global Phase 2b full dataset available on company website at: Investors\Events & Presentations



<sup>1.</sup> Strober, B et al. Maui Derm 2022 Abstract and Poster (and reflects additional data analyses conducted by the Company subsequently)

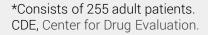
<sup>2.</sup> Silverberg, J et al. Maui Derm 2022 Abstract and Poster (and reflects additional data analyses conducted by the Company subsequently)

<sup>3.</sup> Thaçi et al. J Dermatol Sci. 2019;94:266-75.

Not a head-to-head trial. Differences exist between trial designs and subject characteristics and caution should be exercised when comparing data across trials

## Key Takeaways from Stage 1 CBP-201 Pivotal AD Trial in China

- Successfully achieved all primary and key secondary endpoints at Week 16 for the primary analysis
  population\* of this large China-specific pivotal trial in patients with moderate-to-severe AD with highly
  statistically significant results at Week 16
- In the first 16 weeks of treatment:
  - More than 8 out of 10 (83%) patients achieved 50% improvement (EASI-50)
  - More than 6 out of 10 (63%) patients achieved 75% improvement (EASI-75)
- Data were consistent with our global Phase 2b trial observations of a greater clinical response rate among patients with more active AD
- Overall safety results showed CBP-201 was generally well tolerated
  - Results remained consistent with targeting the IL-4Rα pathway
  - Most TEAEs were mild to moderate in severity and did not lead to study drug discontinuation
- Stage 2 maintenance period is ongoing and could potentially demonstrate sustained efficacy with continued dosing at every two weeks as well as at a more convenient every four-week dose
- Pre-NDA package submitted to CDE and expecting feedback in Q1'23 on NDA timeline in China









CBP-307: A next generation selective sphingosine 1-phosphate receptor 1 modulator (S1P) in development for Irritable Bowel Disease (IBD)

### **Ulcerative Colitis (UC)**

#### Large Opportunity where High Unmet Need Remains Despite Treatment Advances

An autoimmune disease that causes inflammation and ulceration of the inner lining of the colon and rectum (the large bowel)

#### **Current Treatment Limitations**

- Efficacy
  - Less than half of patients achieve long-term remission, and many drugs lose the initial efficacy response <sup>1</sup>
  - Maximal clinical remission may require up to one year of treatment
- Safety concerns with many treatment options
- Biologics can have complicated administration regimens

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#### IBD patients in the US in 2015<sup>2</sup>

IBD patients worldwide in 2017<sup>3</sup>

6.8 M

of IBD patients in the US had UC<sup>4</sup>





- Ulcerative Colitis. Nature Reviews. Disease Primers. 2020. 6:74. https://doi.org/10.1038/s41572-020-0205-x
- Inflammatory Bowel Disease Prevalence (IBD) in the United States. Centre for Disease Control (CDC). August 2020. https://www.cdc.gov/ibd/data-statistics.htm
- GBD 2017 Inflammatory Bowel Disease Collaborators. Lancet Gastroenterol Hepatol 2020; 5: 17–30. DOI: https://doi.org/10.1016/S2468-1253(19)30333-4
- Betteridge, J. et al. Inflamm Bowel Dis 2013:19:1421-1427, https://academic.oup.com/ibdiournal/article/19/7/1421/4604306

- **Key Unmet Needs**
- Improved efficacv
- Faster onset of efficacy
- **Reduced adverse events**
- **Oral therapies**

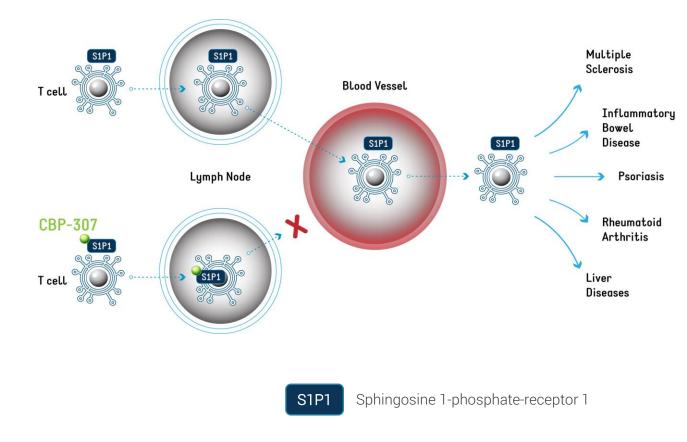


### **CBP-307: A Next Generation S1P Modulator**

In clinical development to treat patients with IBD

#### Mechanism of Action – S1P Modulator – A validated target

- Blocking T Cell Egress from Lymph Nodes Reduces Inflammation Implicated in Many T cell-mediated diseases<sup>1</sup>
- S1P mediates T cell movement from lymph nodes into circulation, and hence migration to tissues to release inflammatory mediators
- Internalizes S1P receptors, trapping T cells inside lymph nodes
- Has molecular design features that offer potential for differentiation
  - High Potency & Selectivity
    - Designed to be the most potent modulator of S1P1
    - No notable activity observed for S1P3, a receptor subtype associated with known safety concerns
    - Substantially lower potency for S1P4 and S1P5 than S1P1 observed





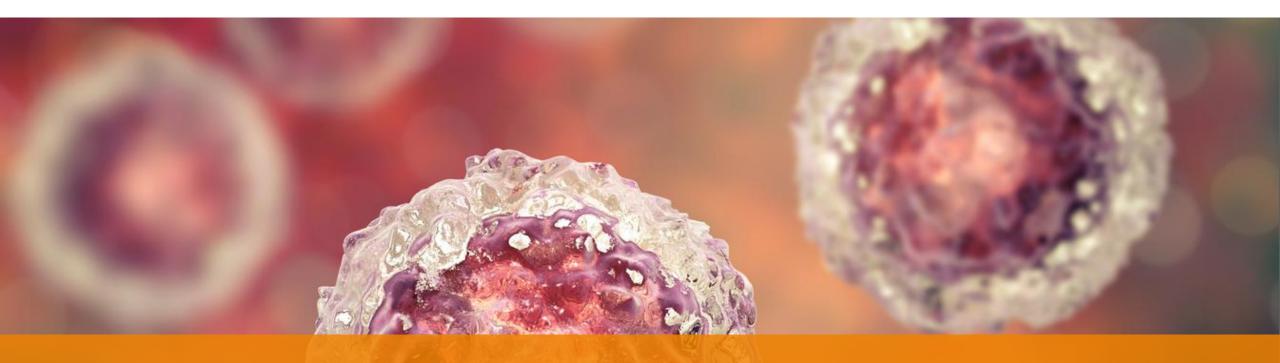
### Key Takeaways CBP-307 Phase 2 UC Trial 12-Week Induction Period

### Patients dosed at 0.2 mg once daily, orally (PO QD)

- Data showed decreased disease severity based on adapted Mayo Score after 12 weeks of treatment, although the change did not reach statistical significance
- Support for potential as a Phase 3-ready asset include:
  - Achieved statistical significance on Clinical Remission, which was an FDA-recommended primary endpoint and was used for approval of a previously approved drug to treat UC
  - Achieved several other key secondary endpoints
  - Confirmed mechanism of action with clear dose-dependent and rapid pharmacodynamic changes observed
  - Overall safety results showed drug to be generally well tolerated
- Next steps include securing a partnership to advance into future trials for UC and Crohn's disease (CD) in order to capitalize on potential to be a competitive asset and welcome addition to the gastroenterologist's treatment armamentarium







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Thank you!