# Connect Biopharma Reports Detailed Positive Dataset from the Global Phase 2b Trial of CBP-201 in Adult Patients with Moderate-to-Severe Atopic Dermatitis

January 5, 2022

*—Phase 2b trial previously reported achievement of both primary and key secondary end points, demonstrating significant improvements in skin clearance, disease severity, and itch compared to placebo—*

*—Additional analyses demonstrate a potentially competitive therapeutic profile for CBP-201 300mg administered every two weeks (Q2W) or every four weeks (Q4W). Company to begin Phase 3 trial of CBP-201 in the second half of 2022—*

*—Company management and Dr. Jonathan Silverberg, MD, PhD, MPH, will review additional data from the Phase 2b trial on conference call on Wednesday, January 5 at 8:30 am ET (5:30 am PST)—*

*—Data to be presented at Maui Derm Conference January 24-28, 2022—*

SAN DIEGO, CA and TAICANG, China, Jan. 05, 2022 (GLOBE NEWSWIRE) -- Connect Biopharma Holdings Limited (Nasdaq: CNTB) ("Connect Biopharma" or the "Company"), a global clinical-stage biopharmaceutical company dedicated to improving the lives of patients with chronic inflammatory diseases through the development of therapies derived from T cell-driven research, today reported detailed positive data from the global Phase 2b clinical trial of CBP-201 administered subcutaneously (SC) to adult patients with moderate-to-severe atopic dermatitis (AD) (WW001) (NCT04444752).

The Company announced topline results from the Phase 2b trial on November 18, 2021 indicating that all three CBP-201 arms (300mg Q2W, 150mg Q2W or 300mg Q4W) met the primary endpoint of eczema area and severity index (EASI) percent reduction from baseline at Week 16 and were statistically superior to placebo. The announcement noted that multiple key secondary endpoints were also met with CBP-201.

CBP-201 was also observed with favorable safety data and, versus placebo, demonstrated a similar incidence of Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and TEAEs leading to study drug discontinuation. For adverse events (AEs) of special interest (AESI) among patients receiving CBP-201, there were low reported incidences of injection site reactions (1.8%) and conjunctivitis (3.5%).

"The results of the WW001 study with CBP-201 in the treatment of moderate-to-severe AD are in line with efficacy expectations for a Phase 2b trial with the IL-4Rα mechanism of action," said Jonathan Silverberg, MD, PhD, MPH, Associate Professor of Dermatology, The George Washington University School of Medicine and Health Sciences and lead author on the second WW001 Phase 2b abstract being presented at Maui Derm 2022. "In addition, the favorable safety data and promising pre-specified and post-hoc analyses explaining CBP-201's depth of clinical response across both the moderate and more severe AD populations provide clear direction for the Phase 3 program that may bolster the strong efficacy already seen in the Phase 2b trial."

**Summary of Primary Data Analyses**

| Key Primary and Secondary Endpoint Results at Week 16 | | | | |
|---|---|---|---|---|
| | 300 mg Q2W n=57 | 150 mg Q2W N=57 | 300 mg Q4W N=56 | Placebo N=56 |
| Least square (LS) mean % EASI score change from Baseline | -63.0*** | -57.5** | -65.4*** | -40.7 |
| EASI-50% responders | 54.4* | 52.6* | 62.5** | 33.9 |
| EASI-75% responders | 47.4*** | 40.4** | 41.1** | 14.3 |
| EASI-90% responders | 24.6 | 14.0 | 25.0* | 10.7 |
| Investigator's Global Assessment (IGA) 0,1 % Responders | 28.1* | 15.8 | 21.4 | 10.7 |
| LS mean change (Peak Pruritus-Numerical Rating Scale) PP-NRS score from baseline | -3.56** | -2.64 | -3.29* | -2.26 |

*$P$<0.05, **$P$<0.01, ***$P$<0.001 vs placebo

Since the CBP-201 Phase 2b trial occurred during the COVID-19 pandemic and the patient population recruited had a markedly lower AD disease severity and higher patient discontinuation rate relative to previous IL-4Rα antibody Phase 3 trials, additional analyses were performed to determine the effects of these factors on the magnitude of the treatment benefit observed with CBP-201 in the Phase 2b study.

**Additional Data Analyses – Key Findings from A Priori and Post-Hoc Analyses:**

- Compared to prior IL-4Rα antibody trials in AD, patients enrolled across all treatment groups in this study had significantly lower disease severity at baseline. The lower severity of disease in the overall study population could have contributed to the lower percentage EASI score changes from baseline across all treatment groups observed in our Phase 2b study versus prior IL-4Rα antibody Phase 3 trials in AD.

| Baseline Disease Characteristics Comparison | | | |
|---|---|---|---|
| Baseline Disease Characteristics | CBP-201-WW001 (n=226) | CBP-201-WW001 China Subgroup (n=32) | Prior IL-4Rα antibody AD Ph3 trials |
| Median Baseline EASI | 20.1 to 22.1 | 25.9 to 32.9 | 29.4 to 31.1 |

| | | | |
|---|---|---|---|
| IGA score = 4 (%) | 25 to 40 | 33 to 50 | 47.2 to 48.9 |
| Median BSA % | 32.5 to 37.0 | 40.0 to 56.0 | 51.0 to 54.5 |

- In the China sub-population (n=32), a pre-defined analysis performed to support ongoing discussions with regulatory authorities in China, versus the overall trial population, patients had a higher median baseline EASI score, greater proportion of IGA score=4 and a higher BSA involvement than the overall trial population. Greater treatment benefit of CBP-201 were noted among patients enrolled in the China sub-population as indicated in the table below.

| Key Endpoint Results at Week 16 – China Subgroup | | | | |
|---|---|---|---|---|
| China Sub-population (n=32) | 300 mg Q2W (n=6†) | 150 mg Q2W (n=11) | 300 mg Q4W (n=9) | Placebo (n=6) |
| LS mean % EASI score change from Baseline | -82.9 | -60.3 | -76.1* | -34.9 |
| EASI-50 % responders | 50.0 | 72.7 | 66.7 | 33.3 |
| EASI-75% responders | 50.0* | 54.5* | 55.6* | 0 |
| EASI-90% responders | 16.7 | 18.2 | 33.3 | 0 |
| IGA 0,1 % Responders | 33.3 | 18.2 | 22.2 | 0 |
| LS mean change PP-NRS score from baseline | -2.75 | -2.12 | -3.61 | -0.78 |

*$P$<0.05 vs placebo; †: n=4 for %EASI change from baseline.

- An analysis of median percent EASI reduction from baseline which reduces the impact of the low median EASI baseline and the non-normal distribution of patients' AD disease severity observed in this trial, showed greater reductions (79.3%, 64.7%, 72.4% for 300 mg Q2W, 150 mg Q2W, 300 mg Q4W, respectively vs. 41.0% in Placebo) compared to the LS means percent EASI reduction from baseline reported above (n=226).
- In an exploratory post-hoc analysis of patients with higher disease severity at baseline based on EASI score (n=69), relative to the overall trial population, results showed both greater reduction of EASI score from baseline and a lower placebo response. Similarly, a post-hoc analysis of patients (n=69) with higher baseline thymus and activation-regulated chemokine (TARC or CCL17), a biomarker associated with disease activity in patients with AD, vs. the overall patient population in this trial, showed that they achieved greater EASI reduction and had a lower placebo response, compared to the overall population.

| Post Hoc Analysis (Highest Tertile EASI Subgroup) | | | | |
|---|---|---|---|---|
| | 300 mg Q2W (n=20) | 150 mg Q2W (n=18) | 300 mg Q4W (n=13) | Placebo (n=18) |
| Median Baseline EASI | 37.5 | 29.6 | 31.0 | 34.4 |
| LS mean % EASI score change from Baseline | -62.9* | -54.9 | -81.4*** | -35.5 |
| Post Hoc Analysis (Highest Tertile TARC Subgroup) | | | | |
| | 300 mg Q2W (n=16) | 150 mg Q2W (n=20) | 300 mg Q4W (n=14) | Placebo (n=19) |
| Median Baseline EASI | 34.4 | 27.2 | 28.1 | 26.2 |
| LS mean % EASI score change from Baseline | -61.7** | -63.2** | -83.0*** | -28.6 |

*$P$<0.05, **$P$<0.01, ***$P$<0.001 vs placebo
Baseline EASI tertiles: Low: ≤ 18.4, Mid: >18.4 and ≤26.4, High: >26.4
Baseline TARC tertiles: Low: ≤ 116 pg/mL, Mid: >116 pg/mL and ≤291 pg/mL, High: >291 pg/mL

- Higher treatment discontinuation rates particularly in the active treatment arms (13%–19%) were observed versus those of prior anti-IL-4Rα Phase 3 trials (6.3–9.5%). The vast majority of the discontinuations in the Phase 2b study were due to patients withdrawing consent or patients being lost to follow-up, and it is likely that movement restrictions related to the COVID-19 pandemic contributed to the higher observed rates. None of the discontinuations in our Phase 2b study were attributable directly to COVID-19 infection.

These additional analyses demonstrate that the significant treatment benefit seen in the primary analyses for CBP-201 are markedly higher in patients with higher baseline AD disease severity based on EASI score and TARC or CCL17. These findings demonstrate that CBP-201 has the potential to show a superior efficacy profile against current IL-4Rα antibody therapy in future studies of patients with higher baseline disease severity.

"The results of the additional analyses provide details of the potential significant benefits of CBP-201 in the treatment of adult patients with moderate-to-severe AD, despite having enrolled a relatively less severe patient population," said Zheng Wei, PhD, Co-Founder and CEO of Connect Biopharma. "We are very encouraged by the findings from the additional analyses and remain confident on the potential for a highly competitive efficacy and safety profile for CBP-201 coupled with a more convenient and differentiated Q4W dosing schedule. We look forward to leveraging the insights from the additional analyses as we initiate a Global Phase 3 clinical trial program in the second half of 2022."

"These new results add to the body of evidence that CBP-201 has the potential to provide clinically meaningful benefit to adult patients with moderate-to-severe AD," said Dr. Bruce Strober, Clinical Professor of Dermatology, Yale University School of Medicine and lead author on the first of two

WW001 Phase 2 trial abstracts to be presented at Maui Derm 2022 in January. “In addition to efficacy data that look at least comparable to current anti-IL-4Rα therapy, CBP-201 may be able to be dosed every four weeks which could reduce patients’ treatment burdens and aid in treatment adherence. I look forward to the planned Phase 3 trial program of CBP-201 commencing in the second half of 2022.”

*CBP-201 Global Phase 2b Clinical Trial Design*

The global Phase 2b clinical trial, “A Randomized, Double-Blind, Placebo-Controlled Multi-Centered Study of the Efficacy, Safety, Pharmacokinetics and Pharmacodynamics of CBP-201 in Adult Subjects with Moderate to Severe Atopic Dermatitis,” enrolled 226 patients (ages 18–75 years) throughout the United States, China, Australia and New Zealand. Patients were randomized to one of three CBP-201 treatment groups or the placebo group. The CBP-201 treatment groups all received a 600 mg loading dose on Day 1 and then received 300 mg Q2W, 150 mg Q2W or 300 mg Q4W. The treatment period was 16 weeks, and all patients were followed for an additional period of 8 weeks. CBP-201 and placebo were administered via SC injection.

The primary efficacy endpoint was percentage reduction in the EASI score from baseline to Week 16 for each CBP-201 group compared with the placebo group; the key secondary endpoints were the proportion of patients with an IGA score 0 or 1 and a reduction of ≥2 points at Week 16; the proportion of patients achieving EASI-50, EASI-75 or EASI-90 from baseline at Week 16; and change from baseline to Week 16 in weekly average PP-NRS. Safety assessments included reported AEs, vital signs, physical examinations and injection site changes; laboratory and electrocardiogram evaluations; and the number of patients displaying anti-drug antibodies.

In the coming months, Connect Biopharma intends to discuss the CBP-201 data with the FDA and other health authorities and seek feedback on its planned Phase 3 trial program in adult patients with moderate-to-severe AD. The Company plans to commence enrollment in the second half of 2022.

**Maui Derm Presentation Information**
Two abstracts related to the CBP-201 Phase 2 trial have been accepted for presentation at the 18th Annual Maui Derm meeting, taking place January 24-28, 2022.

Efficacy and Safety of CBP-201 in Adults with Moderate-to-Severe Atopic Dermatitis (AD): A Phase 2b, Randomized, Double-blind, Placebo-controlled Study (CBP-201-WW001)

The Effect of Baseline Disease Characteristics on Efficacy Outcomes: Results from a Phase 2b, Randomized, Double-blind, Placebo-controlled Trial (CBP-201-WW001)

**Conference Call Information**
Connect Biopharma’s management team, along with Dr. Jonathan Silverberg, will host a conference call and webcast today to review data from its global Phase 2 trial of CBP-201 in patients with moderate-to-severe AD, beginning at 8:30 am Eastern Time.

The conference call can be accessed using the following information:

**Webcast**: https://edge.media-server.com/mmc/p/2pa7xiwr
**U.S.**: 844-646-2698
**Outside of U.S.**: 918-922-6903
**Conference ID**: 7998162

The webcast will also be available in the “Investors” section of the Company’s website following the completion of the call.

**About Atopic Dermatitis**
Atopic dermatitis (AD), which has an estimated lifetime prevalence of up to 20% and is increasing globally, is the most commonly diagnosed chronic inflammatory skin disorder. It is characterized by skin barrier disruption and immune dysregulation. Estimates of prevalence of AD in China show an increase over time and recent longitudinal studies have reported a dermatologist-diagnosed prevalence of 7.8% in Chinese outpatients visiting tertiary hospitals. In the United States, it is estimated that 26.1 million people have AD, of which 6.6 million have moderate-to-severe disease. Further, over 58% of adults with moderate-to-severe AD have disease that physicians consider to be inadequately controlled by approved therapeutic modalities, including topical anti-inflammatory agents and systemic agents.

**About CBP-201**
CBP-201, discovered internally using Connect Biopharma's proprietary Immune Modulation Technology Platform, is an antibody designed to target interleukin-4 receptor alpha (IL-4Rα), which is a validated target for the treatment of several inflammatory diseases, including atopic dermatitis (AD). CBP-201 was well tolerated and showed evidence of clinical activity in a Phase 1b clinical trial in adult patients with moderate-to-severe atopic dermatitis, suggesting a potential for a differentiated efficacy profile compared with data from clinical trials of the current biologic standard of care therapy. CBP-201 has been evaluated in a global Phase 2b trial in adult patients with moderate-to-severe atopic dermatitis (NCT04444752); in a China specific pivotal trial in adults with moderate-to-severe atopic dermatitis (NCT05017480); in a Phase 2b trial in adult patients with moderate-to-severe persistent asthma (NCT04773678); and in a Phase 2b trial in adult patients with chronic rhinosinusitis with nasal polyps (CRSwNP) (NCT04783389).

**About Connect Biopharma Holdings Limited**
Connect Biopharma Holdings Limited is a global clinical-stage biopharmaceutical company dedicated to improving the lives of patients living with chronic inflammatory diseases through the development of therapies derived from our T cell-driven research.

Our lead product candidate, CBP-201 — an antibody designed to target interleukin-4 receptor alpha (IL-4Rα) — has been in clinical trials for the treatment of AD, asthma, and CRSwNP. Our second lead product candidate, CBP-307 — a modulator of a T cell receptor known as sphingosine 1-phosphate receptor 1 (S1P1) — has been in clinical trials for the treatment of ulcerative colitis (UC) and Crohn’s disease (CD). Furthermore, we have started the clinical development of an additional product candidate, CBP-174 — a peripherally acting antagonist of histamine receptor 3 — for the treatment of pruritus associated with AD.

With clinical development activities in the United States, China, Europe, and Australia, and operations in those geographies as well as Hong Kong, Connect Biopharma is building a rich global pipeline of internally designed, wholly owned small molecules and antibodies targeting several aspects of T cell biology. For additional information about Connect Biopharma, please visit our website at www.connectbiopharm.com.

**FORWARD-LOOKING STATEMENTS**
Connect Biopharma cautions that statements included in this press release that are not a description of historical facts are forward-looking statements. Words such as "may," "could," "will," "would," "should," "expect," "plan," "anticipate," "believe," "estimate," "intend," "predict," "seek," "contemplate," "potential," "continue" or "project" or the negative of these terms or other comparable terminology are intended to identify forward-looking statements. These statements include the Company's statements regarding the potential of CBP-201 to achieve a differentiated, competitive, or favorable benefit or profile including on safety, efficacy and/or convenience, and the Company's plans to initiate a Phase 3 trial program to further evaluate CBP-201. The inclusion of forward-looking statements shall not be regarded as a representation by Connect Biopharma that any of its plans will be achieved. Actual results may differ from those set forth in this release due to the risks and uncertainties inherent in the Connect Biopharma business and other risks described in the Company's filings with the Securities and Exchange Commission ("SEC"). Among other things, there can be no guarantee that planned or ongoing studies will be initiated or completed as planned, that future study results will be consistent with the results to date, that CBP-201 will receive regulatory approvals, or be commercially successful. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Connect Biopharma undertakes no obligation to revise or update this news release to reflect events or circumstances after the date hereof. Further information regarding these and other risks is included in Connect Biopharma's filings with the SEC which are available from the SEC's website (www.sec.gov) and on Connect Biopharma's website (www.connectbiopharm.com) under the heading "Investors." All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995.

We have not conducted a head-to-head study of CBP-201 versus any other IL-4Rα antibody. Comparisons 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, safety, convenience, or competitiveness of CBP-201 compared to any other IL-4Rα antibody. The potential benefits of CBP-201 does not imply an expectation of regulatory approval which is solely within the authority of the FDA (or applicable foreign regulator).

**IR/PR Contacts:**
Lazar FINN Partners
David Carey (IR)
T: +1-(212) 867-1768
**david.carey@finnpartners.com**

Erich Sandoval (Media)
T: +1-(917)-497-2867
**erich.sandoval@finnpartners.com**
**Corporate Contacts:**
**info@connectpharm.com**