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Argent BioPharma Ltd.

(Argent BioPharma or the Company)

Phase IIb Clinical Trial Confirms CimetrA®'s Favourable Safety Profile and Faster Recovery Time

Highlights:

- **CimetrA® demonstrated a strong safety profile with no drug-related adverse events.**
- **Patients receiving CimetrA® experienced faster clinical improvement compared to placebo, as measured by the WHO Ordinal Scale for COVID-19 recovery.**
- **A trend toward improved quality of life was observed in CimetrA®-treated patients at the end of the study.**
- **Inflammatory markers (IL-6, IL-1β, IL-12, TNF-α, IFN-γ, CRP, NLR) showed positive vector of modulation with CimetrA®, supporting its potential anti-inflammatory effects.**
- **No significant safety concerns were observed, reinforcing CimetrA®'s suitability for further clinical development.**
- **CimetrA® Demonstrates Strong Safety and Faster Recovery in Phase IIb Study**

Argent BioPharma (ASX:RGT) is pleased to announce positive results from its Phase IIb, double-blind, randomised, placebo-controlled clinical study evaluating CimetrA® in patients diagnosed with COVID-19.

The Phase IIb clinical study confirmed CimetrA®'s strong safety profile, with no drug-related adverse events reported. Patients treated with CimetrA® showed a **positive trend** toward faster recovery and symptom improvement compared to placebo. Additionally, CimetrA® demonstrated promising modulation of **IL-6**, a key inflammatory marker, supporting its potential anti-inflammatory effects.

These findings build upon earlier preclinical and clinical studies that have consistently highlighted CimetrA®'s **unique mechanism of action and therapeutic benefits**. Studies have shown that CimetrA® suppresses the expression of **Interleukin-32 (IL-32)**, a pro-inflammatory cytokine linked to immune overactivation, while also increasing **Heme-Oxygenase-1 (HO-1)**, a key antioxidant enzyme that protects against inflammation-related damage. This dual mechanism may help regulate immune responses and reduce inflammation, **key factors in managing severe viral infections and autoimmune diseases**[1].

Beyond its clinical studies, CimetrA® has also demonstrated **excellent safety in preclinical large-animal trials**, where **no toxicological changes** were observed across tissue, blood, or urine samples in a controlled **14-day swine study**[2].

While additional, larger-scale trials will be required to further validate CimetrA®'s efficacy, the results of this study reinforce its **favourable safety profile and potential as a well-tolerated adjunct therapy**. Given its **demonstrated ability to influence inflammatory pathways**, CimetrA® may have **broader applications beyond COVID-19**, including in **autoimmune and inflammatory conditions**. Argent BioPharma remains committed to advancing CimetrA® through continued clinical development and regulatory discussions to explore its **full therapeutic potential**.

[1] Refer to ASX Announcement dated 7 March 2023
[2] Refer to ASX Announcement dated 14 August 2023

The study assessed CimetrA®'s efficacy, pharmacokinetic parameters, and safety across three arms:

1. CimetrA®-1: Curcuma longa extract (28 mg) + Boswellia serrata extract (60 mg)
2. CimetrA®-2: Curcuma longa extract (19.6 mg) + Boswellia serrata extract (42 mg)
3. Placebo: Identical formulation without active ingredients

Patients received four doses over 48 hours, administered as an adjunct therapy.

Primary Outcomes

1. **Clinical Improvement Over Time in CimetrA® Groups**
   - Patients in the CimetrA® groups experienced progressive improvement in the WHO Ordinal Scale for COVID-19, with scores decreasing from **2.9 (Day 1) to 1.3 (Day 28)** within treatment groups.
   - CimetrA® groups demonstrated greater symptom reduction at Day 7, Day 14, and Day 28, supporting its potential to accelerate recovery.
2. **Strong Safety Profile**
   - No serious adverse events (SAEs) related to CimetrA® were observed.
   - Overall adverse event (AE) rates were lower in CimetrA® groups compared to placebo.
   - The treatment was well tolerated, reinforcing its potential as a safe therapeutic option.
3. **Inflammatory Marker Modulation Suggests Anti-Inflammatory Potential**
   - CimetrA® was associated with notable reductions in inflammatory markers over 28 days, including **IL-6, IL-1β, and TNF-α**, supporting its proposed anti-inflammatory mechanism:
     - IL-6: ↓ 15.5 points (from 16.9 to 1.4)
     - IL-1β: ↓ 0.27 points (from 0.45 to 0.18)
     - TNF-α: ↓ 9.8 points (from 15.9 to 6.1)
     - IFN-γ: ↓ 8.5 points (from 10.5 to 2.0)
     - CRP & NLR also showed clear downward trends.
4. **Trend Toward Improved Quality of Life**
   - Patients receiving CimetrA® reported steady improvements in overall well-being, with QoL scores improving from **2.9 (Day 1) to 1.3 (Day 28)**.
   - This trend indicates CimetrA® may contribute to improved patient-reported outcomes, though larger studies are needed for confirmation.

Roby Zomer, CEO & Managing Director of Argent BioPharma, commented: *"We are highly encouraged by CimetrA®'s strong safety profile and the observed trend of faster clinical improvement. The data supports its potential as a safe and effective treatment for inflammatory conditions beyond COVID-19. These findings pave the way for further clinical development as we explore broader applications for CimetrA® in immune and inflammatory disorders."*

Dr. Nadya Lisovoder, CEO of Galilee Clinical Bio Research (CBR), commented: *"The results of this Phase IIb study reaffirm CimetrA®'s strong safety profile and its potential to regulate inflammatory responses. By modulating key cytokines like IL-6 and IL-32, CimetrA® demonstrates a unique mechanism of action in controlling immune overactivation. These findings, combined with past research, suggest broader applications beyond COVID-19, including autoimmune and inflammatory diseases.*

*Our collaboration with **Rambam Health Care Campus** and the dedicated team at **Galilee Clinical Bio Research (Galil CRO)**, who expertly managed and coordinated this study, has been instrumental in ensuring the highest clinical standards. It has been a privilege to work alongside such esteemed partners, and we look forward to further development and the opportunity to bring CimetrA® to patients in need of safer, more effective treatments."*

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Next Steps
Based on these positive findings, Argent BioPharma plans to:

- Advance regulatory discussions to explore approval pathways for CimetrA®.
- Conduct further clinical investigations into CimetrA®'s broader therapeutic applications in inflammatory diseases.
- Continue engaging with potential commercial partners to maximize CimetrA®'s global market potential.

—Ends—

Authorised for release by the board of directors, for further information please contact:

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About Argent BioPharma

Argent BioPharma Limited (ASX: RGT; OTCQB: RGTLF) is an innovative clinical-stage biopharmaceutical company specialising in neuroimmunology, developing advanced nano-medicines to address unmet medical needs in central nervous system (CNS) disorders and immune-related conditions. By leveraging cutting-edge technologies, including the Neuro-Immune Modulatory (NIM) System and its role in coordinating nervous and immune responses, Argent BioPharma's robust pipeline—featuring lead candidates like CannEpil®, CogniCann®, and CimetrA®—targets complex diseases where effective treatments are lacking. Through a commitment to science-driven innovation and patient-centered outcomes, Argent BioPharma is reshaping the future of care for chronic, inflammatory, and neurodegenerative diseases

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Annexure A

Protocol Title	A Phase IIb, double blind, placebo-controlled clinical study designed to evaluate the effect of CimetrA in patients diagnosed with COVID-19
Study Arms	STUDY DRUG – CIMETRA was administered as the following: Arm 1: CimetrA-1, with a total dose containing a combination of Curcuma longa rhizomedry extract 28 mg, Boswellia serrata resin dry extract 60 mg in spray administration – divided in 4 separate doses given as an add on therapy, total of 4 doses over 48 hours (day 1 and day 2), twice a day (morning and evening). Arm 2: CimetrA-2, with a total dose containing a combination Curcuma longa rhizome dryextract 19.6 mg, Boswellia serrata resin dry extract 42 mg in spray administration – divided in 4 separate doses given as an add on therapy, total of 4 doses over 48 hours (day 1 and day 2), twice a day (morning and evening). Arm 3: Placebo, composed of the same solvent but without active ingredients, given as anadd on therapy in spray administration, total of 4 doses over 48 hours (day 1 and day 2), twice a day (morning and evening). Patients will be randomised in 1:1:1 ratio to one of the three arms.
Study Purpose	This study designed to evaluate the efficacy, pharmacokinetic parameters, and safety of CimetrA on patients diagnosed with COVID-19.
Methodology and study procedures	• Multi-center multinational-controlled study in Israel, Russia, South Africa and the United States. • 29 adult patients who suffer from moderate COVID-19 infection. • Safety was assessed by collecting and analysing adverse events, blood and urine laboratory assessments, and vital signs. • After the Screening visit, the study drug was administered twice a day, morning and evening (every 12 hours) during (day 1 and day 2) • The patients were randomised in 1:1:1 ratio to study drug (CimetrA) in two dosages in addition to Standard of Care - Arm 1, 2 or (Placebo) in addition to Standard of Care- Arm 3.
Study Duration	The study took place during the patient's hospitalisation due to COVID-19 infection. The study last up to 4 weeks, until the conclusion on day 28. In case of hospital discharge within the study period, follow up continued per protocol until day 28 wherever the subject was located, performed via phone call or in-clinic, depending on the status of the patient and study schedule.
Study Endpoints	The primary outcomes: Efficacy endpoint: - Change in WHO Ordinal Scale for clinical improvement (measured on days 1, 7, 14, 28) - Change in COVID-19-Related Symptoms score (measured on days 1,7, 14, 28) Safety endpoint: was assessed by collecting and analysing adverse events, blood and

	urine laboratory assessments, and vital signs. The secondary outcomes: • Number of participants with depending on oxygen supplementation through day 28 since onset of symptoms • Change in inflammatory marker levels – IL-6, IL-1β, IL-12, TNF α, IFN-γ, CRP, NLR (Neutrophil / Lymphocyte ratio) at days 1, 2, 4, 7, compared to baseline • Pharmacokinetic profile of the study drug on day 1 through 24 Hrs. • Incidence and duration of mechanical ventilation • Incidence of Intensive Care Unit (ICU) stay during COVID-19 complication • Percentage of participants with definite or probable drug related adverse events • Long term adverse events of COVID-19 on Day 28 • The impact of COVID-19 on quality of life of patients on Days 1, 14 and 28. The exploratory outcomes: • Course of change in D Dimer levels compared to baseline • Occurrence of secondary infections

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