Atriva Therapeutics announces publication of Proof of Concept (POC) / Phase 2a RESPIRE study data with zapnometinib in patients hospitalized with COVID-19

- **Atriva Therapeutics announces publication of results from the Phase 2a RESPIRE study in eClinicalMedicine (part of THE LANCET Discovery Science)**
- **Results reflect clinically relevant efficacy for zapnometinib, in terms of the primary endpoint - clinical severity status (CSS) at Day 15 with zapnometinib`s safety profile comparable to placebo**
- **Trial results provide solid foundation for further clinical development of zapnometinib in severe Influenza**

Tübingen/Martinsried, Germany, 04 October 2023 – Atriva Therapeutics GmbH, a biopharmaceutical company pioneering the development of host-targeting antiviral therapies, announced today the publication of proof-of-concept data for its oral MEK inhibitor, zapnometinib, in hospitalized patients with moderate-to-severe COVID-19 in the journal eClinicalMedicine.

The double-blind, placebo-controlled RESPIRE trial investigated the safety and efficacy of zapnometinib in hospitalized adults with COVID-19 at 17 sites worldwide. The trial was terminated early as the emergence of the Omicron variant impacted recruitment. Despite the early termination, patients on zapnometinib had higher odds of improved clinical status score (CSS) vs placebo (odds ratio [OR] 1·54 [95% CI 0·72–3·33]; p=0·262). The frequency and intensity of adverse events were low and similar between the zapnometinib and placebo arms. Further details on the study and trial results can be found at: https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(23)00414-5/fulltext

"These results provide proof-of-concept for the innovative approach of targeting the Raf/MEK/ERK pathway in hospitalized patients with moderate or severe COVID-19," said Dr. Stephan Stenglein, Chief Medical Officer of Atriva Therapeutics.

Zapnometinib is an oral, non-ATP-competitive, small-molecule inhibitor of MEK1/MEK2 with immunomodulatory and antiviral properties. Atriva is continuing the development of zapnometinib in severe viral diseases with epidemic or pandemic potential, aiming to confirm the promising results from the RESPIRE study.

Christian Pangratz, CEO of Atriva Therapeutics, concludes: “The encouraging study results from the RESPIRE trial establish a strong foundation for us to advance zapnometinib into the next clinical study in which we plan to demonstrate the molecule’ s efficacy and safety in patients hospitalized with severe seasonal influenza.”

The RESPIRE trial was funded by Atriva Therapeutics GmbH, the German Federal Ministry of Education and Research and co-funded by the European Investment Bank.

About the RESPIRE study

RESPIRE[1] was a randomized, double-blind, placebo-controlled, international, multi-center POC (Proof of Concept) / Phase 2 clinical trial in adult patients with moderate-to-severe COVID-19. Hospitalized patients with or without supplemental oxygen at the time of screening

or randomization were enrolled. On top of standard of care, patients were randomized to receive zapnometinib (ATR-002) 900 mg tablets, once daily on Day 1, followed by zapnometinib 600 mg once daily on Days 2 to 6, or to receive placebo in a matching scheme.

The study was designed to establish the efficacy of zapnometinib; the primary endpoint was CSS on Day 15, using a seven-point ordinal scale as recommended by the WHO COVID-19 Therapeutic Trial Synopsis.[2] Secondary endpoints included time to hospital discharge, changes in clinical signs and symptoms and other relevant clinical parameters. All patients were followed-up for 90 days.

About zapnometinib

The Atriva lead product zapnometinib (ATR-002) was specifically developed to treat diseases caused by RNA viruses, such as influenza and COVID-19. Zapnometinib is a MEK inhibitor targeting the intracellular Raf/MEK/ERK signaling pathway. Many RNA viruses need to activate this pathway to ensure replication, including influenza viruses,[3,4] hanta viruses,[4] the respiratory syncytial virus (RSV),**Fehler! Textmarke nicht definiert.** and corona viruses,**Fehler! Textmarke nicht definiert.** including SARS-CoV-2. Zapnometinib inhibits cellular MEK (MAPK/ERK kinase), blocking the formation of functional virus particles in the host cell, ultimately reducing the viral load in the body.[5,6] In SARS-CoV-2 infected cells, inhibition of MEK1/2 by zapnometinib significantly reduces virus production.[2]

In addition, zapnometinib has the potential to modulate the host immune response and avoid an excessive cytokine/chemokine response that can be caused by viral infections.[8,9] This second host-targeting effect may therefore dampen the overactive inflammatory response, e.g., as seen in the lungs of patients who are severely ill with COVID-19 or influenza.**Fehler! Textmarke nicht definiert.**[10] In SARS-CoV-2 infected cells, inhibition of MEK1/2 by zapnometinib significantly impairs pro-inflammatory cytokine production.**Fehler! Textmarke nicht definiert.** Zapnometinib is under advanced clinical development as a treatment for patients with severe influenza or COVID-19. For the treatment of hantavirus infections, zapnometinib has been granted Orphan Drug Designation (ODD) by the U.S. Food and Drug Administration (FDA).

About Atriva Therapeutics

Atriva Therapeutics' mission is to develop an antiviral therapy platform against severe respiratory and systemic diseases with a high unmet medical need induced by RNA viruses, e.g., influenza and COVID-19. The clinical-stage biopharmaceutical company is pioneering the development of host-targeting antiviral therapies, making development of resistance unlikely, and thereby significantly contributing to pandemic preparedness. The Atriva lead product zapnometinib (ATR-002) is a first-in-class, host-targeting agent that aims to inhibit viral replication and to favorably modulate the body's immune response to RNA viruses. Ten active patent families with broad international coverage grant protection for the use of MEK inhibitors and other kinase inhibitors for antiviral therapies through 2041. Atriva Therapeutics was founded in 2015 by a team of leading scientists in viral research and seasoned industry experts and is based in Munich, Germany.

For further information, please visit www.atriva-therapeutics.com and follow us on LinkedIn and X (formerly known as Twitter).

Contact:

Atriva Therapeutics GmbH
Christian Pangratz, CEO
Phone : +49 69 999916210
pangratz@atriva-therapeutics.com

References:

1. Atriva Therapeutics GmbH. 2022. A Randomized, Double-Blind, Placebo-Controlled, Multi-Centre Clinical Trial to Evaluate the Safety and Efficacy of ATR-002 in Adult Hospitalized Patients with COVID-19 (RESPIRE).
2. https://www.who.int/publications/i/item/covid-19-therapeutic-trial-synopsis.
3. Pleschka S et al. Nat Cell Biol 2001 Feb 3:301-5.
4. Ludwig S et al, Curr. Opin. In Virology 2023, https://doi.org/10.1016/j.coviro.2023.101304
5. Haasbach E et al. Antiviral Res 2017 Jun 142:178-4.
6. Laure M et al. Antiviral Res 2020 Jun 178:104806.
7. Schreiber A et al. 2022. Cell Mol Life Sci. 79(1):65.
8. Planz O Antiviral Res 2013 Jun 98(3):457-68.
9. Pinto R et al. Antiviral Res 2011 Oct 92(1):45-56.
10. Ragab D et al. 2020. Front Immunol. 11, 1446 (2020).