35Pharma Announces Oral Presentation Featuring its Novel Activin and GDF Trap HS135 at the American College of Cardiology's 72nd Annual Scientific Session (ACC)

- HS135 demonstrates enhanced in vivo PAH efficacy across lung and heart readouts, including normalization of RV gene expression
- HS135 entirely normalizes expression of heart failure markers in LV and reverses lung congestion and pulmonary vessel remodeling in a Left Heart Failure model

Montreal, QC, Canada (Mar. 5, 2023)– 35Pharma, a biopharmaceutical company that designs and develops biologics for cardiopulmonary and metabolic diseases, today reported preclinical results from its HS135 program in an oral presentation at the American College of Cardiology's 72nd Annual Scientific Session together with the World Congress of Cardiology (ACC.23/WCC) in New Orleans, LA, USA (Mar. 4 – 6, 2023).

TGF-beta superfamily growth factors Activins and GDFs are validated targets driving the pathophysiology of cardiopulmonary diseases. While previous agents directed against these growth factors have shown considerable therapeutic promise in clinical trials, full pathway inhibition remains a challenge.

HS135, an engineered Activin receptor II ectodomain (ActRII) -based Fc-fusion protein, has been rationally designed for best-in-class Activin and GDF *in vivo* target engagement and optimal pathway rebalancing.

The data reported at ACC.23/WCC today demonstrate HS135's enhanced and differentiated efficacy in pre-clinical models of Pulmonary Hypertension and Left Heart Failure.

Highlights of the data presented include:

- HS135's best-in-class potency profile translates into full *in vivo* target engagement in mice as measured by complete suppression of FSH, a biomarker of Activin and GDF inhibition
- HS135 showed higher and differentiated efficacy in a rat Monocrotaline model of Pulmonary Arterial Hypertension (PAH):
    - HS135 dose-dependently improved pulmonary arterial pressure as well as pulmonary vessel muscularization and normalized inflammatory gene expression in the lung
    - HS135 dose-dependently returned parameters of right heart failure to baseline and normalized gene expression in the right ventricle to levels comparable to normal, naive animals

- HS135 showed enhanced and differentiated efficacy in a mouse therapeutic transverse aortic constriction (TAC) model of Left Heart Disease:
    - HS135 dose-dependently reduced left-ventricular expression of markers or heart failure and fibrosis to baseline
    - HS135 dose-dependently reversed lung congestion and pulmonary vessel remodeling to baseline levels
- In each case, HS135 achieved a deeper and differentiated response compared to dose-matched ActRIIA-Fc

Maureen O'Connor, Chief Scientific Officer of 35Pharma commented: "The data presented today at ACC.23/WCC demonstrate that HS135's best-in-class profile translates into deeper responses *in vivo*. These results illustrate the potential of HS135 as a differentiated disease modifying approach to address Pulmonary Hypertension and Heart Failure."

About 35Pharma

35Pharma is a biopharmaceutical company that designs and develops best-in-class transforming growth factor-beta (TGF-beta) superfamily ligand traps for cardiopulmonary and metabolic diseases. HS135 is a multi-specific receptor ectodomain ligand trap designed to achieve maximum neutralization of Activins & GDFs, clinically validated drivers of cardiopulmonary and metabolic disease. HS135 is undergoing IND enabling development.

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