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Variant Pharmaceuticals Announces Publication of Data Demonstrating 2-Hydroxypropyl-β-Cyclodextrin (2HPβCD) Protects Against Kidney Disease in Experimental Models of Alport Syndrome (AS) and Focal Segmental Glomerulosclerosis (FSGS)

These data, published in Kidney International, reinforce evidence that altered lipid metabolism contributes to pathogenesis of some glomerular disorders

The data also demonstrate 2HPβCD can prevent proteinuria and renal function decline in experimental AS and FSGS

WESTON, Fla., Oct. 24, 2018 /PRNewswire/ -- Variant Pharmaceuticals, Inc. (Variant), a clinical stage orphan drug company developing first-in-class drugs for patients with rare diseases, announced today publication of preclinical data evaluating 2HPβCD in experimental models of Alport Syndrome and FSGS. Data were published in *Kidney International.*[1]

Key findings from the experimental Alport Syndrome model (Col4a3 knockout mice) include:

- Accumulation of esterified and free cholesterol (crystals) in the kidney cortex of Alport Syndrome (AS) mice, attributed to impaired reverse cholesterol transport (based on reduced expression of ABCA1 and ABCG1 in mRNA isolated from glomeruli)
- Demonstration of fibrosis and podocyte foot process effacement in AS mice (based on Picrosirius red staining and electron microscopy)
- Administration of 2HPβCD subcutaneously (4,000mg/kg, 3 times weekly) in AS mice resulted in significantly lower cholesterol ester and crystal accumulation, fibrosis, podocyte foot process effacement, and proteinuria when compared to untreated AS mice

Key findings from the experimental FSGS mouse model (Adriamycin-induced nephropathy) include:

- Demonstration of glomerular injury in FSGS mice, as evidenced by mesangial expansion, and proteinuria
- Administration of 2HPβCD subcutaneously (40 mg/kg, daily via osmotic pump) in FSGS mice protected against glomerular injury (reduced mesangial expansion) and significantly reduced proteinuria when compared to untreated FSGS mice

The authors reported that these data are supportive of that from their previous studies in an experimental model of diabetic kidney disease and a newly established FSGS model (NFAT mouse model), both of which demonstrated a preventive effect of 2HPβCD in progression of kidney disease.

"We are pleased to see the preclinical data published in the prestigious *Kidney International* journal," stated Stephen C. Glover, Variant's Co-founder, CEO and Chairman. "The strength of these data helped support progressing directly into phase 2a clinical trials in adult patients with FSGS, which will significantly shorten our development time. We look forward to advancing our goal to provide a meaningful treatment for FSGS, AS, and other forms of kidney disease."

About Variant

Variant Pharmaceuticals, a clinical stage orphan drug company focusing on restoring health and transforming the lives of patients with rare diseases through innovation, was established in 2014, with the mission to become a leading orphan drug company. Our evolving product pipeline is targeted to the $100+ billion orphan drug market. Our lead candidate is 2-hydroxypropyl-β-cyclodextrin (2HPβCD) for chronic treatment of two orphan indications, Focal Segmental Glomerulosclerosis (FSGS) and Alport Syndrome (AS), progressive forms of kidney disease with an addressable market greater than $3.5 Billion.

References

1. Mitrofanova A, et al. Hydroxypropyl-β-cyclodextrin protects from kidney disease in experimental Alport syndrome and focal segmental glomerulosclerosis. *Kidney Int*. 2018 Oct 6. pii: S0085-2538(18)30518-0. doi: 10.1016/j.kint.2018.06.031. [Epub ahead of print]

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