OTI TOPIC

ADVANCING ASPRIHALE® TO PIVOTAL PK/PD STUDY

Mark Stansfield, Senior Project Manager, and Kambiz Yadidi, Founder and Chief Executive Officer, both of Optitopic, discuss results of their pilot Phase I clinical study of dry-powder inhalation of aspirin.

Dry-powder aspirin inhalation company Otitopic recently completed a pilot clinical study – *"A Phase I, Single-dose, Open-label, Pilot Study to Compare the Pharmacodynamics and Pharmacokinetics of Acetylsalicylic Acid Inhalation Powder with Non-Enteric-Coated Chewable Aspirin in Healthy Adults"*.

The effects of Asprihale® are a distinctly more rapid, potent and consistent pharmacodynamic (PD) response than the current standard of care (reference listed drug). The immediate antiplatelet and inhibitory effects of Asprihale® would be expected to translate to meaningful clinical benefits in the early evolution of arterial thrombosis.

The very high levels of serum thromboxane B2 (TxB2) suppression and complete arachidonic acid (AA)-induced platelet aggregation response – both within two minutes – are unprecedented for a non-parenterally administered antiplatelet therapy. The individual data for both AA-induced platelet aggregation and TxB2 inhibition show more rapid and predictable response in two minutes than chewable aspirin.

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Asprihale® is a novel, proprietary aspirin formulation delivered via a dry powder inhaler (DPI), entering the bloodstream faster than oral tablets. Once the US FDA grants approval, the rapid onset of action indicates a promising role for Asprihale® in the treatment of acutemyocardial infarction.

In the clinical trial, subjects were administered a single dose of acetylsalicylic acid (ASA) as either a chewable tablet (162 mg) or by inhalation. Regarding Asprihale® pharmacokinetics (PK), there is a 1.6-fold greater C_{max} of aspirin when inhaled, which is similar to intravenous

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"This rapid exposure is unprecedented and has enormous implications for early disruption of an emerging thrombus, where differences in time of restoration of blood flow within minutes with different therapies can be life changing."

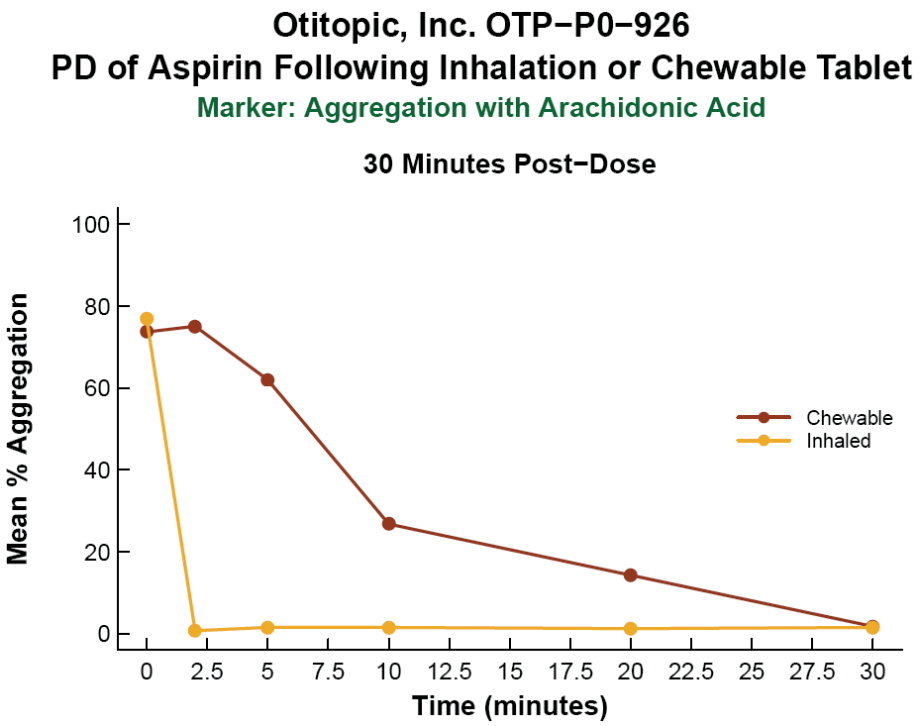

Figure 1: Asprihale® completely inhibits AA-induced platelet aggregation within two minutes versus 30 minutes for chewable aspirin.

administration. Asprihale® aspirin exposure occurred more rapidly compared with chewed aspirin. Asprihale® reaches maximum plasma concentration in two minutes versus 20 minutes for 162 mg non-enteric coated chewable aspirin. This rapid exposure is unprecedented and has enormous implications for early disruption of an emerging thrombus, where differences in time of restoration of blood flow within minutes with different therapies can be life changing.

TxB2 and platelet aggregation were measured and evaluated at baseline and at each PK timepoint post dose – two, five, 10, 20, 30 and 40 minutes, and one, four and 24 hours. Following administration of the inhaled formulation, TxB2 levels fell rapidly over the first two minutes. Asprihale's early and consistent reduction in TxB2 led to early and consistent suppression of platelet aggregation by AA in two minutes.

Figure 1 displays percentage aggregation versus time when aggregation was induced with AA. For the inhaled formulation, AA-induced aggregation was completely suppressed at two minutes post-dose; for the chewable tablet, at 30 minutes post-dose. The effect was maintained for 24 hours for both treatments.

A PK/PD analysis was performed to evaluate the effect of T_{max} on the time to reach 5% platelet aggregation when induced by AA. A strong linear relationship was found between ASA T_{max} and time to onset of its antiplatelet effect. Earlier attainment of C_{max} (i.e. shorter T_{max}) leads to earlier onset of action with Asprihale®.

Otitopic is advancing towards its pivotal PK/PD study following discussions with the FDA. The randomised pivotal study, which is expected to initiate in the fourth quarter of this year, will compare the pharmacodynamics, pharmacokinetics, safety and tolerability of acetylsalicylic acid inhalation powder with non-enteric coated chewable aspirin. The team is looking forward to starting its pivotal study.

Otitopic® is a registered trademark of Otitopic LLC

ABOUT THE COMPANY

Otitopic is a late-stage dry powder inhalation of aspirin company with a track record of success in pharmaceutical product drug delivery and drug device development. Asprihale® is a novel, proprietary aspirin formulation administered via a DPI, entering the bloodstream faster than oral tablets. Otitopic is on track with Asprihale® to file a US NDA in 2021/2022 for a novel drug device combination product to reduce the risk of vascular mortality in patients with suspected acute MI. Otitopic is pioneering a new class of dry-powder inhalation in the cardiovascular medicine field, based on the company's proprietary drug delivery platform. This patented technology leverages inhalation as the route of administration, enabling rapid inhibition of platelet aggregation, aimed at providing powerful new therapeutic capabilities.

ABOUT THE AUTHORS

Mark Stansfield is Senior Project Manager at Otitopic, with more than 11 years' experience in the development of inhaled medications and oral drug formulations. He has extensive product development program management and clinical development and operations experience, including products for the treatment of cancer, chronic obstructive pulmonary disease, asthma, viral infections and acute thrombotic conditions such as heart attack and stroke.

Kambiz Yadidi, Chief Executive Offiver at Otitopic, has over 28 years of management experience across the pharma space. He has been involved in biopharmaceutical businesses in dry powder inhalation drug development, inhalation devices, nasal delivery drug development and nasal drug delivery devices. These companies include Sinus Dynamics and MedQuip. He has also been involved in industry organisations as a board member of Cedars-Sinai Hospital (LA, CA, US) Board of Governors.