Immunotherapy, INO-3107, is Well-Tolerated, Effective, and Elicits an Antigen-Specific T-cell Response in Adults with HPV-6 & 11 Recurrent Respiratory Papillomatosis

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Background: DNA medicine represents an innovative approach that can be applied to multiple diseases, by utilizing optimized DNA plasmids encoding for target antigens/proteins and device-facilitated cell transfection to overcome limitations of other antigen delivery methods (e.g., vector-based vaccines/therapeutics) including the risk of anti-vector neutralizing antibodies. We present data for INO-3107, an immunotherapy designed to generate T-cells against human papillomavirus (HPV)-6 and -11 for treating recurrent respiratory papillomatosis (RRP), as an example of an application of the DNA Medicine platform.

Methods: Thirty-two patients with HPV-6 and/or 11 RRP requiring ≥2 surgeries in the year preceding dosing entered the Phase I/II trial, and received INO-3107 on Day 0, Weeks 3, 6, and 9 via intramuscular injection. Patients were evaluated through Week 52. Primary endpoints: safety and tolerability; secondary endpoints: post-treatment surgical frequency and immune responses. Twenty-eight patients were enrolled in the retrospective extension study for at least 52 additional weeks and assessed for surgical frequency and severe adverse events (SAEs).

Results: INO-3107 induced peripheral T-cell activity against HPV-6/11 and clonal expansion through Year 1 (Y1). Excised papilloma revealed T-cell infiltration inclusive of activation and cytotoxicity. In Y1, 72% (23/32) of patients experienced a 50-100% reduction in surgeries, increasing to 86% (24/28) in Year 2 (Y2). Mean annual surgeries declined 78%, from 4.1 (pre-treatment, n=32) to 0.9 (Y2, n=28). INO-3107 was well-tolerated; 41% (13/32) reported treatment-related adverse events, most commonly transient injection site pain (31%) and fatigue (9%). No treatment-related SAEs or long-term safety concerns were identified.

Conclusion: INO-3107 elicited a robust and persistent antigen-specific cellular immune response, was well-tolerated, and showed sustained clinical benefit with reduced surgery frequency through Year 2. These findings support DNA medicine as a promising alternative to current antigen delivery platforms, with the added advantage of repeat dosing due to the absence of immunogenic viral vectors.