PhysioPD™ Research Enhances Dermatology Research and Drug Development Using Mechanistic Physiological Modelling

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Objectives: To elucidate the mechanistic details of etiology and pathogenesis in a variety of dermatologic diseases and conditions. To improve the identification of promising candidate therapies and reduce risks associated with drug development. To increase research efficiency for new treatments.

Methods: With participation from industry clients, Rosa developed PhysioPD Research Platforms for acne, atopic dermatitis (AD), psoriasis, skin aging, and erythema in over a dozen research projects. PhysioPD Platforms are quantitative systems pharmacology (QSP) models that incorporate engineering approaches and scientific analysis to clarify physiology and drug interactions. Each Platform was qualified in accordance with Rosa’s Model Qualification Method (MQM), including conducting simulated experiments to ensure that Platform results were qualitatively and quantitatively consistent with relevant published and/or proprietary research. Simulated experiments were then run to test hypotheses, elucidate the connections between treatments and physiological outcomes, explore efficacy, toxicity, and therapeutic dose range, select the correct drug or treatment targets, and define and refine the target patient population.

Results: In acne, PhysioPD research identified sebogenesis and inflammation as top drivers for acne pathophysiology and demonstrated that only one compound out of three was likely to be superior to the standard of care. In skin aging, a sensitivity analysis highlighted hyaluronic acid and other key drivers for improvements in skin appearance as promising treatment targets. In AD, PhysioPD research clarified mechanisms of action and helped prioritize acquired assets for development. Each of these research projects has elucidated interactions between skin structure/function and immunology and enabled investigation of hypotheses linking pathologies to clinical outcome scores, e.g., SCORAD.

Conclusions: In the context of dermatology R&D, PhysioPD Platforms are efficient tools for increasing confidence in a candidate therapy. Mechanistic QSP modeling also enables focused use of resources by informing go/no-go decision points early in the drug development process.