Barriers and Opportunities: A View across the Developmental Divide

Twenty-four years ago, I first had the privilege of working in a research laboratory in dermatology for three years during medical school. It was my first exposure to immunodermatology, and I marveled at the extent to which the molecular culprits of various immunologic diseases had been systematically identified and cataloged—especially given the rudimentary nature to which the molecular mechanisms of diseases in other physiologic systems and specialties had been worked out.

Since then, having subsequently spent 15 years as a practicing clinician and 10 years concurrently as an investment professional, I have personally found it even more interesting that none of those discoveries was really ever carried forward for the development of targeted therapies. Having both witnessed and participated in the financing of companies whose business plans centered on treating rare diseases involving other organ systems—which were successful in both raising capital and developing treatments to help patients—the question that inevitably emerged was why did this phenomenon not happen with diseases in dermatology even though groundwork arguably had been laid to a greater extent than for many of the conditions that ultimately ended up as the basis for companies? We have begun to see interest from investors and companies in developing treatments for a rare disease such as epidermolysis bullosa, but there are many other diseases within dermatology that remain unaddressed—some represented within the ranks of the patient groups making up the Coalition of Skin Diseases, but countless others that are not.

Dermatology is indeed a specialty of a few very common afflictions, as well as many, many rare ailments, of which the aforementioned immunologic represent but a subset and for which the quality of research continues to advance and improve. Yet the focus of product development remains squarely centered on those few common diseases, to the detriment of the field. Many view dermatology as a medical specialty with few conditions affecting sufficient patient numbers to support a viable commercial enterprise; consequently, outside of those few entities, investment interest has historically been lukewarm. It seems almost necessary that, given the characteristics of the field, the orphan disease business model should be embraced as a means to both increase the breadth and depth of therapies within dermatology and reestablish the legitimacy of dermatology as a "serious" medical specialty.

The calculus to change the perception of investors has precedent and does not require extensive spreadsheet manipulation. Pioneered at Genzyme, which developed billion-dollar product franchises based on enzyme replacement therapies for genetic diseases affecting a handful of patients, the orphan disease model posits that a scarcity of affected individuals need not make a disease less lucrative as commercial opportunity. Indeed, it makes each of those individuals much more valuable and even more worthy of close attention and care. Annual courses of therapy cost not hundreds, but hundreds of thousands of dollars—and the regulatory exclusivity granted to such treatments (Seven years' worth in the United States and 10 years' worth in Europe) because of the presumed limitations of their scope of utility further buttresses this value. If suitably chosen and priced accordingly, a company with a single drug for an indication with a prevalence of one to five cases per million can generate well over a billion dollars in sales or more. According to Thomson Reuters, almost a third of orphan drugs currently generate more than a billion dollars of sales in a year, with more

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than $50 billion in global sales for the category. Moreover, there is always the potential for an unexpected upside from indications not previously considered at the time of initial development—both rituximab and recombinant erythropoietin, now mainstays of therapy in several medical specialties and bellwethers of biotechnology drug development, started out as orphan drugs.

Of course, positing pie-in-the-sky scenarios on the back of an investor's napkin does neglect certain real-world considerations. The main requirement to achieve this rarefied status in the eyes of the regulatory agencies is simply the number of patients afflicted, but, of course, the social and commercial viability of such a model requires evidence that the investment in each patient is justified—that their lives are sufficiently transformed for the better to warrant the burden of cost, both to government and private payers and to society as a whole. Such an undertaking will necessitate comprehensive efforts to provide validation of outcome measures and documentation of natural histories, similar to the work done by the International Dermatology Outcome Measures group for psoriasis and as has been the case with other conditions outside dermatology, such as muscular dystrophies.

It is ultimately this demonstration of value—showing that diseases of the skin are as functionally debilitating to the individuals who are unfortunate enough to have them as those found with other specialties—that is required to compel reimbursement. If payers can be convinced to pony up for biologics costing tens of thousands of dollars a year for a condition as prevalent as psoriasis, then there is no reason why they cannot be swayed in similar fashion for treatments for isolated conditions within dermatology and at a higher per capita rate to make the rare disease business model feasible—opening up a heretofore largely unexplored vista of value creation to attract investors and help patients, as well as improve the stature of dermatology within medicine and society as a whole.

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