

## TRANSLATIONAL TOOLBOX

# How to Start a Biomedical Device Company

## Physicians Can Lead the Team Effort



J. Michael DiMaio, MD,<sup>a,b</sup> Brittany A. Potz, MD,<sup>c</sup> Jeffrey E. Thatcher, PhD,<sup>a</sup> John J. Squiers, MD<sup>a,d</sup>

### SUMMARY

Taking a solution for a clinical unmet need from a mere idea to a profitable medical device company is a long and complex process. After developing a prototype solution, the physician-inventor must quickly file a patent to protect his or her intellectual property. After the patent is secured, the first major business decision arrives: should the inventor sell the patent or maintain ownership? If the inventor decides to maintain ownership, he or she will face a series of hurdles from obtaining additional funding to device development, and ultimately, commercialization and marketing of the product. Although this process is daunting at first glance, and physicians certainly face unique challenges in this endeavor, clinicians are uniquely and strategically positioned to identify clinical unmet needs and, therefore, have the ability to fundamentally transform the way we treat our patients. (J Am Coll Cardiol Basic Trans Science 2017;2:328–34)  
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Although medical school and residency typically do not provide formal training regarding biodesign or business principles, physicians should be leaders at the cutting-edge of innovation in health care. After all, physicians are uniquely positioned to identify clinical unmet needs and to develop practical solutions with the potential to widely affect patient care. These unmet needs manifest in a variety of ways, but the best method is for the physician to simply pinpoint a problem that routinely bothers him or her during everyday clinical activities. This step of the biomedical design process is the easiest and, unfortunately, is the one at which the vast majority of physicians cease their efforts. After all, successfully addressing a clinical unmet need by developing a novel drug, device, or process

is neither straightforward nor guaranteed. Any physician with an insatiable passion to improve some element of patient care, big or small, can nevertheless find success, which may then afford him or her the opportunity to commercialize the solution. Herein, we will provide an overview of the fundamental principles for starting a company in the medical device industry based on our own experience in taking a potential solution for a clinical unmet need from the bench-top to in-human clinical trials.

### THE “3 IS” PROCESS (IDENTIFICATION, INVENTION, IMPLEMENTATION)

The initial steps in starting a successful medical device company center on the “3 Is” process

From <sup>a</sup>SpectralMD, Inc., Dallas, Texas; <sup>b</sup>Department of Cardiothoracic Surgery, The Heart Hospital Baylor Plano, Plano, Texas; <sup>c</sup>Division of Cardiothoracic Surgical Research, Department of Surgery, Rhode Island Hospital, Warren Alpert Medical School of Brown University, Providence, Rhode Island; and the <sup>d</sup>Baylor Scott & White Research Institute, The Heart Hospital Baylor Plano, Plano, Texas. Drs. DiMaio and Thatcher receive salary from and have ownership through stock in SpectralMD, Inc. Dr. Squiers has received consulting fees from SpectralMD, Inc. Dr. Potz has reported that she has no relationships relevant to the contents of this paper to disclose. All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Basic to Translational Science* [author instructions page](#).

(identification, invention, implementation). A detailed description of this process, as implemented in the Stanford Biodesign Program, was provided in a recent issue of *JACC: Basic to Translational Science* (1). Briefly, a commercial venture begins with the identification of an unmet clinical need. Physicians, more than potentially any other group of professionals, can provide important expertise at this stage due to their first-hand experience with the need as well as their understanding of the pathophysiology underlying and current treatment methodologies available for the need. Once identified, the unmet clinical need informs the invention of a solution that will ultimately be commercialized. However, this solution cannot be invented by the physician alone; instead, a team approach is often imperative for success. If the physician identifies an unmet need that may be solved by a medical device, for example, he or she might enlist an engineer with the skills to design such a device, from prototyping through final aspects of development. Finally, after a solution has been invented, the team may incorporate a business expert to assist with implementation of the device into the market, including considerations regarding intellectual property, credible reimbursement options, and investment strategies for further research and development (R&D) and commercialization efforts. Fundamentally, the “3 Is” process characterizes the dynamic relationship among professionals in at least 3 different arenas (medicine, engineering, and business) that is required to identify, invent, and implement a commercially viable medical device.

## PATENTING AN INVENTION

After the physician and his or her team have identified a clinical problem and invented a solution, patenting this solution is critical for protecting the team’s ability to commercialize their medical device. There are 3 important milestones in the process of patenting an invention: the date of conception, the date of actual reduction to practice, and the date of constructive reduction to practice. The date of conception describes when the invention was first conceived in its completed form. The date of actual reduction to practice refers to the date when a working model or prototype was completed. The date of constructive reduction is the date on which the patent application was filed.

Prior to 2013, the United States followed a “first-to-invent” patent system. Under this system, when 2 inventors filed patents for the same invention, an interference hearing before the Board of Appeals and Interferences at the U.S. Patent Office was scheduled

to determine the legal date of priority based on the date of conception for each inventor. Although this system was designed to protect inventors’ intellectual property, several major flaws, including the lengthy and costly legal process and difficulties in determining accurate dates of conception, limited its effectiveness. Therefore, in 2011, the U.S. Congress passed the America Invents Act, which introduced a “first-to-file” patent system that gives priority to the inventor who first files a patent application. Beginning on March 16, 2013, the first-to-file system took legal precedent in the United States, the final country to adopt this system worldwide. Therefore, the date of constructive reduction to practice is now used to determine which inventor has priority over a patented technology.

Inventors must navigate the patent system under the first-to-file system in a dramatically different fashion than under the first-to-invent. Previously, inventors who were confident that their date of conception would hold legal precedent had little incentive to keep their inventions secret or to rush toward a patent application. Instead, they could take their time to diligently reduce their invention to practice and to prepare a patent application, knowing that their date of conception would give them priority to the patent. Under the first-to-file system, however, inventors are now most likely to secure a patent by keeping their technology secret from others and by filing for a patent (demonstrating constructive reduction to practice) as quickly as possible. Otherwise, the inventor risks losing the patent to someone who files first, even if the first-to-file party had conceived of the patented technology second.

Another key consideration when filing for a patent is the patent policy at the inventor’s institution. If a physician conceives or creates a patentable medical device or technology through research conducted at his or her institution, it is very likely that the university, practice group, and/or employer has rights to both the patent and any royalties that stem from commercialization of the device that is patented. In fact, many universities generate a significant income from technology and patent licensing of their faculty’s inventions (2).

Finally, although it may be possible for physicians to patent an invention on their own, hiring a patent lawyer is strongly recommended given the complexities of the patenting system and the speed with which a patent application needs to be filed under the governing first-to-file patent system. A strong relationship with a patent lawyer is also essential to ensure that the inventor is ready to protect his or her

## ABBREVIATIONS AND ACRONYMS

<b>FDA</b>	= Food and Drug Administration
<b>NIH</b>	= National Institutes of Health
<b>R&amp;D</b>	= research and development
<b>SBIR</b>	= Small Business Innovation Research
<b>STTR</b>	= Small Business Technology Transfer

invention against potential patent challenges and infringements that may arise after the patent is secured.

### LICENSE, ASSIGN, OR MANUFACTURE?

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After the solution has been successfully patented, the inventors are well positioned to bring the patented medical device to the marketplace. The first key decision during this process is whether to license, to assign, or to manufacture their invention. Which option is best depends on a number of factors, including the invention itself, the inventors' long-term goals and/or level of desire to maintain control over their invention, and the existing market competition for the invention (3).

When an inventor licenses an invention, he or she allows a third party to commercialize the invention for a certain time period. In return, the inventor receives an agreed upon compensation, also termed a "royalty," which is typically either a percentage of sales or a 1-time payment. At the conclusion of the licensing agreement, the original inventor regains complete control over the invention from the third party. When an inventor assigns an invention, he or she sells (and therefore relinquishes) ownership of the invention to another party in exchange for a 1-time payment or series of payments. Although the inventor at least temporarily cedes control over the invention in both cases, he or she is no longer faced with the daunting tasks of development, mass manufacturing, commercialization, and marketing of the invention. If, however, the inventor is committed to maintaining absolute control over the invention, he or she can proceed to manufacture the medical device. In this case, it remains the inventor's responsibility to further develop, mass manufacture, commercialize, and market the product. These activities require significant expertise and financial investments. Fortunately, the necessary financial support required to manufacture and commercialize a medical device can be acquired through a variety of avenues.

### SOURCES OF FUNDING

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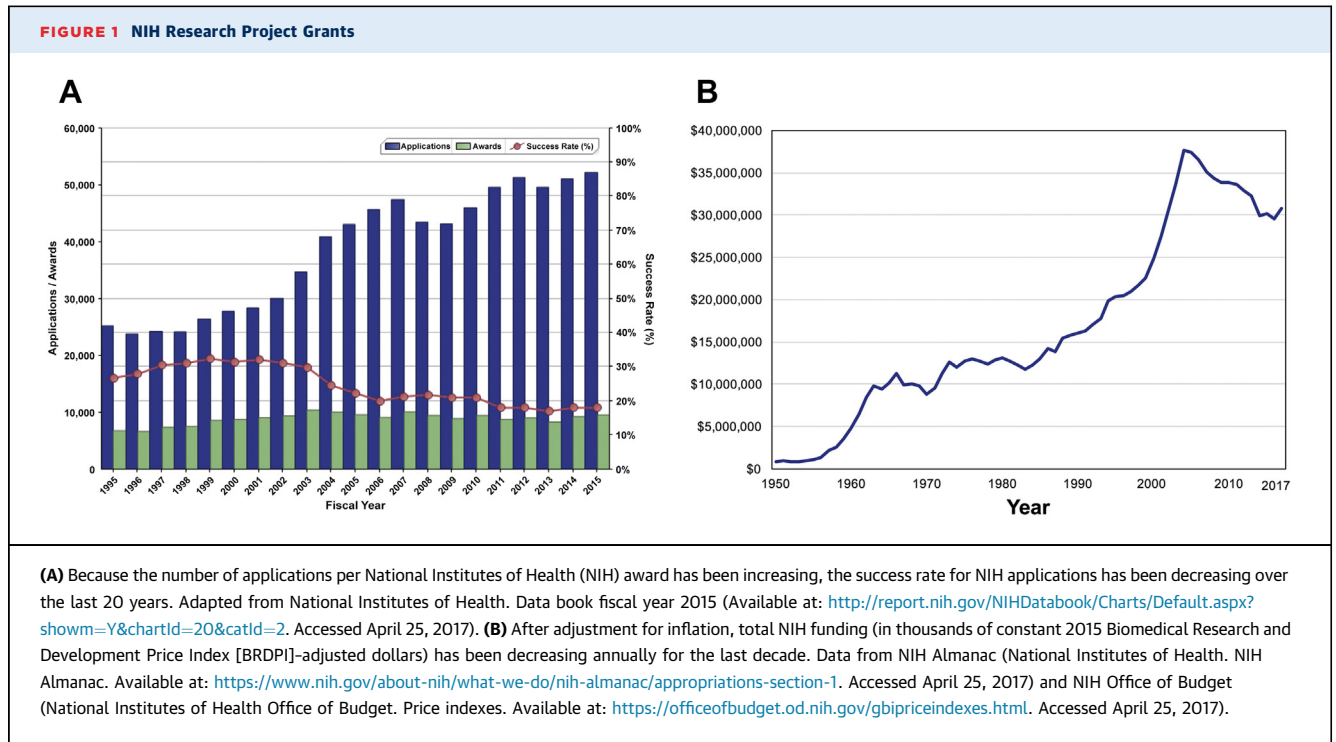
The primary difference between licensing/assigning and manufacturing a product is that the inventor will need to secure significant funding to begin commercialization of the product if he or she chooses to manufacture. The inventor should expect a net deficit, with costs accumulating due to further development of the invention, mass manufacturing, and marketing expenses, until the product has been successfully commercialized and available on the

market for several years. Recent estimations of R&D costs suggest that well over \$1 billion are often invested to bring a single new drug to market (4). R&D costs related to medical devices are significantly less, but are nevertheless typically on the order of tens of millions of dollars per device. Thus, to fully commercialize their product, inventors will likely have to acquire funding from more than 1 source. The 2 primary sources of funding for biomedical companies are the public sector (i.e., the government) (5) and private sector (i.e., venture capitalists) (6,7).

The primary source of government funding for health care innovation and medical device development is the National Institutes of Health (NIH). The NIH spends 53% (\$16.5 billion) of its budget on Research Project Grants and 11% (\$3.5 billion) on R&D contracts. The rest of the budget is split among research centers, other research grants, research training, intramural research, research management and support, and miscellaneous costs. The Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs funded through the NIH's R&D budget are of particular use to physician inventors aiming to commercialize their solution to a clinical unmet need. The intricacies of these programs were outlined in a recent issue of *JACC: Basic to Translational Science*, and funding can support virtually any project performed by a small business, from preclinical research to in-human clinical trials (5). Fortunately, the SBIR/STTR Reauthorization Act of 2011 (P.L. 112-81) requires that the NIH actually increase its funding of small business through these programs. Applying for SBIR/STTR funding from the NIH is very similar to the grant-writing and application process with which physician-scientists are already familiar.

Despite the support available from the NIH and other government agencies, the likelihood that an inventor will be able to fully commercialize an invention with public funding alone is unlikely. In fact, over the last 2 decades, the number of applications per NIH award has been increasing, with a corresponding decrease in the percentage of successful applications. Worse yet, the total amount of inflation-adjusted funding awarded by the NIH has actually been decreasing for nearly a decade (Figure 1). Even if the inventor does secure NIH funding, the award amount is generally insufficient to advance the medical device through the litany of Food and Drug Administration (FDA) clearance milestones (5). Therefore, support from the private sector is almost certainly necessary to acquire as well.

Private sector funding, termed "venture capital," is typically sought from investors who are willing to



tolerate a substantial element of risk inherent to a small business that has not already capitalized its product. Applying for private funding is, therefore, a very different process compared with the grant application process with which physicians are more familiar. Securing venture capital for one's company requires the physician-inventor to shift from the details of grant applications toward streamlined business proposals. When pitching an investment opportunity to venture capital investors, inventors should use the "10-20-30 Rule of PowerPoint" (8). This rule calls for the PowerPoint presentation to be no more than 10 slides, covering the 10 topics listed in Table 1. The presentation should last no more than 20 min, and all text should be no smaller than 30-point font. If the significance of the clinical unmet need, the innovativeness of the solution, and the details of the business plan take more than 20 min (or a font smaller than 30 points) to explain, then the inventor has not sufficiently distilled the concept and cannot expect a venture capitalist to take a risk on the idea.

Beyond NIH funding and venture capital, other potential sources of funding include grants from private organizations such as the American Heart Association, governmental agencies such as the National Science Foundation, intramural support via universities, and even friends and family. Although the amount of money needed to get a medical device business off the ground is daunting, always

remember that if a clinical unmet need is significant enough and the inventor's solution is strong enough, funding can be secured.

### EQUITY DISTRIBUTION

Whereas grants from government agencies or private organizations typically do not dilute the inventor's ownership of their technology, the inventor must realize that venture capital investments are secured in exchange for equity in the company. In general, equity is initially distributed based on what each of the founding members of the company brought to the table early in the company's lifecycle. When negotiating with private investors, a number of additional factors will weigh into equity negotiations, including relatively quantifiable aspects, such as the value of intellectual property and patents, business plans and projections, and the amount of capital sought by the inventor, as well as more qualitative aspects, such as the nature of the relationship between the inventor and the investor. Of course, inventors who retain more equity during these negotiations will ultimately retain more voting power, and therefore more control in their company. Inventors can expect to exchange a percentage of equity in the company, as valued by the investor, that is equivalent to the capital investment they are seeking. For example, if an inventor needs to raise \$50 million and their investor believes the

<b>TABLE 1 10-20-30 Rule of PowerPoint</b>
10 topics
1. The problem (unmet clinical need)
2. Your solution (invention)
3. Business model
4. Underlying magic/technology
5. Marketing and sales
6. The competition
7. The team
8. Projections and milestones
9. Current status and timeline
10. Summary and call to action
20-min presentation
30-point font (minimum)
Presentations to venture capital investors should follow the 10-20-30 rule of PowerPoint, which requires the presenter to cover 10 specific topics, in 20 min, using 30-point font.

company is worth \$500 million, then the inventor will cede 10% equity and voting control in the company to the investor. Venture capitalists are savvy investors, so significant amounts of negotiation should be expected before they are willing to sign official agreements with the inventor.

## REGULATION AND THE FDA

After funding has been secured, the inventor must ensure that the company meets quality control standards per FDA requirements if they plan to market the device in the United States (9). These standards, termed design control, include quality assurance practices throughout the lifecycle of medical device design that work to verify and to validate that design outputs (the medical device) correspond to design inputs (user needs) (Figure 2). Verification (was the device designed correctly?) and validation (was the correct device designed?) are the 2 sides of the design control coin. All aspects of the design control process must be documented and stored within a “design history file,” which ultimately captures the entire history of design for a completed medical device.

Prior to marketing a medical device, companies typically must obtain FDA clearance or approval, depending on the classification of the medical device. Devices are classified as Class I, II, or III based primarily on the risks associated with the use of the device. Class I devices are considered to be low risk and are subject to the least regulatory controls. These devices (e.g., examination gloves) are often exempt from FDA clearance prior to marketing. Class II devices are incrementally higher-risk devices than Class

I and thus require greater regulatory controls to provide reasonable assurance of device safety and effectiveness. These devices (e.g., infusion pumps) require FDA *clearance* via Premarket Notification, also known as a 510(k) application, that proves substantial equivalence of the device to an existing device that has already been cleared by the FDA. Class III devices are at the highest risk and are subject to the highest level of regulatory control. Class III devices (e.g., implantable heart valves) require FDA *approval* via a Premarket Application.

With increasing risk, the FDA will require an increasing quality of evidence to support the safety and efficacy of the device for its proposed labeling and indications. Class III devices, for example, usually must be vetted in pre-market clinical trials that require investigational device exemption from the FDA. Very often, these clinical trials require randomization of patients to treatment with the new device or the current standard of care. Additional details regarding medical device classification and FDA approval processes were provided in a recent issue of *JACC: Basic to Translational Science* (10).

In general, keeping the design control process current and preparing applications for FDA clearance/approval are both laborious and time consuming. In fact, bringing a medical device from initial conceptualization to market takes, on average, between 3 and 7 years (10), and even longer for drugs (11). It is therefore advantageous to work with an experienced quality assurance engineer and a regulatory expert who have previous experience with these tasks to ensure that the medical device can move through the regulatory process quickly and efficiently.

## COMMERCIALIZATION AND MARKETING

After FDA approval has been secured, the company can commercialize and market its medical device, the final steps of product development. Although the goal of advertising is to encourage the commercial adoption of the product, marketing involves analytically identifying consumer behavior to advertise and commercialize efficiently and effectively. The inventor should assemble a team of marketing and commercializing experts who can effectively portray how the medical device solves a previously unmet clinical need and why the value-proposition of the medical device justifies its cost to the consumer.

## 3 RULES OF SUCCESS

When inventors take on the challenge of manufacturing their own product, a myriad of difficult

decisions will inevitably arise. However, 3 simple rules (12), if followed throughout all phases of commercialization, will allow the inventor to be successful:

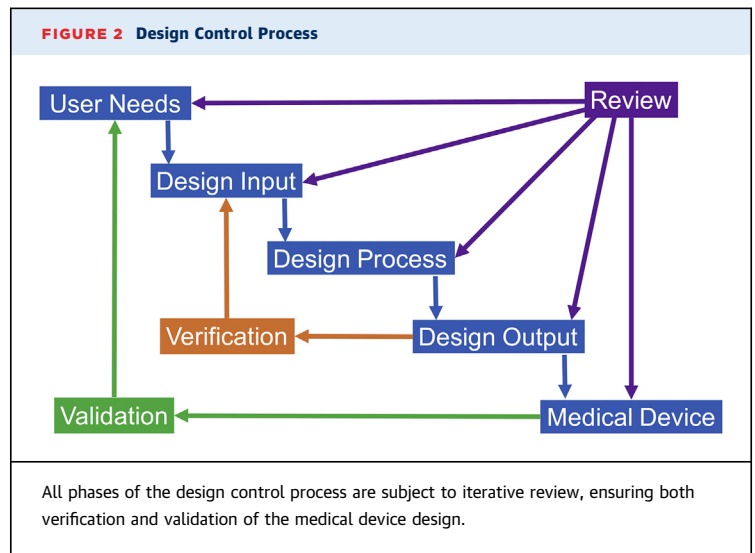
1. *Better before cheaper.* Although it may be beneficial in the short-term to choose the least expensive and/or time-consuming option, a successful company always chooses the best, most reliable option for the long-term.
2. *Revenue before cost.* Successful businesses drive profitability with higher volumes of product or higher prices, not by lowering the cost of the product.
3. *There are no other rules.*

Finally, and most importantly, when the inventor elects to see an idea through the manufacturing process, he or she must be aware that this decision means accepting a new leadership role. As such, the inventor must approach subsequent problems just as he or she approaches clinical work: with the goal of perpetual learning toward mastery of the environment and tools. The leader should develop a team of coworkers who excel in their professions, and he or she should lead by setting an example of hard work and friendly collaboration. It is imperative that leaders first fully trust those with whom they have chosen to work and then naturally relinquish complete control over decisions that they are not the most qualified to make. The leader, like the physician for the patient, must focus on listening, understanding, supporting, and building the team toward shared goals. The leader must also strive to understand the various elements of each multifaceted issue within the company so that he or she can confront future problems with improved decision making. As with most things in life, balance is important, and decisiveness is ultimately a game winner.

### UNIQUE CHALLENGES FACED BY PHYSICIANS DURING COMPANY DEVELOPMENT

Due to their identification of the clinical unmet need and mastery of the clinical environment, physicians are uniquely positioned to develop a company based on their novel solution to this need. Although all of the hurdles discussed previously are presented to any leader of a start-up company, physicians face a host of additional, unique challenges when starting a company due to a variety of factors, including educational background, possible attitude toward lawyers, and a reframing of expectations compared with clinical practice.

During training and while in practice, physicians learn by *doing*—evaluating new patients, performing



procedures, and actively learning from mistakes. When starting a company, however, a new learning mentality is required, one that is more similar to the beginning of a physician's education in medical school. Rather than learning by doing, a physician entrepreneur should consider the importance of reading and studying to gain essential knowledge and important experience. Recommended reading materials include the Stanford biodesign course textbook (*Biodesign: The Process of Innovating Medical Technologies* [13]), the Harvard Business Review *HBR Guide to...* books, and the current series of "Translational Toolbox" articles, including this one, in *JACC: Basic to Translational Science*. Physicians may also consider taking a short intensive course in entrepreneurial leadership, such as the Entrepreneurship Development Program offered annually by the Massachusetts Institute of Technology.

Physicians must constantly remember the importance of seeking out, listening to, heeding, and implementing sound legal advice when starting a company. Although legal professionals are often viewed as adversaries to the practicing clinician, in the form of both potential lawsuits and the increasing bureaucracy of medical practice, expert lawyers should be strongly embraced by the physician entrepreneur at all stages of company development. More often than not, the potential hazards identified by lawyers when reviewing contracts and essential company documents will manifest themselves if the advice of the lawyer is brushed aside. The immediate investment in what may appear to be relatively expensive legal advice is absolutely worth long-term protection against legal troubles down the line in a company's life cycle.

Finally, many clinicians enjoy practicing medicine due to the instant gratification that arises from providing excellent care to their patients. The immediate joy that accompanies a difficult, but correct, diagnosis of a curable disease or a challenging, but successful, procedure is often not available to motivate physicians as they develop their company. The design control process that dictates progress in any biomedical device process, by definition, requires years of incremental progress toward the final product. Gratification is certainly available at many stages throughout this process, but will likely not be a daily, or even weekly, occurrence. Therefore, physicians must reframe their expectations of and timelines for success when starting a new company.

## CONCLUSIONS

Taking a solution for a clinical unmet need from a mere idea to a profitable medical device company is a long and complex process. After developing a prototype solution via the “3 Is” process, the inventor must

quickly file a patent to protect his or her intellectual property. After the patent is secured, the first major business decision arrives: should the inventor sell (license or assign) the patent or maintain ownership (manufacture)? If the inventor decides to maintain ownership and proceed with manufacturing, he or she will face a series of hurdles from obtaining funding (government or private) to device development (design control and FDA regulation), and ultimately commercialization and marketing of the product. Although this process is daunting at first glance, and physicians face unique challenges throughout, clinicians are uniquely and strategically positioned to identify clinical unmet needs and, with collaboration and conviction, can fundamentally transform the way we treat our patients.

**ADDRESS FOR CORRESPONDENCE:** Dr. J. Michael DiMaio, SpectralMD, Inc., 2515 McKinney Avenue, Suite 1000, Dallas, Texas 75201. E-mail: [dimaio@spectralmd.com](mailto:dimaio@spectralmd.com).

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