ErectiSTIM ED
bioelectric treatment of erectile dysfunction

Executive Summary

MyoStim ED is a bioelectrical stimulator (BES) that may not only provide transient erectile dysfunction (ED) treatment, but also lead to longer-term recovery of function. Unlike other ED therapies, it is multi-modal: improving blood circulation, managing inflammation, stimulating nerve regeneration and enhancing smooth muscle performance and recovery.

Unmet needs in the large and global erectile dysfunction market are highly significant. An estimated 332 million people will be affected by ED worldwide by 2025; the U.S. alone will account for >40 million people between the ages of 35-74 years. Despite high awareness, PDE-5 inhibitors (e.g., Viagra, Cialis) are not the answer for all ED sufferers due to contra-indications, medication drug interactions, side effects and the presence of non-responders. Other competitive ED offerings are effective, but often affect intimacy, have side effects or are invasive (e.g., injections, implant)

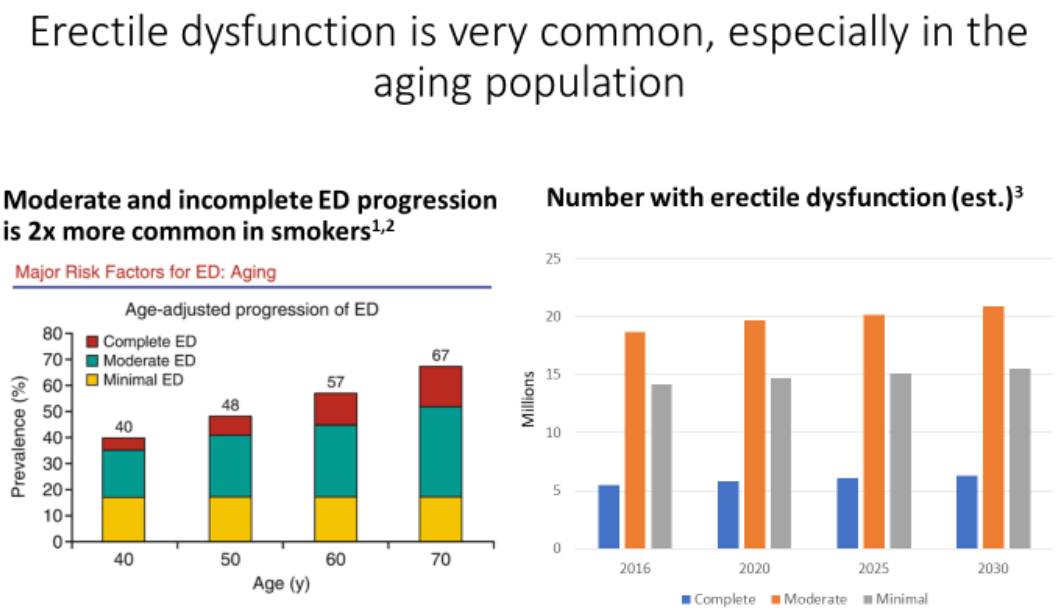
Myostim ED clinical data (preliminary) is suggestive of high efficacy, ease-of-use and limited, if any, side effects. Feasibility data has been obtained from XX patients with very promising (statistically significant) results. It reflects xx years of research in electrical conduction, is rooted in science and protected by patents (two issued, seven pending) and proprietary algorithms.

The Myostim ED development team collaborates with a high level of technical and clinical expertise. Investment to-date totals $2.0 million, with another $1.5 million required for completion of pre-clinical R&D and clinical studies. Pre-money valuation is $XXX. The goal is to further development, increase conviction regarding efficacy and exit through sale to a third party. The comparative valuations of consumer-oriented ED companies are high.

II. Details

Unmet market in the large and global ED market and highly significant

Erectile dysfunction (ED) is extremely common, projected to affect 332 million males by 2025.[1] ED frequency increases with age, affecting 40% of the 40-year old population and rising to 67% in the 70-year old population.[2] ED severity also increases with age from minimal to complete; the majority of patients are classified as moderate. The International Index of Erectile Function is a validated and commonly used scoring system for ED classification.[3]



[1]Pathophysiology of Erectile Dysfunction, Penn Clinical Manual of Urology https://www.progressivemenshealth.com/age-major-risk-factor-erectile-dysfunction-2/. Feldman HA, Johannes CB, Derby CA, et al. Erectile dysfunction and coronary risk factors: Prospective results from the Massachusetts male aging study. PrevMed 2000; 30:328.[2] https://www.ncbi.nlm.nih.gov/pubmed/10731462 3Calculated based on U.S. census projections by age

Approximately 40-50 million males are affected in the U.S., Europe and Brazil; an estimated 134 million are affected in China.[4-10] Reporting by market may vary based on survey methodology and timing, cultural factors (i.e., willingness to admit sexual dysfunction), population age distribution and other factors.

ED is a complex problem associated with aging, vascular disease and neurological conditions

Erectile dysfunction has been associated with a variety of factors including aging, hypertension, cardiovascular disease, depression, diabetes, neurological diseases, prostatic surgery and other conditions. [11] For example, diabetics have twice the age-adjusted risk and often exhibit symptoms 10-15 earlier than other men.[12] Antidepressants, antihistamines and medications to treat high blood pressure, pain or prostate conditions may contribute to ED. Non-organic causes such as stress, anxiety, depression and other psychological issues account for 10-20% of erectile dysfunction.[13] Smoking and obesity represent common risk factors.

Aging, compounded by the presence of co-morbidities been associated with vascular alterations, pressure imbalances and penile structural changes that result in erectile dysfunction. Historically, solutions have targeted patient sub-populations and short-term needs, and did not address the underlying pathophysiology.

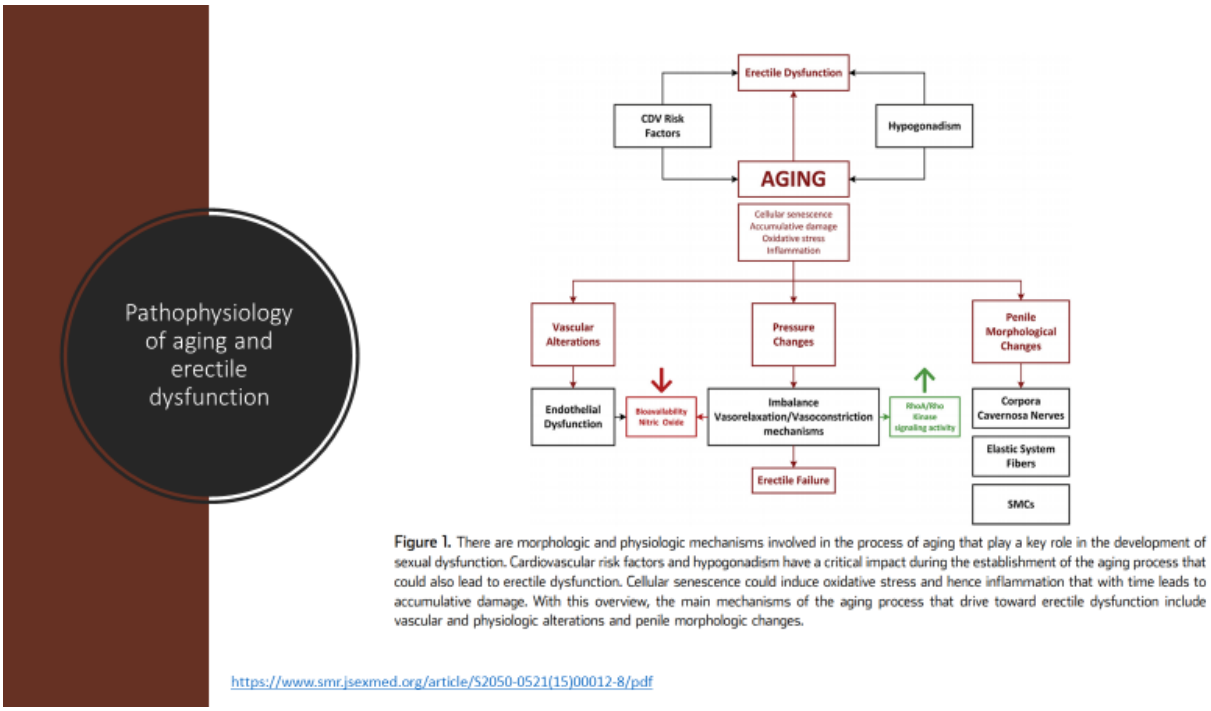


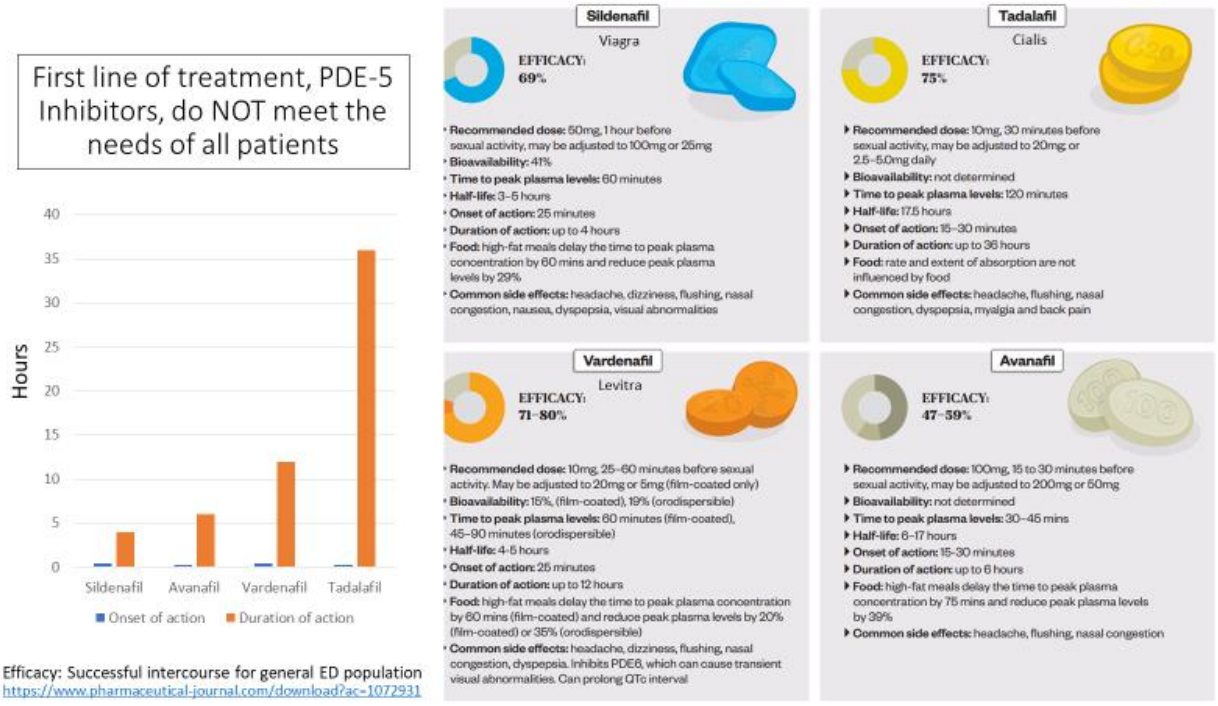
Figure 1. There are morphologic and physiologic mechanisms involved in the process of aging that play a key role in the development of sexual dysfunction. Cardiovascular risk factors and hypogonadism have a critical impact during the establishment of the aging process that could also lead to erectile dysfunction. Cellular senescence could induce oxidative stress and hence inflammation that with time leads to accumulative damage. With this overview, the main mechanisms of the aging process that drive toward erectile dysfunction include vascular and physiologic alterations and penile morphologic changes.

https://www.smr.jsexmed.org/article/S2050-0521(15)00012-8/pdf

Despite high awareness, PDE-5 inhibitors (e.g., Viagra, Cialis) are not the answer for all ED sufferers

First line therapy for erectile dysfunction are PDE-5 Inhibitors are not curative; they provide symptomatic relief. Best known PDE-5s include Viagra (sildenafil) and Cialis (tadalafil).

Global Viagra revenues approximated $2.0 billion in 2012, prior to the availability of generics in Europe (2012) and the U.S. (2017); 2018 revenues were $636 million.[14] Global Cialis revenues in 2018 were $1.9 billion (U.S.: $1.2 billion), a decline of 20% due to the availability of generics in selected markets.[15] U.S. prescriptions increased by 25% following generic approval.[16] Levitra and avanafil are minor products.



Efficacy: Successful intercourse for general ED population
https://www.pharmaceutical-journal.com/download?ac=1072931

PDE-5 inhibitors are contra-indicated in patients with unstable angina and uncontrolled hypertension and have been shown to interact with drugs such as nitrates and alpha-blockers used for these (and other) conditions. Efficacy ranges from 69-80%. Common side effects of limited duration (5-6+ hours). include headache (up to 28%), pharyngitis (up to 18%), dyspepsia (up to 17%), abnormal vision (11%), flushing (10%) and nasal congestion (10%).[17] Of patients that have tried pharmacological treatment, up to 45% are non-responsive or discontinue treatment due to co-morbidities, side effects or cost.

Other competitive ED offerings effective, but often affect intimacy, have side effects or are invasive

Second line therapies include intra-urethral and topical alprostadil, vacuum erectile devices and most recently low intensity shock wave therapies. Intra-urethral and topical alprostadil have been associated with penile pain, local redness, burning and bleeding, thereby somewhat limiting utilization.[18] Vacuum erectile devices (with constricting band) are readily available and inexpensive, though affecting intimacy, requires manual coordination and may be difficult to use in obese men; they have been associated with minor pain and bruising, unnatural erections and absent or painful ejaculation.[19] Third-line invasive therapies such as intra-cavernosal injections and penile implant have not been widely accepted.

Competitive product offerings may impact intimacy, result in local adverse events or be invasive

	Efficacy[1]	Impact on intimacy	Functional recovery period	Immediacy of effect	Sustainability of effect	Adherence	Safety	Cost
First-line								
PDE5 inhibitors	70%	Low	NA	15-30 minutes	4-36 hours	NA	systemic side effects; drug interactions. Contra-indicated CV disease	$25-60/pill x 40 pills/year ~$1,000-2,400/annum
Second-line								
Topical alprostadil[2]	39-75%	Moderate	NA	5-30 minutes	1 hour	Dose titration often required	Local burning, pain erythema; resolve 2 hours	
intra-urethral (IU) alprostadil (suppository)	68%	Moderate	NA	5-20 minutes	1 hour	Dose titration may be required	Penile pain (36%), urethral burning and pain (13%), erythema, bleeding	$66/suppository
Vacuum devices	50-80%	High	NA	2-3 minutes	30 minutes	Difficult in obese men; need coordination	Numbness, pain, bruising, painful ejaculation; unnatural feeling	$300-500/unit
Low-intensity shock-wave[3]	60-65% in patient subsets	None	16 weeks	Spontaneous		12 office visits x 20 minutes divided by 60-90 day break to allow vascular regrowth	Painful during administration	$2,500-3,000; platelet rich plasma extra
MyoStim ED	**70-80%**	**None**	**4-8 weeks**	**Spontaneous**	**>6 months**	**Two 45 minute office visits per week x 4-8 weeks**	**No side effects**	**$1,600**
Third-line								
Intra-cavernosal injections	94%	High	2 session injection training	5-15 minutes	<2-4 hours	Penile injection required	wrong injection site, trauma, fibrosis, priapism	$3-6/dose, syringes
Inflatable penile prosthesis (IPP)[2]	80-90%	Moderate	2-4 weeks	NA	Manual controls	Permanent	Infection, bleeding, scar tissue	$20-30,000

[1] Based on patient selection criteria; [2] Pending FDA approval; [3] FDA status unclear

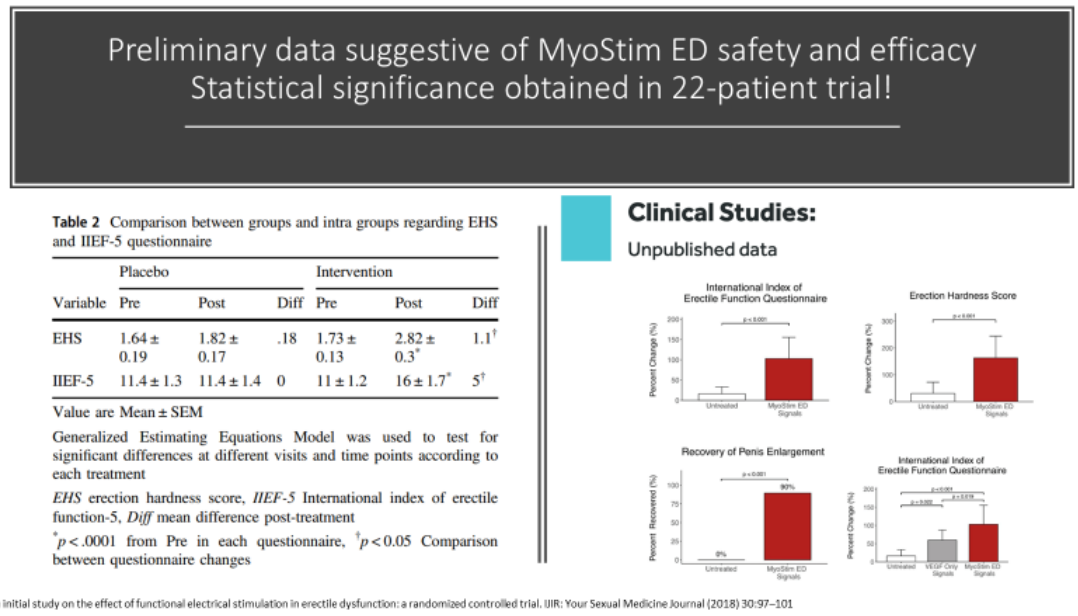
More recent developments include low intensity shockwave therapy +/- platelet derived growth factors and stem cell injections. Shockwave therapy appears promising, though without FDA approval. It requires 16 weeks of treatment, inclusive of a 60 to 90-day period free of therapy to allow vascular re-growth.[20] It's believed to breakup micro-plaques in the penile blood vessels and stimulate new blood vessel growth. The promise of stem cell therapy for regenerative medicine is being explored, including use for erectile dysfunction.[21]

Myostim ED clinical data (preliminary) suggestive of high efficacy, ease-of-use and limited, if any, side effects

Myostim ED is a bioelectric stimulator connected with self-adhesive patch electrodes (3cm) applied to the dorsum of the penis programmed to generate precise signals for improving blood circulation and smooth muscle relaxation, reducing inflammation, and accelerating healing of damaged penile tissue.

In a randomized trial, 22 patients with ED who were not taking any ED-related medications were assigned to treatment with electrical stimulation for four weeks (two 15-minute sessions per week) or a placebo electrical stimulation device. Despite the small sample size, those receiving electrical stimulation treatment showed *statistically significant improvements* in erectile function and quality of life (as measured by the International Index of Erectile Function, Erection Hardness Score, and the WHOQOL questionnaire).[22]

A second trial (n=30) examined the potentially additive effect of adding a third arm to the previous protocol (VEGF) with electrostimulation signals targeting three proteins: endothelial nitric oxide (eNOS), a regulator of endothelial vasoreactivity (venous vasodilation); platelet derived growth factor (PDGF), an enhancer blood flow; and follistatin, a potent stimulator of muscle function and contractility leading to enhanced erection. Unpublished data suggests additional efficacy as compared to the initial randomized clinical trial highlighting the incremental benefits of Myostim ED proprietary algorithms. Anecdotal evidence also suggests improved recovery during the non-erectile state. An effect may also exist with oral PDE-5 medication recalcitrant patients whereby bioelectrical stimulation muscle regeneration increases receptively to oral drugs.[23]



Electrical stimulation has also been shown to be effective in penile rehabilitation for patients that have undergone prostatectomy. Patients who had undergone a nerve sparing radical prostatectomy that received biweekly electrical stimulation treatment for 6 months showed improvement in erectile function not only during treatment but for the six months following treatment. No adverse events related to the treatment were reported[24]

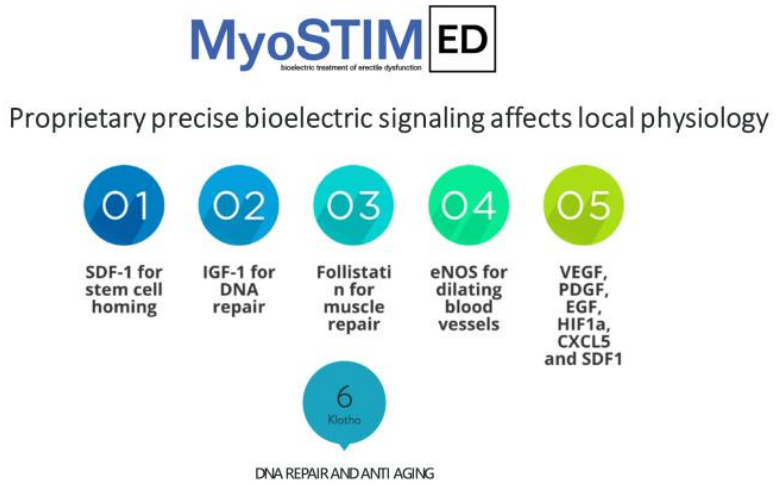
Myostim ED reflects xx years of research in electrical conduction, is rooted in science and protected by patents and proprietary algorithms

It's important to emphasize the scientific basis of Myostim ED as a differentiator to potential "knock-off" competitors; not all bioelectrical stimulators are alike. The Myostim ED algorithms are based on safely modulating various electrical signals to stimulate or inhibit the expression of specific key genes; i.e., to counteract the known molecular patho-physiology of ED and not just induce vasodilation. Multiple pathways are involved.

Myostim ED is the first ED treatment to treat muscle and nerve damage recovery and not just address temporary blood flow improvement.

The MyoStim ED technology has two issued patents; seven are pending:

- US20170266371 - Stimulator, pump & composition
- US20180064935 - Bioelectric stimulator



Myostim ED development team collaborate with a high level of technical and clinical expertise

The Myostim ED development team has invested $2.0 million in product development, pre-clinical studies, clinical studies and patents. The comparatively low level of investment reflects a focused effort and a high level of proficiency, including the conduct on non-U.S. feasibility studies where the cost per patient are a fraction of the U.S.. 30 patients have ben enrolled to-date with positive results, thereby providing confidence to likely outcomes.

Founding Team

Howard Leonhardt, CEO and Executive Chairman, is an inventor and serial entrepreneur with over 21 issued and dozens of pending U.S. patents. He has founded more than 30 start-ups and has had numerous successful exits including the leading endovascular stent graft system and the first percutaneous heart valve sold to Medtronic.

Dr. Cristiane Carboni, Chief Scientific Officer, is a physiotherapist and expert in the treatment of erectile dysfunction with electrical stimulation. She has Mater Degree in pelvic floor rehabilitation – University of Barcelona. Master degree in Rehabilitation Science - Federal University of Health Sciences of Porto Alegre –UFCSPA, Porto Alegre, Rio Grande do Sul, Brazil.

Dr. Nestor Gonzalez-Cadavid, Chief Scientific Advisor, is Professor of Urology, at David Geffen School of Medicine at UCLA and Director of Urology Research Laboratory, LA Biomed at Harbor UCLA Medical Center. He is also Professor of Medicine, Division of Endocrinology, Metabolism and Molecular Medicine at Charles R. Drew University of Medicine and Science.

Leslie Miller MD, Vice President Clinical Affairs

Alex Richardson, Vice President Engineering & Product Development

Jorge Genovese PhD, Vice President Bioelectric Research

Stuart Williams PhD, Vice President Biologics Research

Robert Gelfand PhD, Research Lab Los Angeles Manager

Michael Angerbauer, Chief Bioengineer

Kapil Sharma, Lead Bioengineer

Alonzo Moreno PhD, Senior Advisor, Research Lab Utah Co-Manager

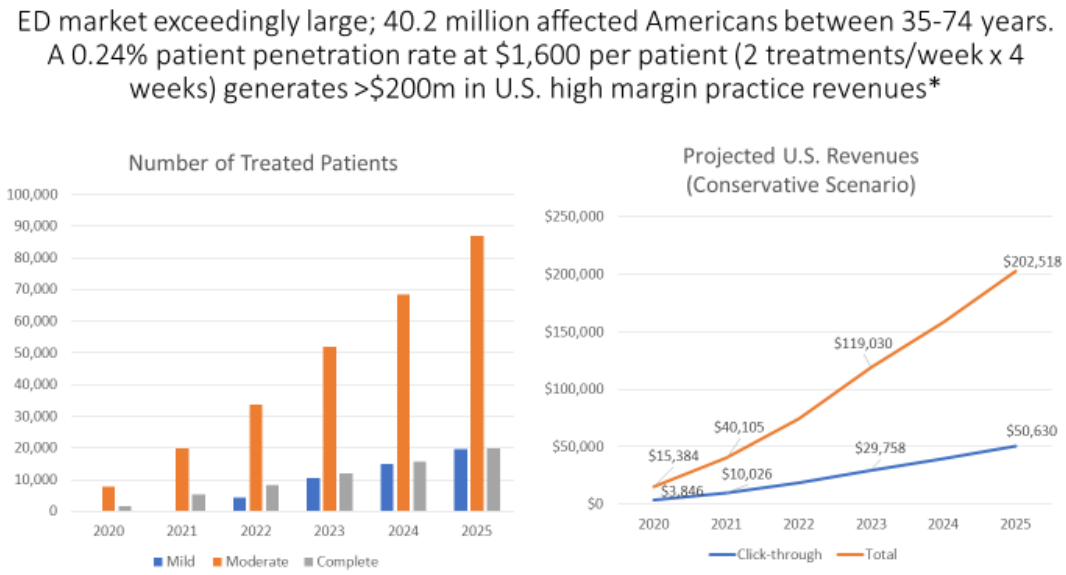
Myostim ED has potentially a highly profitable business model with global and DTC potential

Companies focused on men's sexual health have seen tremendous success in this market. Roman, founded in 2017, provides medications online and has raised a total of $176 million, including a $85 million Series B round based on a valuation of $500 million.[25] They have targeted smoking cessation and plan on expanding into other areas.[26] Hims, also founded in 2017, has raised $197 million, including a Series C round based on a valuation of $1.1 billion. Hims also targets men for baldness and acne, and more recently women for birth control and other conditions.[27] Roman and Hims provides access to physicians and products without the infrastructure costs associated with physician practices and retail pharmacies; their $15 physician telehealth prescription service is not reimbursed by third parties.

Myostim ED also targets men's sexual health, but from a clinical and scientific perspective. It is not targeting the middleman but creating a new product category for a large unmet need based

on clinical and scientific data. According to the American Urology Association (AUA), there are 12,517 urologists in 2,500-3,000 practices, the latter figures assuming 4-5 physicians per practice. The AUA also identifies 226 urologists specializing in erectile dysfunction, a highly focused target opportunity.[28]

Our preliminary business model conservatively assumes limited market penetration, with 125-130,000 patients treated by 2025. Assuming a 25% click-through rate implies high margin revenues of $50 million in the U.S. alone; Europe, China, Japan, Australia and Canada, among others also represent sizable markets.



*Excludes use of Myostim as commercially available consumer product. European ED market (patients) > U.S. > Brazil. China has 3-4x number of ED patients as compared to the U.S.

An alternative business model is potentially based on sale of the professional device and specialty electrodes; i.e., razor and razorblades. An electronic "handshake" can be used to limit the number of generic electrodes. Software upgrades based on the generation of additional clinical data are planned to further justify annual subscription fees and to ensure sustainable differentiation. A direct-to-consumer device is also being considered, though for launch after the professional model to ensure medical and scientific credibility. Consumer oriented apps could also be developed.

III. Footnotes

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