

# SPEECH DELIVERED BY MR. DILIP SHANGHVI, CHAIRMAN AND MANAGING DIRECTOR OF SUN PHARMA ADVANCED RESEARCH COMPANY LIMITED AT THE 11th AGM OF THE COMPANY

Dear Shareholders,

I take great pleasure in welcoming all of you to the 11th AGM of your Company.

# **KEY ACCOMPLISHMENTS IN 2015-16**

I would like to begin by highlighting some of our key achievements of financial year 2016.

At SPARC, we are attempting to continuously improve standards of care for patients globally through innovation in therapeutics and delivery. In pursuit of that vision, your company has built a promising portfolio of potential drugs with many of them now entering human clinical trials across the world.

Most of SPARC's proprietary drug delivery platforms are validated with product approvals and commercialization globally. Our late stage programs are in pivotal clinical trials, paving the way to marketing authorizations in regulated markets such as the US which can unlock substantial commercial value for SPARC.

Your company has made significant progress in advancing key programs last year. We have accelerated recruitment in the phase III clinical studies of Baclofen GRS and initiated work on pivotal studies for Dry Powder Inhaler (DPI) and PICN. We completed 3 pre-IND consultations with USFDA and obtained guidance for the required development data for registration of these programs in US. Your company also filed 4 INDs and initiated first in human studies for 4 programs.

We have had couple of unforeseen regulatory challenges with rescindment of marketing authorisation of ELEPSIA<sup>™</sup> XR by USFDA and delay in XELPROS<sup>™</sup> approval. Both of these events were linked to the compliance status of the manufacturing site of our partner. This has resulted in delay in generating revenues from these promising programs.

PICN, an efficacious and safer anticancer agent which obtained marketing approval in India last year, was successfully launched and commercialised this year with the brand name BEVETEX<sup>™</sup>. BEVETEX<sup>™</sup> offers a safer alternative to existing therapies with the convenience of a shorter infusion time while eliminating the need for premedication with steroids. We are happy to report that BEVETEX<sup>™</sup> is well received by cancer physicians across India.



While building on the momentum of these programs, we continued our focus on augmenting capabilities by scaling our clinical development and regulatory team and making additional capital investments in enhancing biology infrastructure at our Vadodara facility. We will continue to collaborate closely with our affiliate Sun Pharma and its group companies to maintain access to its world class capabilities including their global presence and institutional understanding of the commercial landscape. Your company has taken several measures to ensure such interactions are carried out at arm's length, protecting the interests of both parties and creating synergies.

As you will see in our detailed review of current programs, FY2016 was an important transition year for your company. Not only because of the progression of several products to clinical testing, but also because of the evolution of our early stage portfolio with a purposeful shift towards more innovative, higher valued products.

## INDUSTRY OVERVIEW

Our Industry comprising pharmaceutical, biotech and healthcare delivery segments is in the midst of a recovery globally, sustained in part due to launch of newer and expensive drugs, emerging markets' demand and encouraging catalytic economic and demographic trends. Aging populations, increasing prevalence of chronic and lifestyle diseases, ongoing economic expansion of emerging-markets, and scientific & technology innovation are expected to sustain the momentum of the life sciences sector.

This recovery is made possible by a number of positive fundamentals including recent increases in R&D productivity, which has resulted in a turnaround in drug approvals, and the emergence of breakthrough drugs. There is tremendous excitement and anticipation around new therapeutic approaches like Immuno-Oncology, Genetic Engineering, and Precision Targeting, all leading to potentially high impact treatments addressing hitherto unmet clinical needs worldwide. However, an effort by governments, healthcare providers, and health plans to reduce costs, improve outcomes, and demonstrate value is altering the nature of healthcare demand and delivery landscape. It is becoming increasingly evident that the global life sciences sector is operating through a transformation which is fast reshaping the rules of the game. This transformation has the potential to antiquate proven strategies and enable new ways of winning.

Pharmaceutical industry's business model is also rapidly evolving from captive R&D and traditional closed partnerships to creating multi-stakeholder, multi-national relationships focused on solving scientific and



business challenges. Drug developers are increasingly participating in risk-sharing relationships and other strategic partnerships with academic innovators, patient groups, contract research organizations, and other developers to improve R&D productivity. It is our belief that such dynamic networks making smart use of data, analytics and 'out of the box' regulatory approaches will shape the future of our industry.

## INDIAN INNOVATION INDUSTRY CONTEXT

In India we are at the very beginning of a long term upswing in pharmaceutical innovation following our success in the global generics market, which can propel our industry beyond our generic roots and current comfort zones. Lower cost of failure gives us the strategic space and leverage 'to do More with Less'. Overall cost of development continues to be significantly lower in India, compared to other viable geographies. Our own example powerfully illustrates this advantage. When we compare our cost of global clinical development with comparable programs in similar indications globally, our costs are considerably lower than our international peers. When it comes to discovery efforts and translational research, the costs are even lower. We have also built a diverse pool of world class capabilities in areas such as Medicinal Chemistry, Formulation Sciences, Operational Scaling, Pharmacological and Toxicological evaluations and Project Management in a quarter century of successful global market participation in industries such as Pharmaceuticals and Information Technology. A combination of global market changes, structural advantages and competencies is shaping a compelling opportunity for innovation driven businesses from India.

But as we have learned from our initial experiments in innovative drug development, there are profound challenges constraining us from realizing this opportunity. Indian Pharmaceutical innovation is handicapped by knowledge gaps in critical areas like Biology and Clinical Sciences. It is also crippled by difficulties in scaling up high quality operations. Our belief is that Indian companies such as ours should and will start seeing themselves as global companies driving a value chain that is 'appropriately located'. Your company is already embracing this model by moving global clinical and regulatory leadership to the US. That allows us an opportunity to leverage experienced clinicians and pursue innovative designs and agency engagement.

A lion's share of our efforts is still focused on leveraging our delivery systems understanding to solve problems, improve efficacy and safety. Our success with Liposomal Doxorubicin is a great example of this possibility. A whole host of applications involving nano-technology, liposomes and other encapsulation



and targeting technologies, material science, simulation and modeling techniques are being similarly pursued for incremental efficacy or safety for existing standards of care.

But at least a few early movers are now looking beyond this comfort zone and setting more aspirational objectives. We believe these companies and their successes have the potential to be transformative. We believe SPARC is on the forefront of this effort to develop original solutions from India. We have several novel compounds pursuing substantial improvements to existing standards of care in a diverse set of diseases. Your company has moved most of its first generation innovations in to clinical testing, in the process transitioning our portfolio from a predominantly pre-clinical mix to a balanced blend of clinical, pre-clinical and discovery programs. We are focused on rebuilding our discovery pipeline with a pronounced slant towards innovative programs which can meaningfully improve patient choices.

It is important to highlight this exhilarating journey is certainly riskier and tougher than our path to leadership in the generics industry. A combination of factors including high regulatory hurdles, low probability of success and lack of predictive models to identify winners and prioritize investments escalate our risk profile. Your company is focused on improving the quality of decision making and navigating the increasing development load with utmost financial prudence. But as an ambitious clinical stage company our costs are going to increase and may grow faster than our revenue in the medium term. But our endeavor is to fully prosecute the promise of our innovations if scientific evidence and market potential supports such development while minimizing our overall cash burn. We believe this approach gives us the best chance to maximize shareholder value in the long term.

#### FINANCIAL PERFORMANCE

Our financials for 2015-16 have been published and are available with you. This year your company earned revenues of Rs.16421.91 lacs. The main source of revenue is royalty and milestone payments we receive from the products that we licensed to Sun Pharma for India, emerging markets and USA. We closed the year with a net loss of Rs. 6999.20 lacs. The major expenses were attributed to conduct of clinical trials associated with our late stage programs and employee costs. We also made considerable investments in enhancing our labs at Vadodara to support ongoing projects.

As I mentioned, with several programs advancing to clinical trials and investments in augmenting critical competencies like Clinical Development and Regulatory Management, we expect our expenses to go up in the next few years. To facilitate and fund the anticipated increase in development costs, we



successfully raised Rs.250 crore through a rights issue. This additional funding will help us complete clinical development of several of our late stage programs over next few years, enabling us to generate additional licensing and royalty revenue. Successful completion of our pivotal programs, marketing authorization in target geographies and identification of appropriate commercialization partners are critical for achieving the financial independence which we are hoping to realize in the short term.

## UPDATE ON KEY PROGRAMS

Now I'll discuss progress on key programs in SPARC portfolio.

#### **XELPROS**

SPARC has developed XELPROS<sup>™</sup>, a BAK or Benzalkonium Chloride free Latanoprost eye drops with our proprietary Swollen Micelle Microemulsion (SMM<sup>™</sup>) technology. BAK is a preservative which has many ocular side effects on long-term use. XELPROS<sup>™</sup> is expected to be safe for eyes on long-term use in Glaucoma patients.

SPARC's New Drug Application (NDA) for XELPROS<sup>™</sup> is under review with USFDA. The approval has been delayed pending the cGMP clearance of the manufacturing facility of Sun Pharma (SPIL), our manufacturing partner. Sun Pharma has undertaken detailed remediation at Halol for restoring cGMP compliance status for the site.

#### **ELEPSIA™ XR**

ELEPSIA<sup>™</sup> XR is a novel once-a-day formulation of the anti-epileptic drug Levetiracetam. ELEPSIA<sup>™</sup> XR is designed as higher strengths of 1000mg and 1500mg once-a-day tablet for reducing the overall pill burden of epilepsy patients. Although the dose per tablet is high, the proprietary Wrap Matrix<sup>™</sup> Technology of SPARC helps ELEPSIA<sup>™</sup> XR tablets to be formulated using relatively lower excipient levels, thereby making the tablet compact and better acceptable to patients.

ELEPSIA<sup>™</sup> XR was the 1st NDA approval of SPARC in USA; however, SPARC received a Complete Response Letter (CRL) from the USFDA rescinding its earlier approval, citing that the compliance status of the manufacturing facility was not acceptable on the date of approval. ELEPSIA<sup>™</sup> XR was filed from Sun Pharma's Halol manufacturing facility.



Earlier this month SPARC closed a licensing agreement with a subsidiary of Sun Pharma for commercializing ELEPSIA<sup>TM</sup> XR in the US market. SPARC will receive an up-front payment of US\$10 million from Sun Pharma. It is also eligible for certain additional milestone payments and defined royalties linked to any future sales of ELEPSIA<sup>TM</sup> XR.

# **BACLOFEN GRS**

Baclofen GRS is a novel once-a-day formulation of Baclofen, based on SPARC's proprietary Gastro Retentive Innovative Device (GRID<sup>™</sup>) technology. Baclofen GRS is currently in pivotal phase-3 clinical trials in the USA. Till date, 190 patients of the required 240 have been enrolled in the study. We have taken several steps to accelerate the recruitment like weeding out non-performing sites and adding new sites. We have also opened recruitment at sites in Europe.

Additionally, Duration of Action Study is ongoing in the USA, 84 patients have completed the study against a plan of 135 patients. We expect to complete the enrollment by Q4FY17.

We expect to file the NDA for Baclofen in FY18.

# PICN (TACLANTIS™)

PICN is novel nano formulation of a very successful cytotoxic, Paclitaxel. PICN is developed using SPARC's proprietary Nanotecton<sup>™</sup> technology. Unlike marketed Paclitaxel formulations, PICN is a Cremophor® and Albumin free formulation with advantages of simpler infusion method and shorter infusion time. PICN also eliminates the need for high dose corticosteroids as premedication.

The trade name, TACLANTIS<sup>™</sup>, was conditionally approved by USFDA for PICN in US. SPARC has completed initial exploratory studies to establish bioequivalence with nab-Paclitaxel. The data suggests TACLANTIS<sup>™</sup> may meet the bioequivalence criteria as defined by USFDA. SPARC therefore is planning to initiate pivotal BE study. The protocol has been finalized and submitted to regulators and ethics committee for approval. Subject to receipt of this approval, SPARC expects to commence patient enrollment in FY17.

The bioequivalence route provides a shorter time to get to market and at much lower costs compared to the pivotal phase 3 clinical studies. We therefore are keeping clinical trials in Breast cancer and Cholangiocarcinoma indications as an alternate strategy and will consider only if necessary.



## SUN-K0706

SUN-K706 is a novel and highly selective Bcr-Abl kinase inhibitor, intended for treatment resistant Chronic Myelogenous Leukemia (CML). Currently, there are very limited treatment options for patients who have failed two lines of treatment and especially if they have mutations like T315I. SUN-K706 is a potent inhibitor of Bcr- Abl and its mutant forms, including the T315I mutant. Safety pharmacology data indicates that SUN-K706 has no adverse effect liability on hepatic, neurologic, pulmonary and cardiac functions and the planned clinical study will find whether this translates into a benefit in humans.

SPARC completed necessary preclinical and toxicology studies for initiating the first in human studies and successfully filed IND. The first in human clinical study is initiated in USA.

#### SALMETEROL- FLUTICASONE DRY POWDER INHALER (DPI)

SPARC's DPI is a pre-metered, 60 doses, and breath activated device to administer combination of Salmeterol and Fluticasone by inhalation.

SPARC's DPI is a very efficient device, as it has shown comparable PK profile to Seretide<sup>®</sup>, Accuhaler<sup>®</sup> at half the dose. This device offers uniform delivery of dose, independent of inspiratory flow rate. It consistently delivers higher amount of drug to lungs. The device is small, convenient and easy-to-use and it is compliant with the global regulatory standards.

In a market research conducted by SPARC, physicians viewed SPARC DPI better than Seretide<sup>®</sup> and Accuhaler<sup>®</sup> on all characteristics. After obtaining guidance from regulatory agencies in EU, SPARC has initiated patient enrollment in EU for pivotal studies and we expect to complete necessary trials in a year's time.

#### **BRIMONIDINE OD**

SPARC is developing once-a-day formulation of Brimonidine using proprietary TearAct<sup>™</sup> Technology. Brimonidine is one of the most commonly used drugs for Glaucoma. Brimonidine has to be administered thrice a day, leading to patient compliance issues. In preclinical studies, our product has demonstrated IOP reduction at 24 hours when administered once daily, comparable to currently marketed innovator product administered three times a day. We plan to conduct the proof of concept clinical study in Eastern Europe and the patient recruitment would be initiated in Q2FY17.



# SUN-597 TOPICAL

SPARC has developed a topical formulation of its novel corticosteroid SUN- 597 for steroid responsive dermatoses. In preclinical studies the efficacy of SUN-597 topical was found to be equivalent to currently marketed potent steroids, and superior to marketed low potency steroids. SUN-597 topical formulation, has also demonstrated low potential for skin thinning and other systemic side effects associated with conventionally used topical steroids in the safety studies conducted. SPARC successfully filed IND with USFDA after obtaining guidance for potential registration pathway in a pre-IND meeting.

SPARC completed a Vasoconstrictor Assay (VCA) study in healthy human volunteers in USA. We plan to initiate additional preclinical toxicology studies in Q2FY17 which will help us to initiate proof of efficacy study in Atopic Dermatitis and Psoriasis patients which we intend to start by end of FY17.

#### ABUSE DETTERENT FORMULATIONS

SPARC is working on a Novel Delivery Platform to help address the escalating problem of prescription drug abuse. It is estimated that every day in the United States—46 people die of overdose from prescription painkillers. These deaths have more than quadrupled in the past decade and a half. Today, more people die from prescription opioid overdose than from heroin, cocaine, and all other illegal drugs combined, an alarming trend that led the U.S. Centers for Disease Control to declare it an epidemic in November 2011.

SPARC has developed a platform technology to make a formulation which can deter oral multi-pill abuse. We have filed initial patent for this technology. We have had pre-IND meetings with USFDA for programs under this platform. We also filed IND for one program and completed initial proof of concept studies. This study has demonstrated viability of our technology and we are now working to optimize formulation so that we can initiate pivotal studies.

As you've seen, we have made significant progress in the year 2015-16 and set the stage for critical revenue generating opportunities and milestones going forward.



## OUTLOOK

As we take our programs ahead on the development pathway, we're learning how to manage the complexities of a rapidly changing economic & regulatory environment, respond to the technical demands of innovation, while balancing the requirements of projects with short, medium and long-term horizons.

While some of our delivery systems' projects are considerably closer to the market; we are still in early clinical development of our new chemical entities. In the short term, we will work towards completing the clinical development programs for Baclofen GRS, Salmeterol Fluticasone DPI and PICN. We will also endeavor to fast track other priority clinical stage programs we discussed earlier.

Your company is aggressively replenishing its early stage pipeline as we transition promising candidates to the clinical stage. Our early stage portfolio will continue to be diverse with a mix of delivery system innovations, new chemical entities addressing next generation of opportunities in known and validated biological pathways and in a very small set of opportunities, addressing novel targets. While our focus will predominantly be on molecular targeting using small molecule, new chemical entities, we will also pursue other therapeutic modalities in an exploratory fashion. Oncology, Centre Nervous Systems disorders, Ophthalmology, and Dermatology will remain as our therapeutic focus.

## FOCUS ON PARTNERSHIPS AND CAPABILITY DEVELOPMENT

We are working on building partnerships with several reputed academic institutions to get access to early translational research so as to bring truly novel first in class drugs which may help treat diseases with suboptimal standards of care. We are working on 3 such programs in Oncology in collaboration with globally acclaimed scientists and Key Opinion Leaders. We also established a partnership with a small startup company emerging from a leading university in Europe for developing a next generation treatment for ocular allergies.

In the past few years, your company focused on augmenting internal competencies in core elements of the value proposition, our ability to execute on the development and translation of novel solutions for unmet medical needs faster and cheaper, while partnering with other eco-system players for sourcing ideas and commercializing products. We will continue to build competencies which will help us continuously improve our ability to execute better than our peer group. Such focus includes areas like molecular biology, disease modeling and pharmacology, medicinal chemistry, clinical sciences and informatics. We will also make necessary and sufficient investments in technology and data systems in



order to leverage the speed and intelligence such investments can bring, to differentiate in a competitive market place.

No account of the state of your company would be complete without a mention of its talented, dedicated staff that pursues our programs with great passion and commitment every day. We are very proud to have the team we built across our three locations. We continue to strive to attract and retain the best talent in the industry, both from campuses through our early talent program and lateral hiring. Our talent retention levels continue to be above industry benchmarks. These men and women, who live our core values and strive to achieve our purpose, are the pillars of our differentiation. Please join me in recognizing their dedication and commitment to making the SPARC story possible.

# COMMITMENT TO GOVERNANCE

Before I bring this to close, I want to emphasize our commitment to quality, transparency and highest standards of governance. We take the sensitive character of our industry as a provider of life saving medicines to vulnerable patients very seriously. Our resolute intent to do the right thing for the patient is a key constituent of who we are. We take our commitments as a public company and responsibilities to our shareholders equally seriously. We continue to invest and build resources, processes and systems to exceed expectations placed on us as a player in regulated market places and as a public company. Your company will continue to focus on this critical aspect as we scale and grow as we believe our commitment to quality and transparent governance is critical to long term sustainability of our enterprise.

In closing, we have come a long way together in creating a high value, innovation led business which aspires to be a world leader one day. Your company has built a strong portfolio and operating model which allows it to legitimately claim the pole position in the race for leadership in a still-very-nascent 'second wave' of pharmaceutical innovation from India. We have an opportunity to set a powerful example for Conceiving and Making, globally competitive products from India. Hopefully examples such as ours would inspire higher aspirations and prudent risk taking in our industry, leading to greater success and shareholder value.

Thank you very much for your continued support.

Place: Vadodara

Date: July 29, 2016

Dilip S. Shanghvi Chairman & Managing Director