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Update on R&D Pipeline

4th September 2018

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Agenda

1 **SPARC Strategy & Key Growth Drivers**
Anil Raghavan – CEO

2 **Financial Highlights**
Chetan Rajpara – CFO

3 **Abl Kinase Inhibitor**
SiuLong Yao – Sr. V.P. Clinical Development & Operations

4 **S1PR1 Agonist**
Kristine Nograles – V.P. Dermatology & Rheumatology

5 **Extended Ocular Retention**
Hany Michail – V.P. Ophthalmology

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Yashoraj Zala – V.P. Formulation Development

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Yashoraj Zala – V.P. Formulation Development

8 **Pipeline Build-up Strategy**
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Jaydeep Issrani – G.M. Business Development

10 **Q&A**

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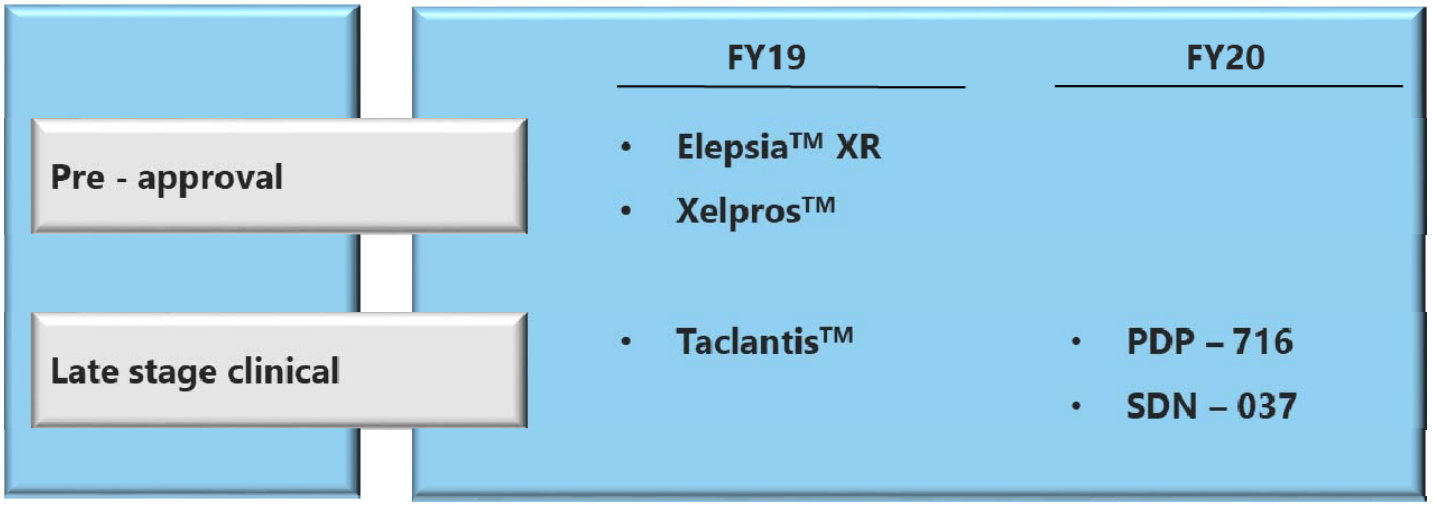
SPARC's Journey

Poised to reach important milestones….



- SPARC responded to US FDA CRLs indicating facility compliance and readiness, resetting the regulatory clock for approval
  - Xelpros™ : PDUFA date – Nov'18
  - Elepsia™ XR : PDUFA date – Jan'19

CRL = Complete Response Letter, PDUFA = Prescription Drug User Fee Act; PDP – 716 = Brimonidine OD, SDN – 037 = SDP – 037 FY = Financial Year
US FDA = United States Food & Drug Administration Taclantis is provisionally approved trade name by US FDA

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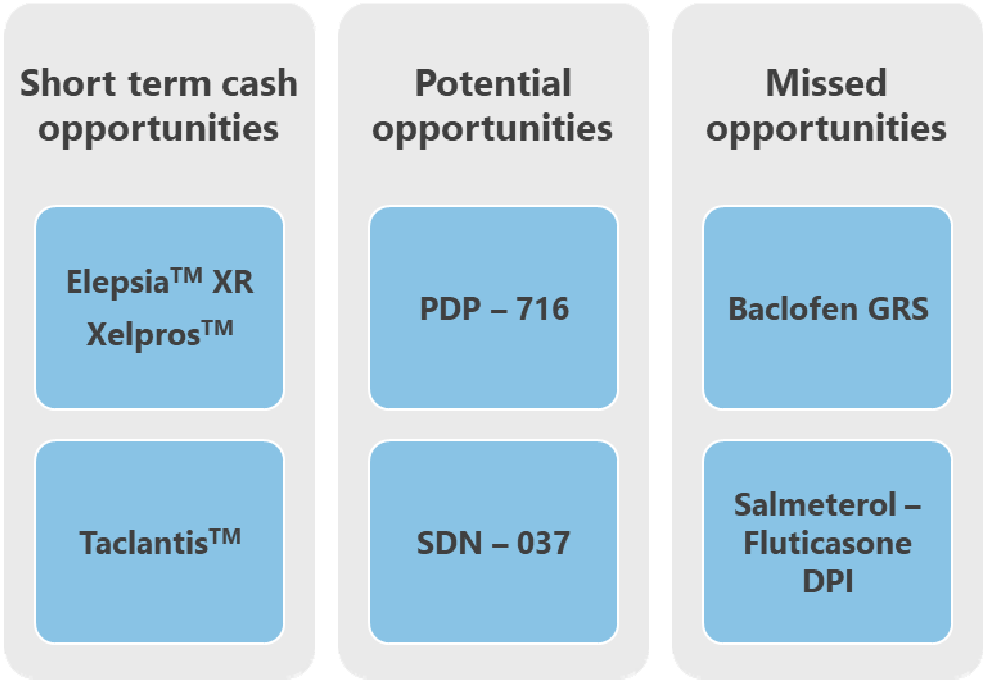
…marking the conclusion of our initial set of delivery solutions



- Baclofen GRS
  - Pivotal studies did not meet the primary end point
  - Met several clinically significant secondary end-points (E.g.: Spasm Frequency, SGIC, etc.)
  - Plan to submit additional registration studies while exploring opportunities to partner
- Salmeterol – Fluticasone DPI
  - Completed regulatory consultations with multiple European regulatory agencies
  - Registration pathway may involve additional BE and clinical endpoint studies
  - Challenging commercial and reimbursement environment
  - Currently exploring partnership opportunities

PDP – 716 = Brimonidine OD, SDN – 037 = SDP – 037, SGIC: Subject Global Impression of Change DPI = Dry Powder Inhaler BE = Bioequivalence

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Key takeaways from our initial programs

- Need for enhanced translational rigor
- Challenging reimbursement environment – Need for balanced risk profile
- Importance of versatile, multi-indication platforms
- Narrow therapeutic focus
- Prudent risk raking

Abl kinase inhibitors	▪ SCO – 088: Chronic Myeloid Leukemia ▪ SCC – 138: Parkinson's Disease ▪ SCO – 125: Chronic Myeloid Leukemia
S1PR1 agonist	▪ SCD – 044: Autoimmune disorders
Abuse & overdose deterrent formulations	▪ SDN – 021: Oral multi-pill abuse deterrence ▪ SDN – 118: Oral multi-pill overdose prevention
Extended ocular retention	▪ PDP – 716: Glaucoma ▪ SDN – 037: Ocular pain & inflammation
Nanoformulations & long acting depots	▪ SDE – 124: Type 2 diabetes ▪ SDD – 098: Acne

Platforms under early clinical development will drive our portfolio value and resource allocation in the short/medium term

SCO – 088 = K0706 CML, SCC – 138 = K0706 Parkinson's Disease, SCO – 125 = K0954, PDP – 716 = Brimonidine OD, SDD – 098 = Minocycline topical SDN – 037 = SDP – 037

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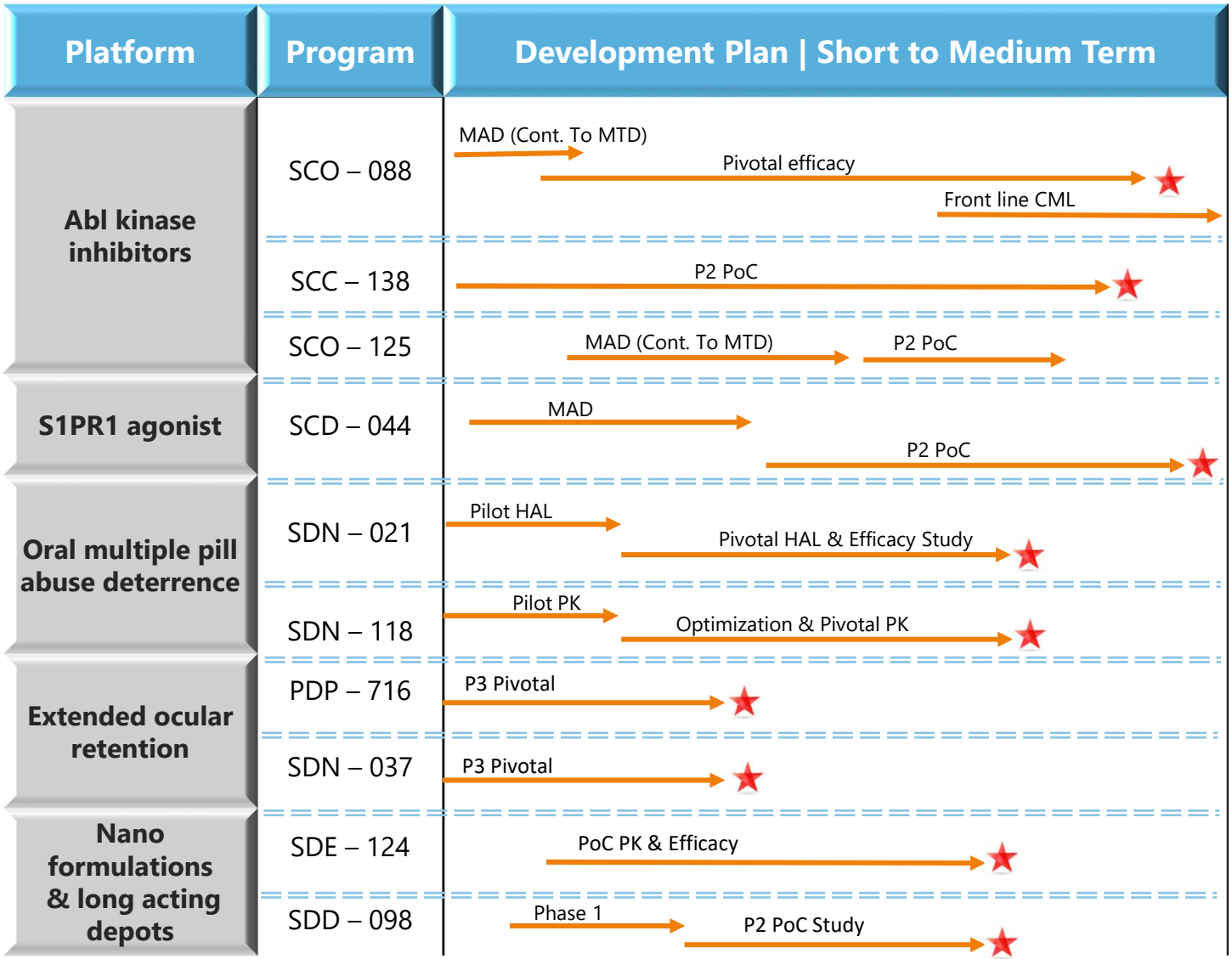
Possible value inflection points & resource allocation

A snapshot of next 24 months



Data read out, SCO – 088 = K0706 CML, SCC – 138 = K0706 Parkinson's Disease, SCO – 125 = K0954 CML, PDP – 716 = Brimonidine OD, SDD – 098 = Minocycline topical
SDN – 037 = SDP – 037

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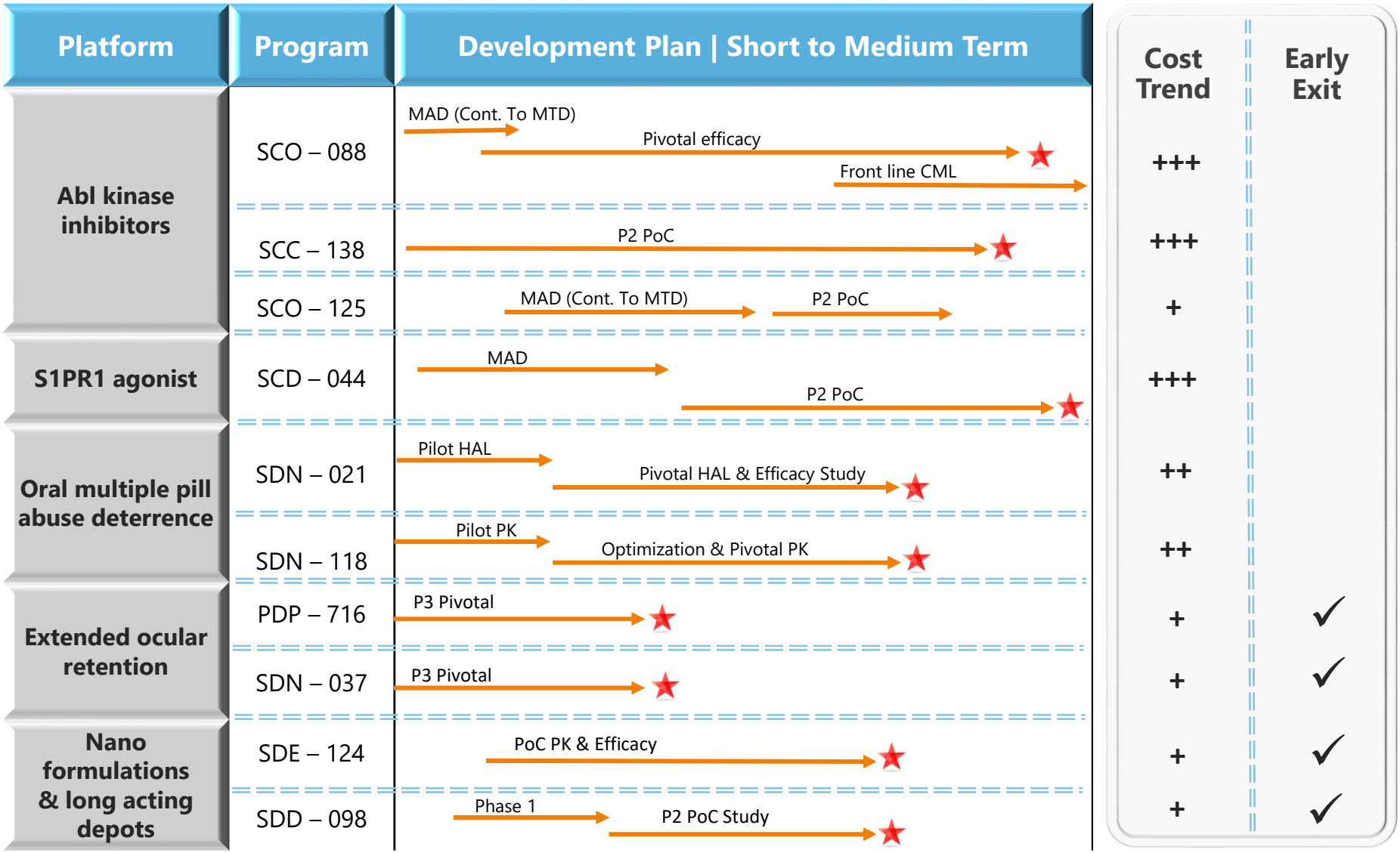
We will continue to be in the investment mode in the medium term



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SDN – 037 = SDP – 037

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SPARC R&D priorities

Execute on SPARC clinical portfolio on schedule and budget to achieve financial sustainability

Increase the **rigor of portfolio decision making** to ensure quality of assets transitioning from pre-clinical to clinical development

Leverage **computational capabilities and external strategic partnerships** to grow discovery funnel

Continue **to invest in SPARC operational model** build up

SPARC will continue to focus on building versatile platforms which can advance the standards of care meaningfully in chosen therapeutic segments

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Dedicated research facility at Savli, Vadodara

- Dedicated, modern campus with world class infrastructure
- Augmenting research capabilities with state of the art technology and equipment
- Plan to shift to new facility by Q4 FY19

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Financial summary

(INR mn)	FY18	FY17	FY16	FY15	FY14
Total Income	832	1,947	1,642	1,588	1,770
Total Expenses	3,292	3,137	2,342	1,983	1,427
Exceptional Item	490	-	-	-	-
Profit (Loss) after Tax	(1,970)	(1,190)	(700)	(395)	303
Total Comprehensive Income (Net of tax)	(1,984)	(1,195)	N.A.	N.A.	N.A.

Liquidity Status

- Cash and cash equivalents INR 1,764 mn as on 31-Aug-18
- Higher working capital need due to GST

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Financial Summary

- Expected cash outflows
  - Increased number of clinical programs
  - Higher operating expenses
  - Refurbishing cost of new facility at Savli
- Expected cash inflows
  - Raised INR 5,000 mn through Preferential Issue of Warrants (70% received, INR 1,500 mn to be received in Jan-19)
  - Milestone payments upon approval of Xelpros™ and Elepsia™
  - Out-licensing of Taclantis™, if pivotal BE study outcome is positive

BE = Bioequivalence

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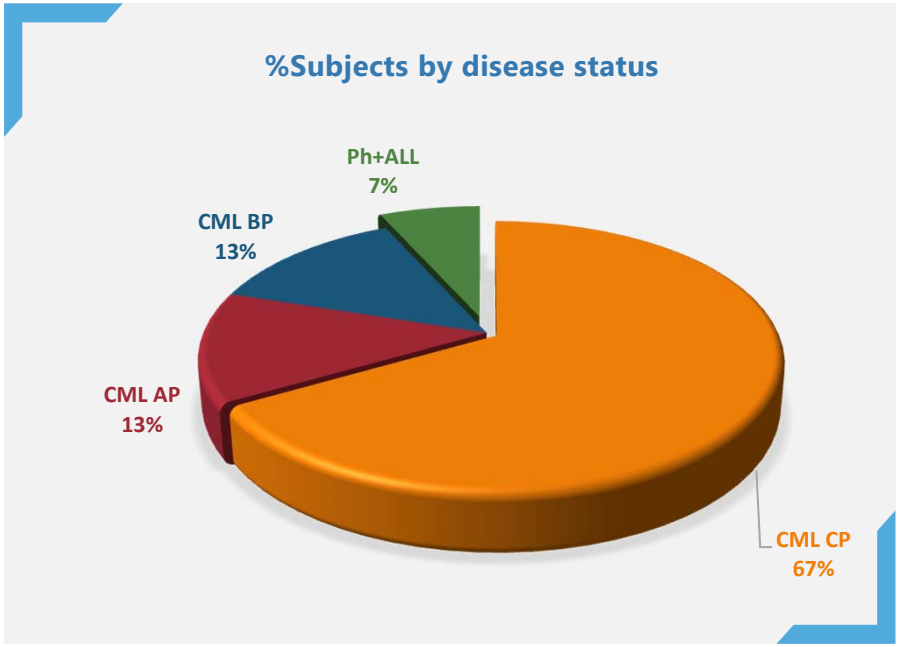
SCO – 088

Encouraging preliminary efficacy and safety observed

- Effective against BCR-ABL and its mutants, including T315I mutation
- Multiple Ascending Dose (MAD) study ongoing in CML patients
  - Completed 5 dose escalations
  - PK supports once-a-day dosing
  - 1st subject continuing treatment, completed 17 cycles



SCO – 088 = K0706 CML, CML = Chronic Myeloid Leukemia CP = Chronic phase AP = Accelerated phase BP = Blast phase Ph+ALL = Philadelphia positive Acute Lymphocytic Leukemia

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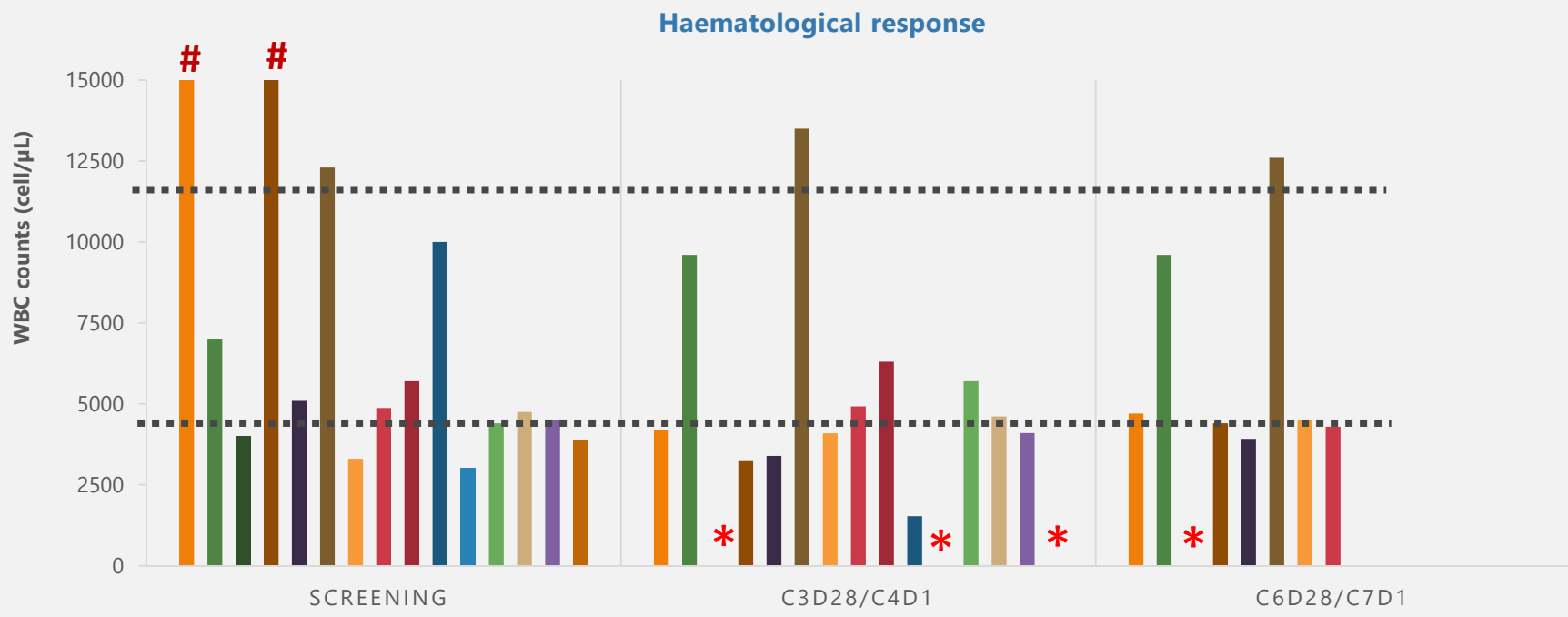
SCO – 088

Haematological response in CML patients



- Haematological response rate ~80% in subjects enrolled
- No cardiovascular events reported till date
- Transient self-limiting grade 1/2 neutropenia reported in one patient only

SCO – 088 = K0706 CML, CML = Chronic Myeloid Leukemia, C3D28 = Cycle 3 Day 28. C4D1 = Cycle 4 Day 1, C6D28 = Cycle 6 Day 28, C7D1 = Cycle 7 Day 1

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SCO – 088
Development status update

- Plan to complete MAD study by Q4 FY19
- Phase 2 pivotal efficacy study
  - Single arm, open label, efficacy study in 150 subjects failed on ≥ 3 TKIs
  - Protocol submission to US FDA by Q2 FY19
  - Study initiation by Q3 FY19

SCO – 088 = K0706 CML, CML = Chronic Myeloid Leukemia, TKI = Tyrosine Kinase Inhibitor, US FDA = United States Food & Drug Administration MAD = Multiple Ascending Dose

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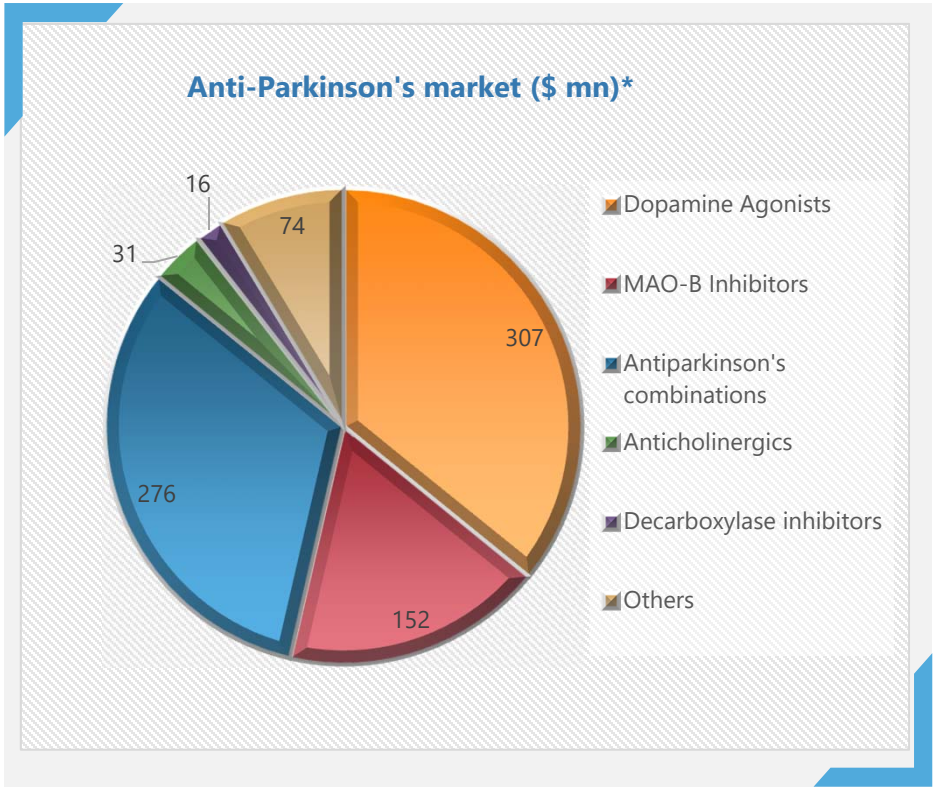
Parkinson's Disease

Increasing incidence due to the aging population



- Over 1 mn people living with Parkinson's Disease in the US^
- Expected to grow to ~1.35 mn by 2022 with about 60,000 new patients diagnosed every year
- No disease modifying therapy available
  - Currently available therapies provide symptomatic relief only

*IQVIA MAT June 2018 ^Parkinson's Disease Foundation - http://www.pdf.org/parkinson_statistics

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SCC – 138

Supporting pre-clinical data in Parkinson's Disease

Pre-clinical development

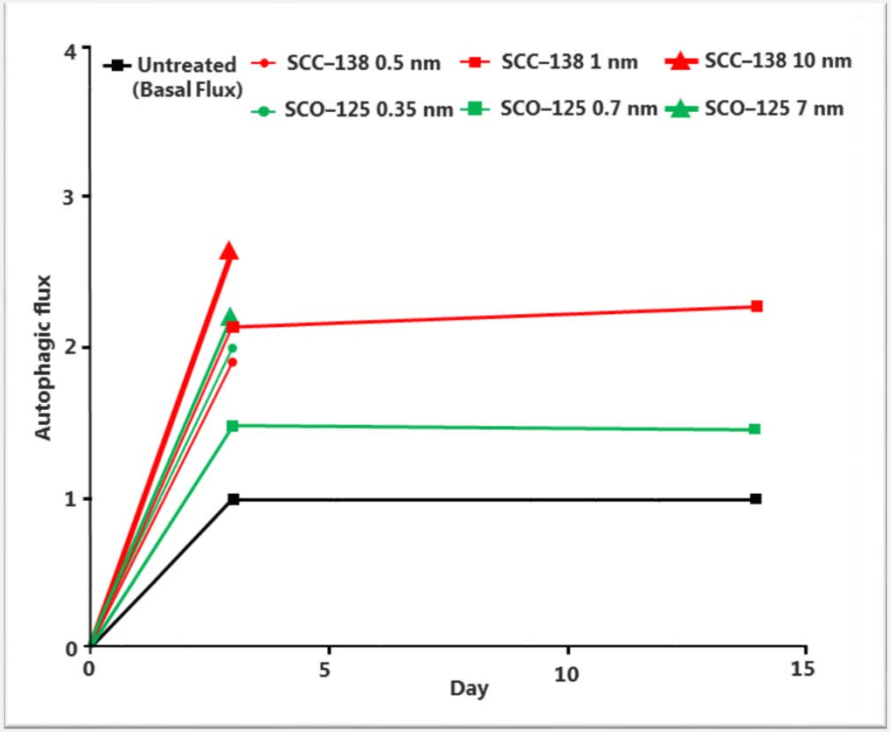
Therapeutic potential in α-synuclein PFF induced model

Role of SCC – 138 in human IPSC-derived neurons

1) Augmenting Parkin activity
2) Modulating autophagic flux and α-synuclein metabolism
3) Altering α-synuclein inclusions

Therapeutic potential in AAV1/2 α-synuclein rat model

Effect of 3-day vs. 14-day treatment of the SPARC c-Abl inhibitors on the autophagic flux.



SCC – 138 = K0706 Parkinson's Disease, SCO – 125 = K0954 PFF = Pre Formed Fibrils IPSC = Induced Pluripotent Stem Cells AAV = Adeno Associated Virus

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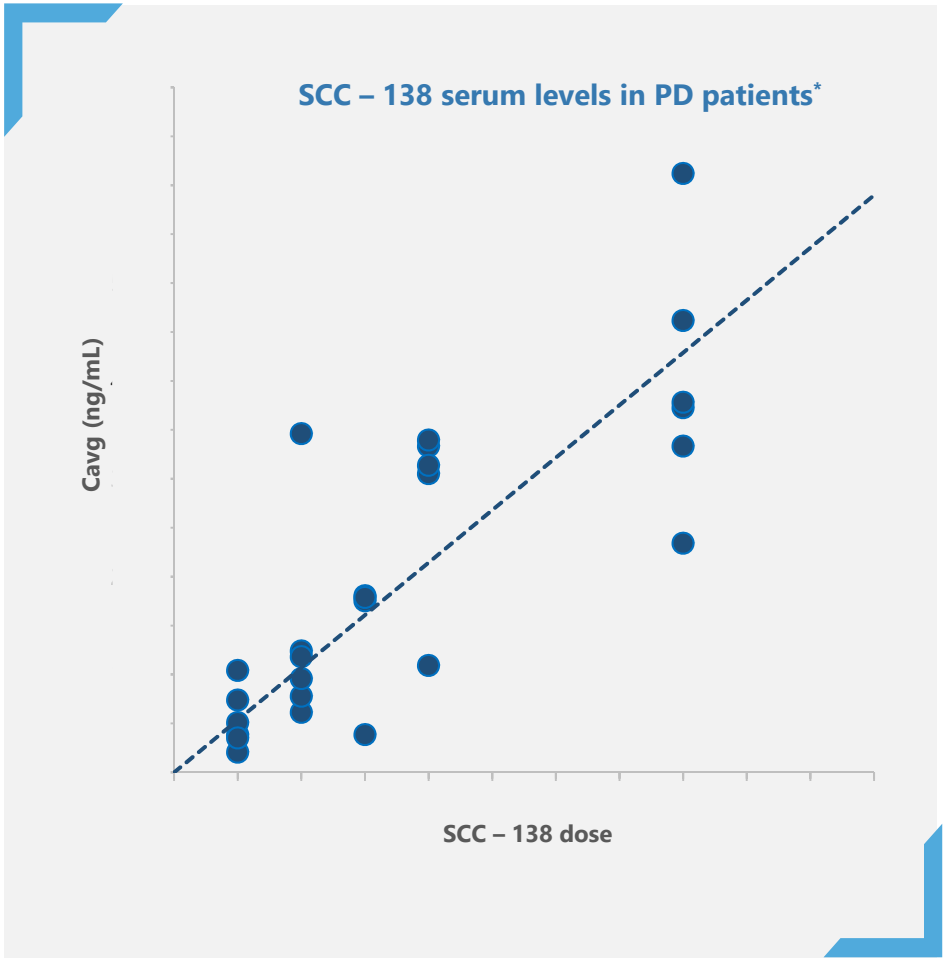
SCC – 138
1st in class disease modifying treatment

- Orally active, disease modifying treatment with potential neuro-protective activity
- Inhibits Abl and Fyn kinase – relevant to neurodegeneration
- Completed 6 dose cohorts in Phase 1 PD patients study
- No significant adverse events observed in highest studied dose level*
- Preliminary human PK data demonstrates drug presence in CSF



*Data available up to 48mg cohort, SCC – 138 = K0706 Parkinson's Disease, CSF = Cerebrospinal fluid PD = Parkinson's Disease

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SCC – 138
Development status update

- MAD study on-going; plan to add higher dose levels
- Phase 2 PoC to be initiated in PD patients by Q3 FY19 at multiple centres across North America, Asia and Europe

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SCD – 044

Selective S1PR1 agonist for autoimmune diseases

- SPARC is developing a novel orally bioavailable, potent and selective S1PR1 agonist in collaboration with Bioprojet, France
- S1PR1 agonists cause diminished migration of lymphocytes out of lymphoid tissues leading to decrease in circulating lymphocytes thereby reducing inflammation
- Encouraging results in animal models of autoimmune diseases, including psoriasis
- First-in-human study is currently ongoing to establish safety profile in healthy volunteers

S1PR1 = Sphingosine-1-phosphate receptor 1

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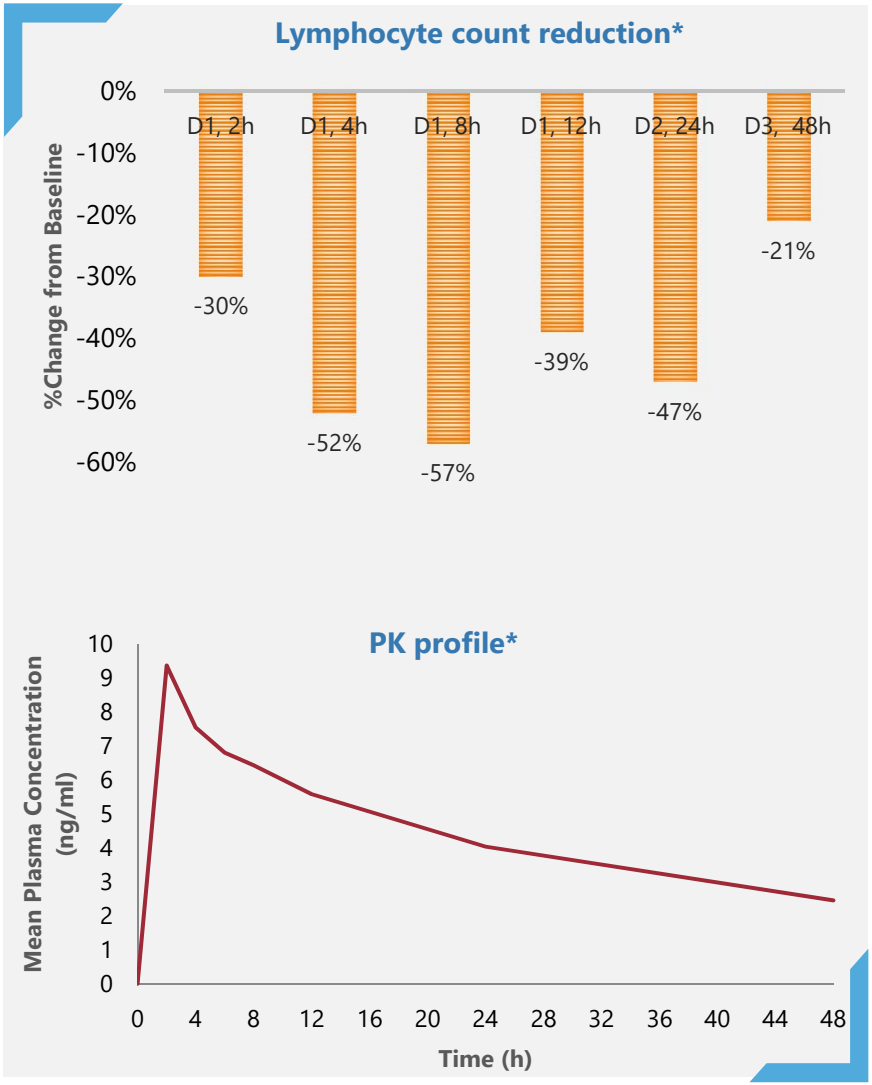
SCD – 044
First-in-Human Study is well underway

- Multi-part study in healthy volunteers
  - **Part 1**: Single ascending dose study completed
    - 6 dose groups evaluated compared to placebo
    - Decrease in lymphocyte counts was observed at all dose levels evaluated
    - Established a maximum tolerated dose
    - Terminal elimination half-life ($t_{1/2}$) of ~34 h, independent of dose
  - **Part 2**: Food effect study completed
  - **Part 3**: Multiple ascending dose study ongoing



*Phase 1 part 1 SAD study, 2 mg dose.

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SCD – 044
Development status update

- Planned completion of Phase 1 study by Q1 FY20
- Phase 2 study initiation anticipated by Q1 FY20
  - Indications under consideration include Psoriasis, Inflammatory Bowel Diseases, Atopic Dermatitis & others

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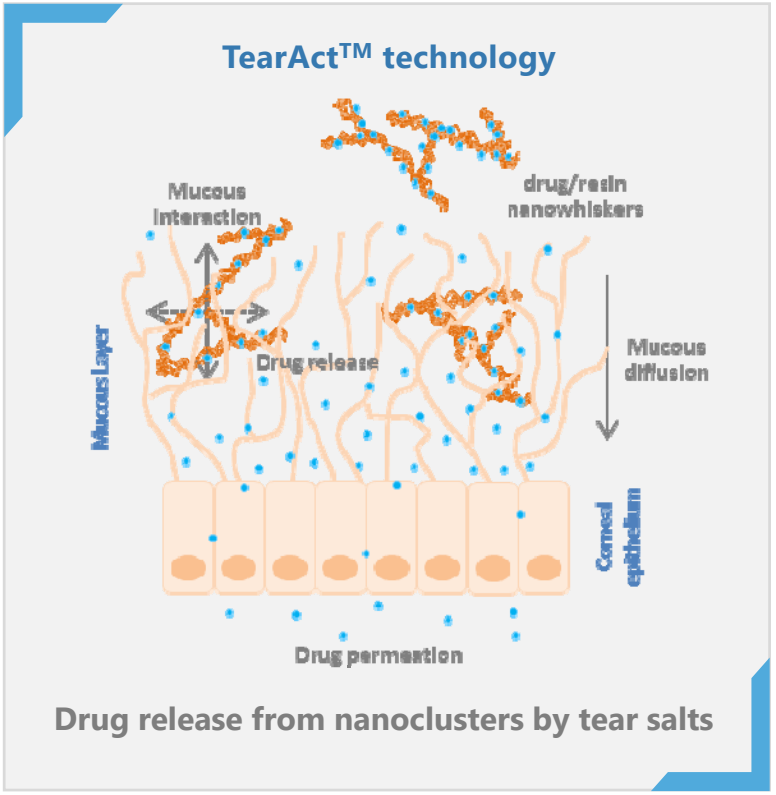
PDP – 716

Novel once-a-day eye drops for Glaucoma

- Existing formulations of Brimonidine, an α2 adrenergic agonist, are administered TID in the second line treatment of Glaucoma
- TID dosing often results in lower treatment adherence rates in patients*
- SPARC is developing improved formulation of Brimonidine for once-a-day dosing utilizing its proprietary TearAct™ technology



Drug release from nanoclusters by tear salts

IOP = Intra Ocular Pressure, *J Glaucoma. 2011 Oct;20(8):502-8; TID = Three times-a-day, PDP – 716 = Brimonidine OD

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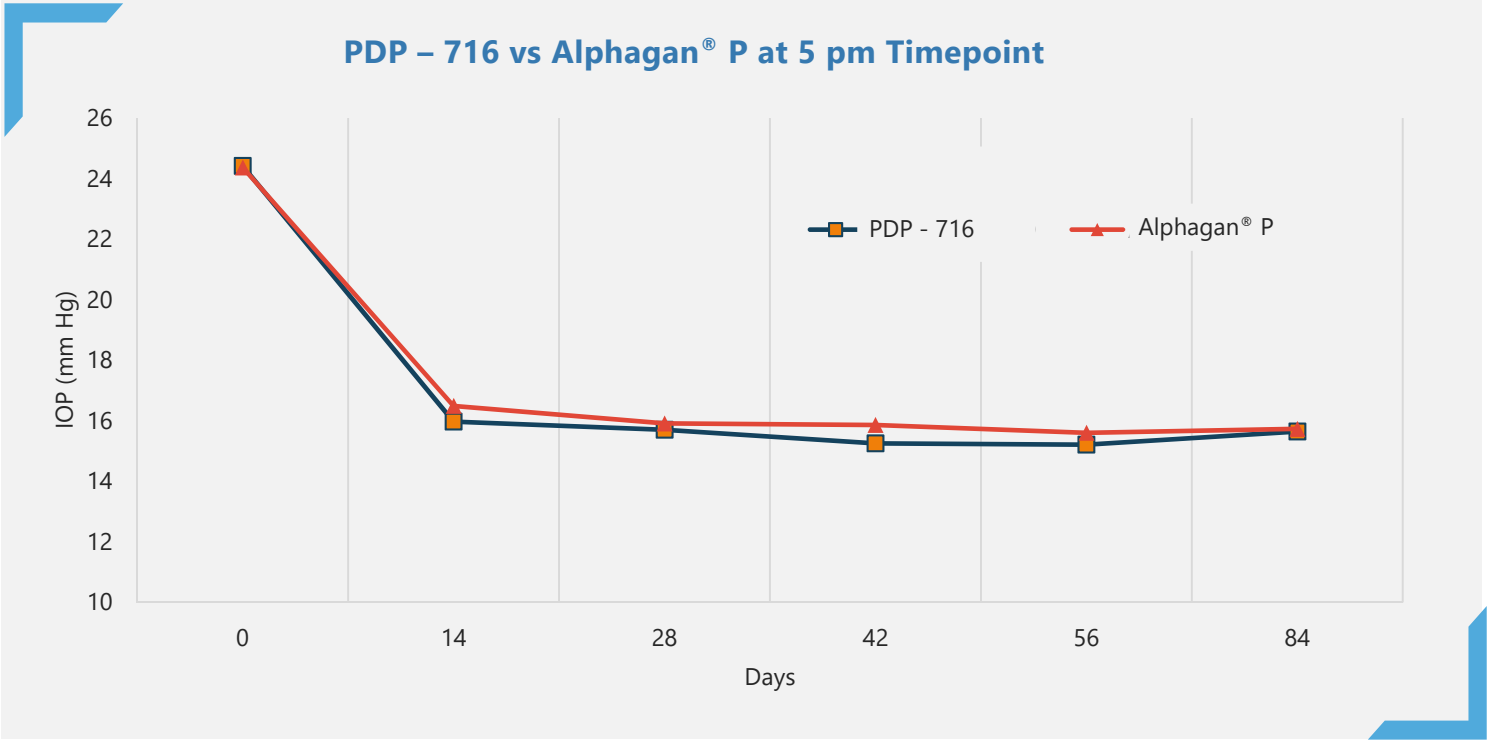
PDP – 716

Phase 2 data supports once-a-day dosing

- Proof of concept demonstrating equivalence to Alphagan® P dosed TID was completed in human trial
- Met pre-specified clinical equivalence efficacy criteria compared to Alphagan® P TID at all time points
- No new adverse events reported



IOP = Intra Ocular Pressure, PDP – 716 = Brimonidine OD, TID = Three times-a-day

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PDP – 716
Development status update

- IND submitted in Q4 FY18
- US FDA alignment on single, active controlled Phase 3 study with Alphagan® P as a comparator to support NDA submission
- Phase 3 study initiated in Q1 FY19
  - Target enrolment of 666 subjects
  - Recruitment at ~27 sites across the US
- NDA submission planned by Q4 FY20

PDP – 716 = Brimonidine OD, IND = Investigational New Drug, US FDA = United States Food & Drug Administration, NDA = New Drug Application

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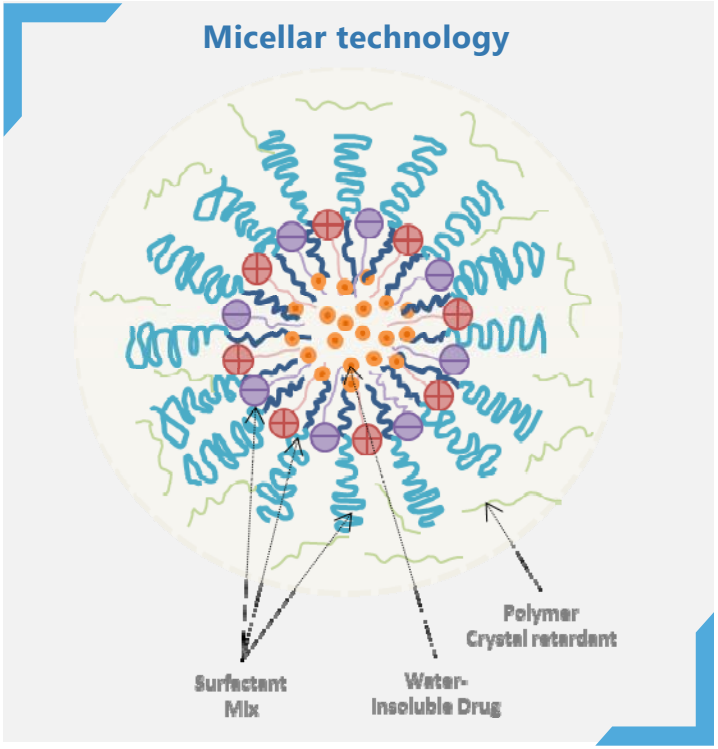
SDN – 037

Improved ocular steroid with reduced dosing frequency

- Currently marketed steroid eye drops are approved for QID dosing
- Additionally, marketed products have hazy/milky appearance which may blur the vision upon administration
- SPARC is developing novel formulation of an existing steroid utilizing its Micellar technology
- Differentiated topical steroid eye drops with BID dosing & clear/transparent appearance is expected to provide meaningful benefit to the patients



QID = Four times- a- day, BID = Two times- a- day SDN – 037 = SDP – 037

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SDN – 037
Development status update

- US FDA alignment on single, vehicle controlled Phase 3 study to support NDA submission
- Phase 3 study initiated in Q1 FY19
  - Target enrolment of 386 subjects
  - Recruitment at ~15 sites across US
- NDA submission planned by Q2 FY20

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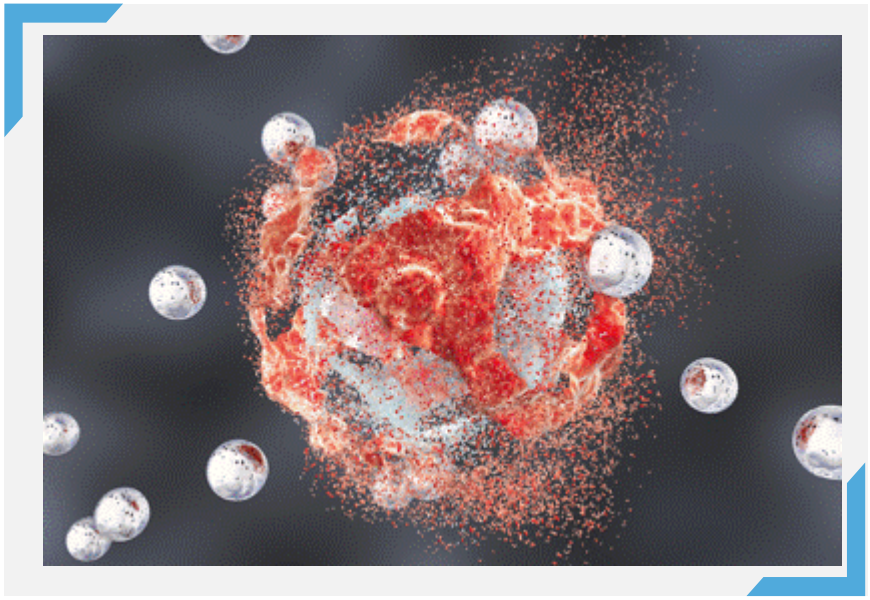
Taclantis™
Establishing bio-equivalence to Abraxane®

Novel formulation of paclitaxel using SPARC's proprietary Nanotecton™ platform technology



- Pivotal BE study fully enrolled
  - 142 patients randomized
  - 99 evaluable patients
  - No hypersensitivity reactions observed
- Data read out expected by Q3 FY19
- Planned NDA filing by Q4 FY19

BE study = Bioequivalence study NDA = New Drug Application

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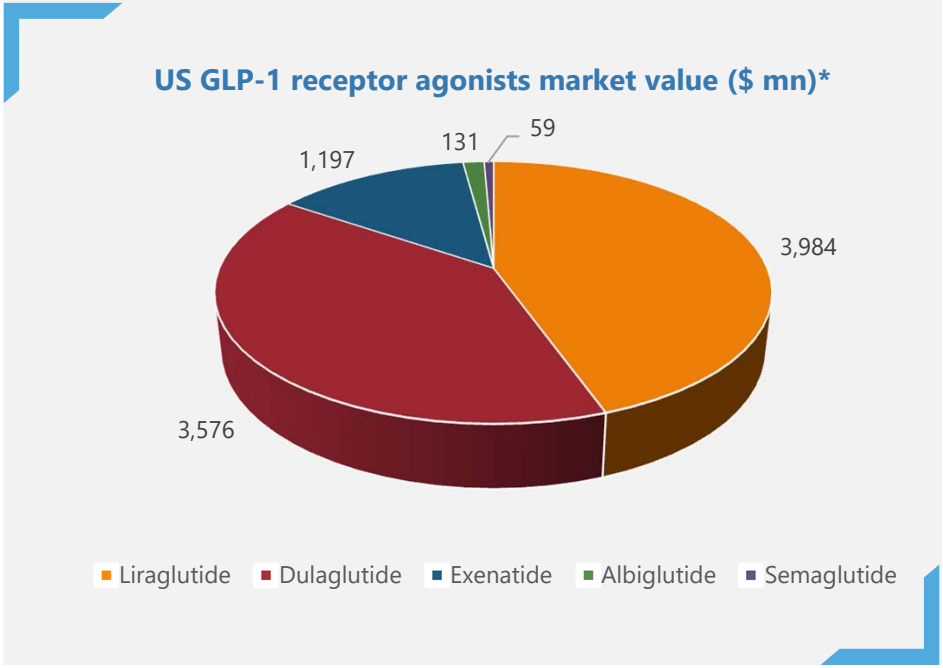
SDE – 124

Long acting formulation of GLP–1 receptor agonist

- 21 mn diagnosed cases of type 2 diabetes in the US#; estimated 1.5 mn new cases diagnosed annually^
- GLP-1 receptor agonists reported annual sales of ~$9 bn with 39% YoY growth*
- Currently marketed reference product available as a daily injection
- Developed long acting, subcutaneous injection for self administration
- Nanostructured gel; harnesses drug and excipient's self-assembling property
  - Drug release by erosion
  - Employs GRAS excipients



*IQVIA Mat June 2018 National Diabetes Statistics Report 2017 #Prevalence of Diagnosed Diabetes in Adults by Diabetes Type — United States, 2016 Weekly / March 30, 2018 / 67(12);359–361 GLP -1 = Glucagon–like Peptide – 1 Zheng SL et.al. JAMA. 2018;319(15):1580-1591, GRAS : Generally regarded as safe, GLP 1 = Glucagon Like Peptide 1

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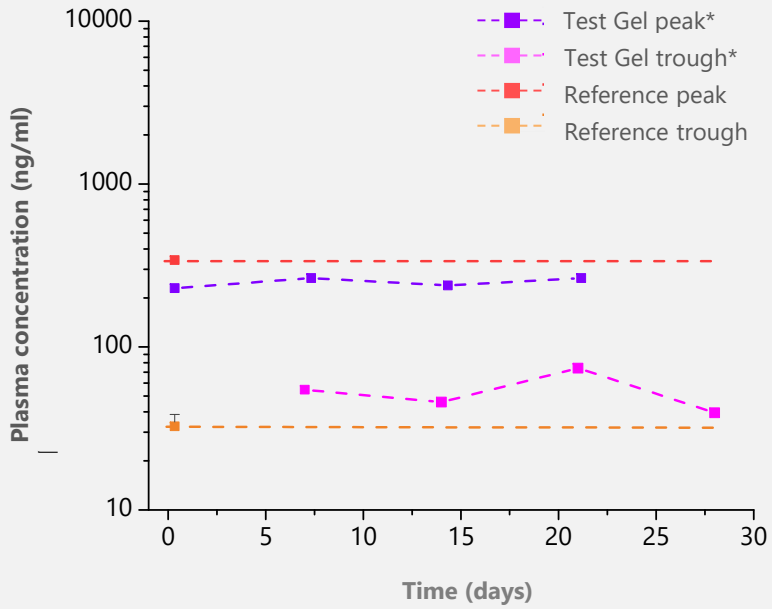
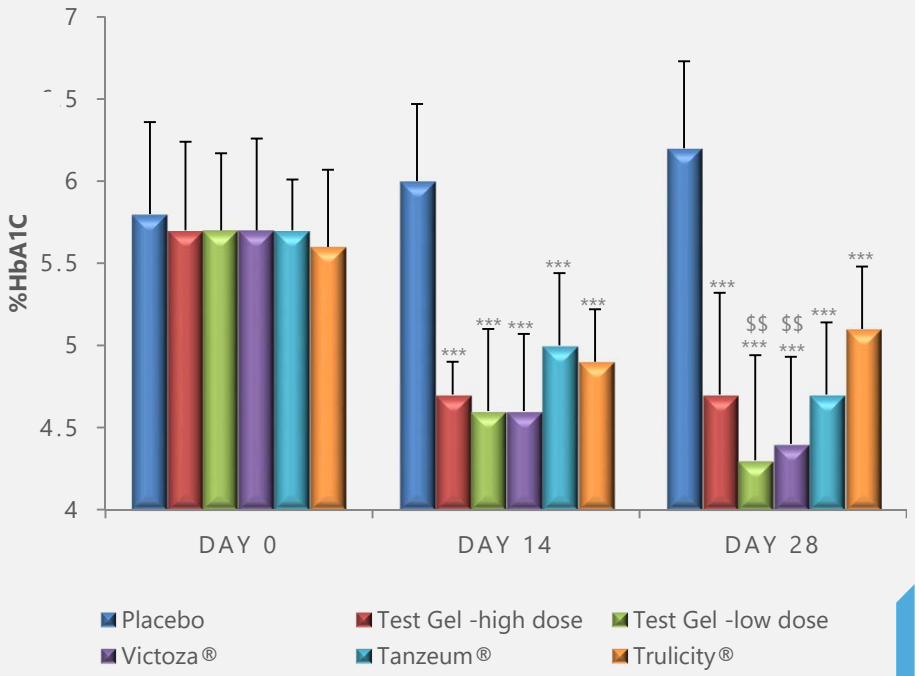
SDE – 124

Encouraging efficacy in pre-clinical setting

Comparative PK profile in SD rats



Comparative HbA1C profile in Fatty-Zucker rats



- Therapeutically effective levels maintained for desired duration in SD rats
- Significant reduction in %HbA1C was observed after multiple SC injections

*Extrapolated to expected human equivalent dose, Two way ANOVA followed by Bonferroni post test, ***p<0.001 as compared to Placebo, $$p<0.01 as compared to Trulicity
SD rats = Sprague Daeley rats SC = Sub-cutaneos

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SDE – 124
Development status update

- Prototype formulation ready; short term stability study ongoing
- Pre-IND meeting with US FDA completed
- IND enabling toxicology studies planned to be initiated by Q3 FY19
- IND submission by Q3 FY20
- Phase 1 human PoC study initiation by Q4 FY20

US FDA = United States Food & Drug Administration IND = Investigational New Drug PoC = Proof of concept

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SDD – 098
Development status update

- According to AAD, more than 5 mn people seek medical treatment for acne and has significant impact on productivity for affected individuals
- SPARC is developing novel topical formulation of Minocycline designed to reduce systemic side-effects associated with oral dosing
- Phase 1 enabling toxicity study ongoing
- Pre-IND meeting completed with US FDA
- IND filing expected by Q4 FY19

SDD-098 = Minocycline topical AAD = American Academy of Dermatology IND = Investigational New Drug NDA = New Drug Application
US FDA = United States Food & Drug Administration

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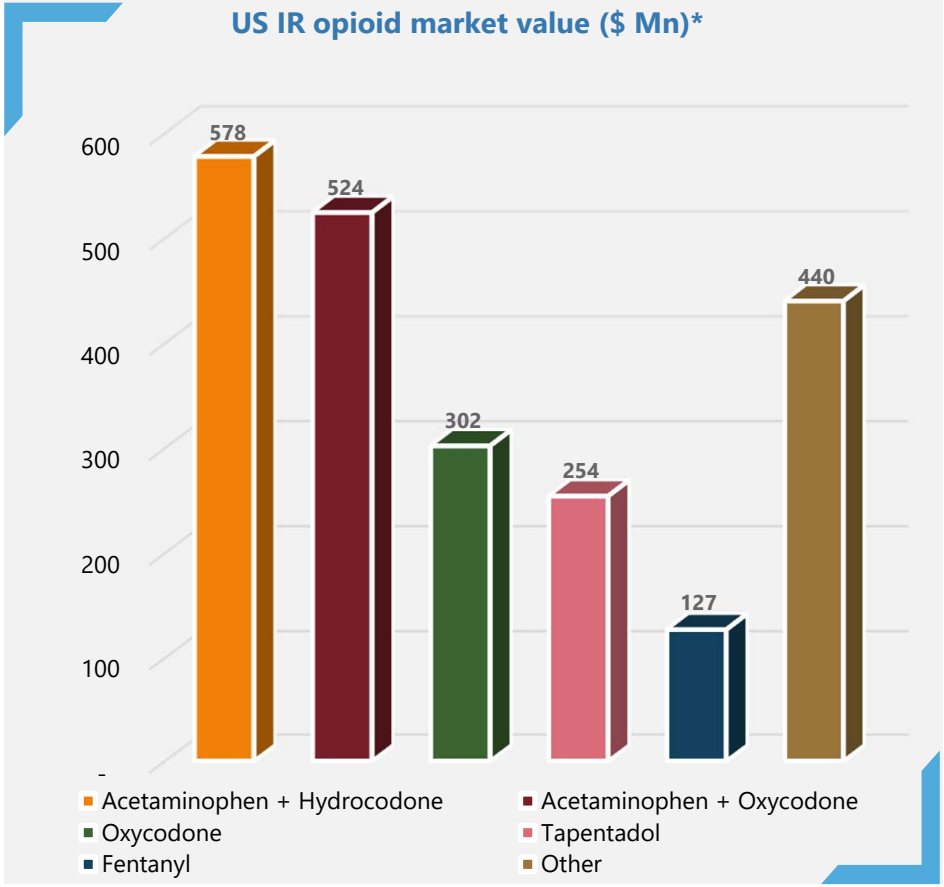
SDN – 021

Potential to deter oral multiple pill abuse

- 187 mn prescriptions generated for IR opioids with estimated value of ~$2 bn*
- 66% of the abusers prefer IR formulations due to ease of manipulation^
- SPARC developed IR opioid formulation with abuse deterrent properties for oral, nasal and IV abuse
- Includes presence of an aversive agent to further deter abuse if tampered
- Encouraging results in Category I *in-vitro* tamperability evaluation



*IQVIA MAT June 2018, ^Postgraduate Medicine, 2016, 128:1, 85-96 IR = Immediate release IV = Intra venous

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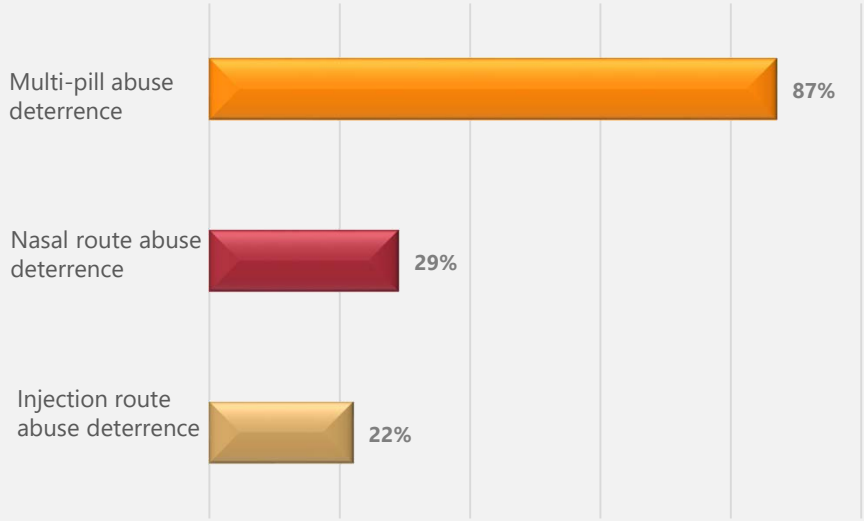
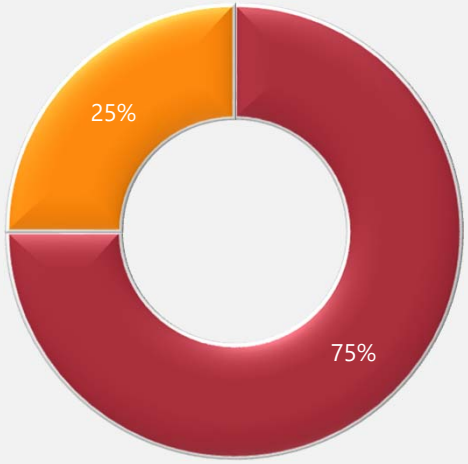
SDN – 021
Multiple pill abuse deterrence – main driver to adoption*

SDN – 021 Adoption drivers*



SDN – 021 Perceived key benefit *



87% of physicians see oral multi-pill abuse deterrence as a driver to utilize SDN-021*

75% of payers view oral multi-pill abuse deterrence as a major benefit*

Q: What are the main drivers of your utilization? (n=44)

Q: What are the major benefits of SDN-021? (n=12)

*Based on primary market research conducted on behalf of SPARC by third party in the US

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SDN – 021
Development status update

- Pilot Human Abuse Liability (HAL) study ongoing
  - Primary endpoint: Drug Liking – E_{max}
  - Cohort A recruitment completed
  - Cohort B recruitment ongoing
  - Topline data expected by Q3 FY19
- Phase 3 clinical study planned in concurrence with US FDA guidance; planned initiation by Q3 FY19
- Pivotal Category 1 studies planned in Q1 FY20

US FDA = United States Food & Drug Administration E_{max} = Maximum effect

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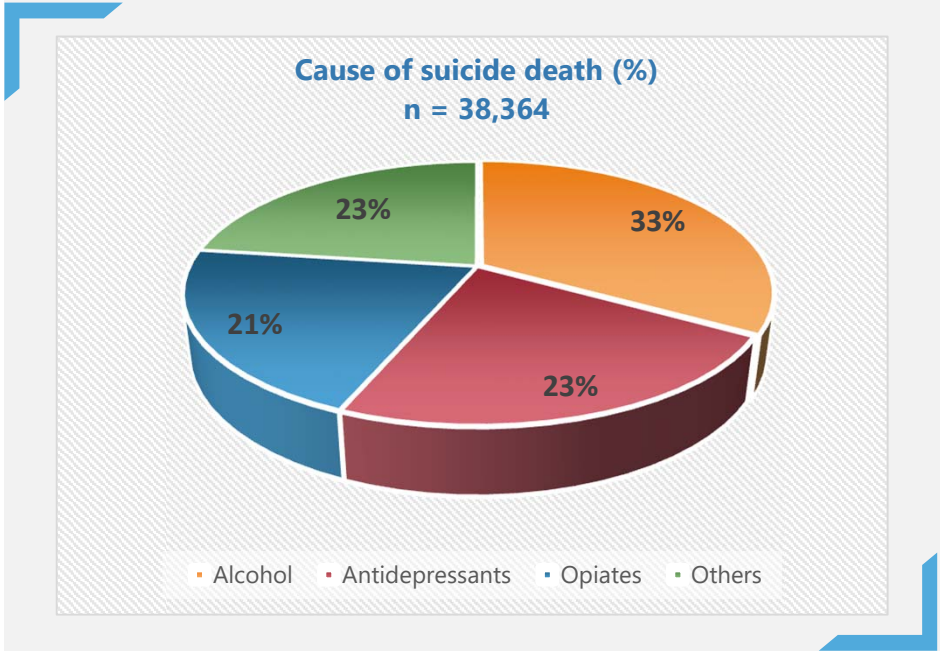
SDN – 118

Addressing prescription drug overdose

- Suicide, one of the top 10 leading causes of death in the US
- SPARC has developed an anti-depressant product based on overdose prevention technology platform
- Technology works to curb release on ingestion of multiple pills either intentionally or accidentally
- Single dose preliminary PK studies encouraging



PK = Pharmaco kinetic Morbidity and Mortality Weekly Report, Vol. 61, No. 6, September 2012

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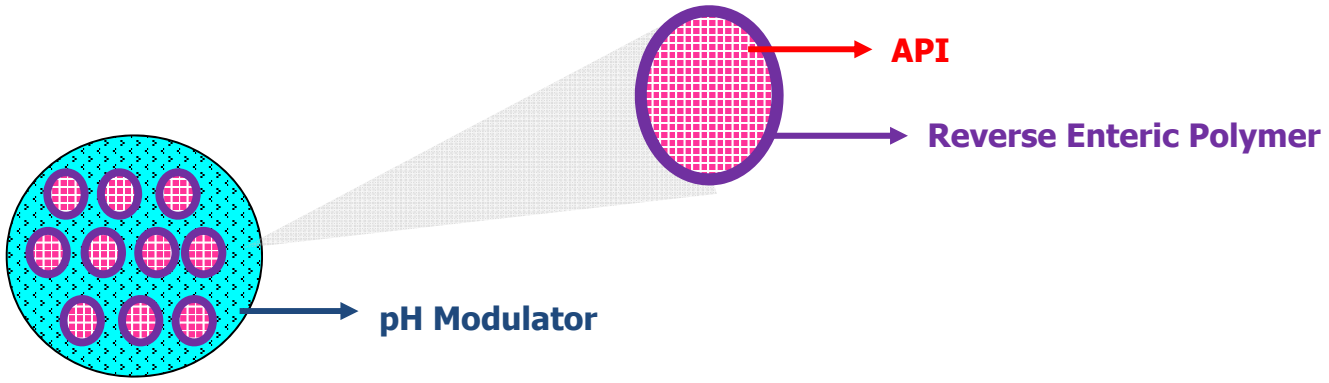
SDN – 118

Overdose prevention technology



- Mechanism of release from one pill
  - Quantity of pH modulator released from 1 pill does not affect the microenvironment of stomach
  - Polymer solubilizes
  - Therapeutic dose delivered
- Mechanism of release from multiple pills
  - Quantity of pH modulator released from multiple pills changes the microenvironment of stomach
  - Changed microenvironment restricts solubility of polymer and thus drug release
  - Harm due to multiple pill overdose may thus be reduced

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SDN – 118
Development status update

- Pre-IND advice received from the US FDA
- IND filing planned in Q3 FY19
- Overdose PoC PK studies planned in Q4 FY19

IND = Investigational New Drug NDA = New Drug Application US FDA = United States Food & Drug Administration PoC = Proof of Concept

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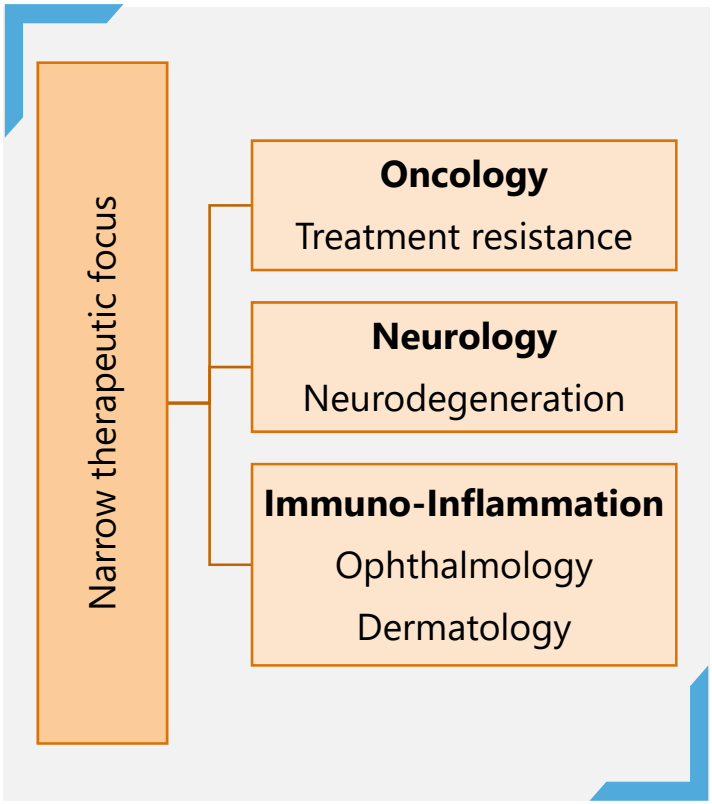
Early stage pipeline building strategy

- Internal ideation
  - Chase validated drug targets in select therapeutic areas
  - Leverage capabilities in complex drug delivery systems to pursue commercially attractive 505(b)(2) opportunities
- External innovation network
  - Partnerships with leading global academic centers to source promising early stage innovative science/biology
  - Pursue novel first-in-class or best-in-class opportunities with high unmet clinical needs
- Exploratory programs
  - Augmenting capabilities to pursue new treatment modalities outside of traditional small molecule drug discovery



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Attacking treatment resistance in cancer

- Fast follower approach in a clinically and commercially validated space
- A number of molecularly targeted therapies against the indications of interest
- Emerging evidence of the development of resistance to targeted therapies
  - Resistance often attributed to mutations in the molecular targets rendering the targeted therapeutic being chased ineffective
  - Resistance due to adaptation to an alternative signaling pathway(s)
- Resistance to hormonal therapies against carcinomas of breast and prostate
  - ERα targeting by tamoxifen or fulvestrant
  - AR targeting by enzalutamide or apalutamide
- Targeted therapy for B lymphoid malignancies
  - Targeting ibrutinib/acalabrutinib resistance

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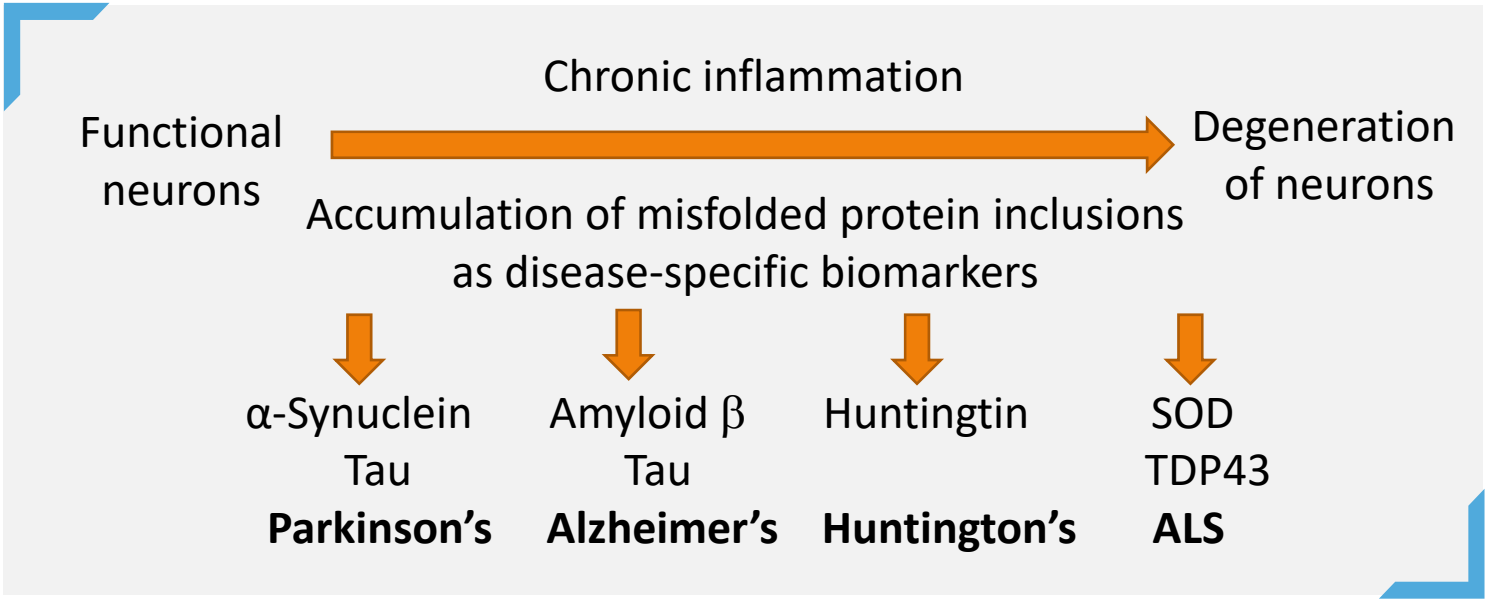
Neurodegeneration

- A common pathway of neuronal death irrespective of disease-specific misfolded protein inclusions in distinct neurodegenerative diseases



- Autophagy, a process by which cells try to eliminate nonfunctional misfolded proteins and organelles
- Inability of neurons to mediate autophagy often leads to neurodegeneration
- SPARC's emphasis is on prevention of neuronal death in these neurodegenerative diseases

SOD = Super oxide dismutase TDP43 = Transactive response DNA binding protein 43 ALS = Amyotrophic lateral sclerosis

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Update on collaborations

- Pursue active collaborations with global academic centres and research institutes
- Unique academic partnering proposition for significant value creation
  - Cash investment
  - In-kind contribution leveraging internal infrastructure in preclinical & clinical development
- Flexible partnering structures
  - Standard in-licensing
  - Grant funding with option to license
  - Material transfer with option to license
  - Sponsored research

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SPARC – Washington University Collaboration

- SPARC partnered with Skandalaris Center of Washington University, St. Louis, US
  - Identifying translational inventions and advancing them towards commercialisation
- SPARC supported Skandalaris Center's LEAP (Leadership in Entrepreneurial Acceleration Program) Inventor Challenge Program
  - Up to $250,000 per program in awards every year for three (3) years
  - Additional in-kind support utilizing internal R&D capabilities at SPARC
  - Option to license IP on worldwide exclusive basis

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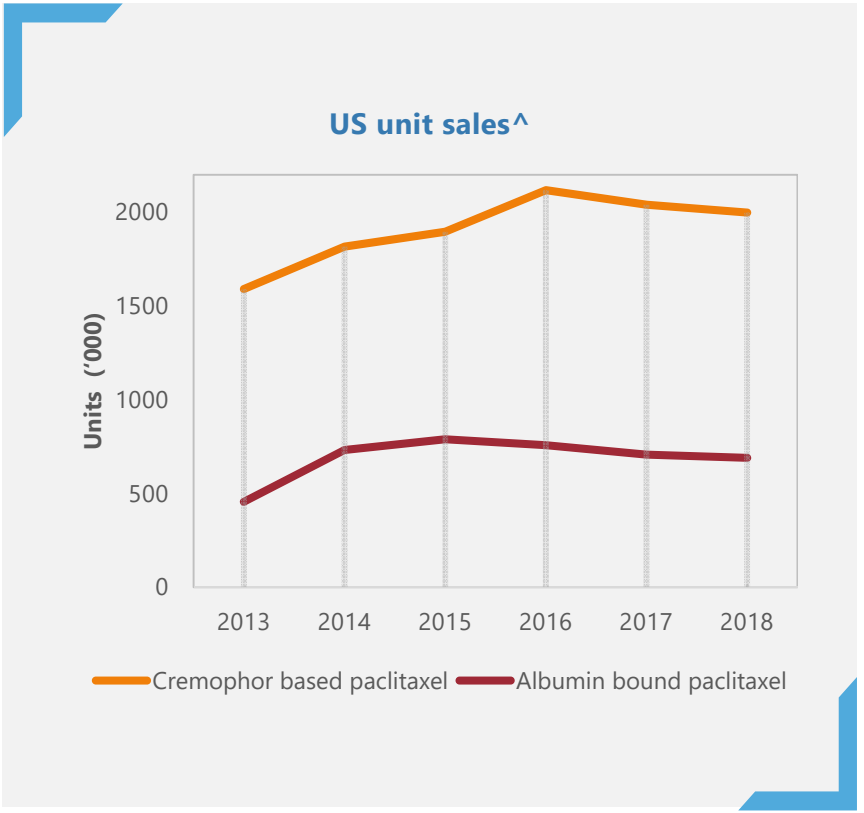
Taclantis™
Albumin free nanoformulation of Paclitaxel

- Over 45% of US clinicians documented hypersensitivity reactions in more than 10% patients treated with Cremophor ® based paclitaxel*
- More than 60% of US physicians view risk of hypersensitivity and ease of administration as important factors influencing choice of therapy*
- Cremophor® based formulations account for ~70% of total Paclitaxel units prescribed#
- Significant opportunity for conversion to novel formulations like Taclantis™



*Based on primary market research conducted on behalf of SPARC by third party in the US, #Internal estimates ^IQVIA MAT June 2018 (Units equivalent to 100 mg)

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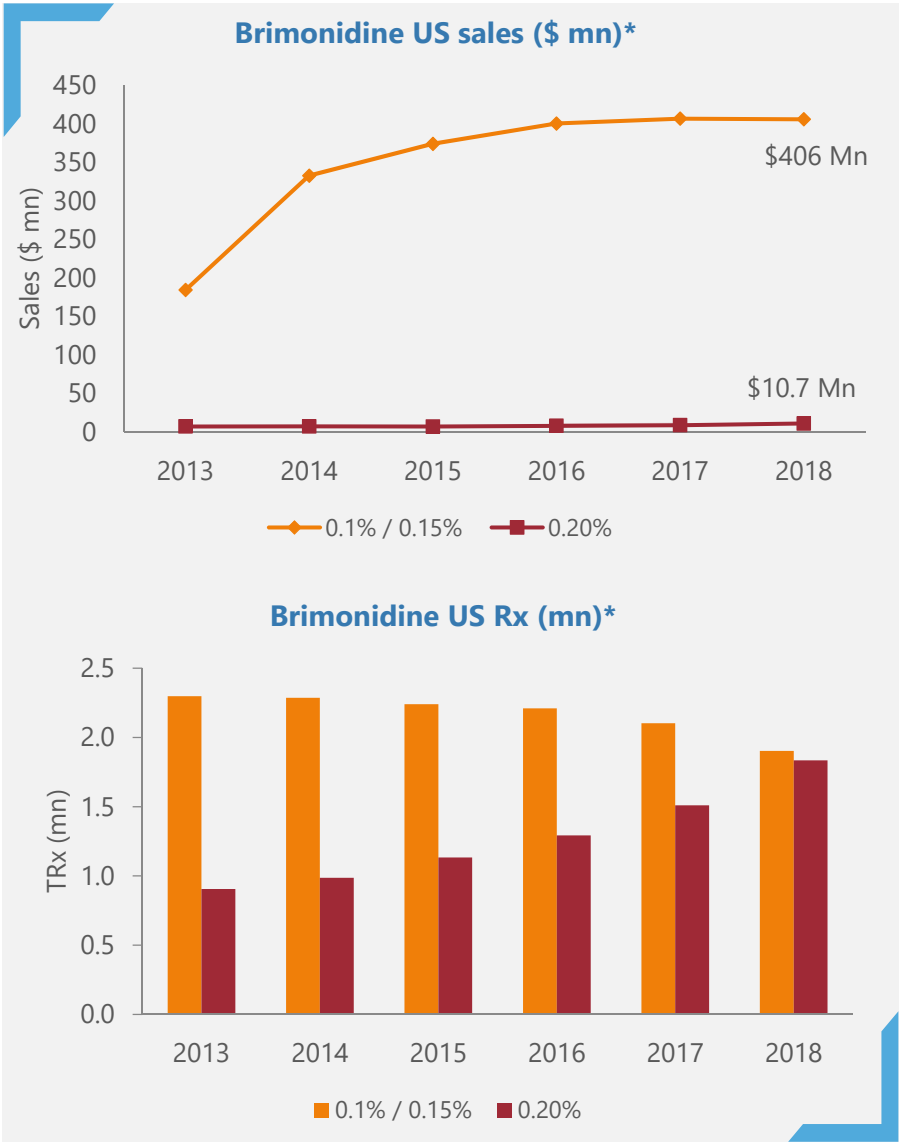
PDP – 716
US market opportunity

- US Glaucoma market is estimated at $ 3.0 bn in 2017*
- Brimonidine is one of the most widely prescribed anti-glaucoma drug with sales of $ 417 mn and 3.7 mn prescriptions dispensed annually*
- Brimonidine branded product commands significant market share inspite of genericization of higher strength formulation



*IQVIA MAT June 2018 PDP – 716 = Brimonidine OD

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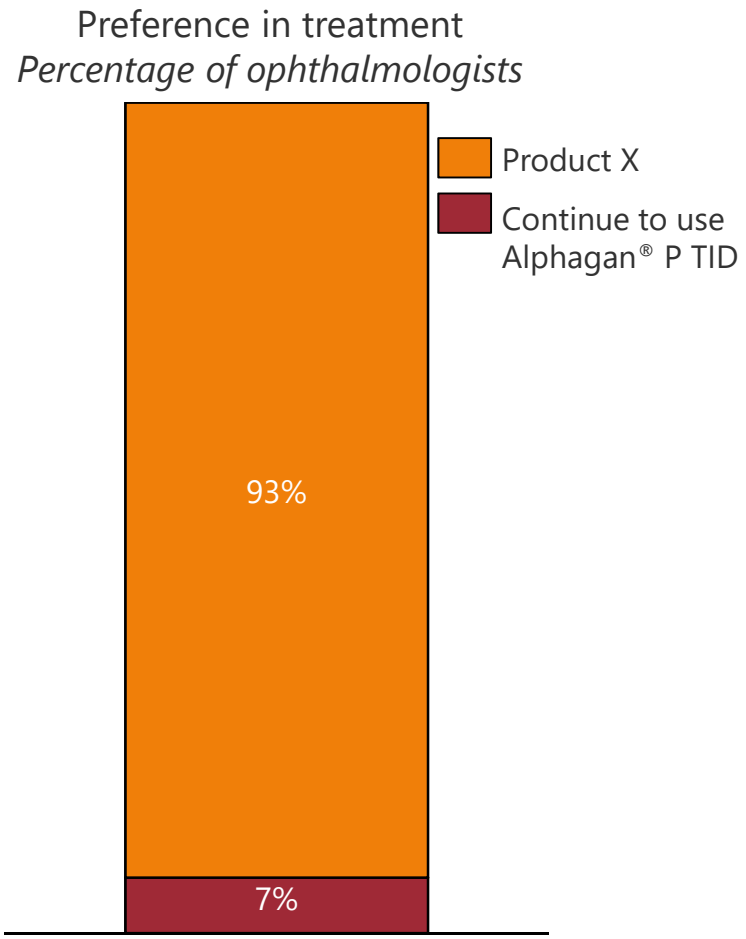
PDP – 716

Once-a-day eye drops perceived favourably by physicians

- Clear preference of physicians for PDP – 716*
- 93% of physicians would prefer to prescribe once a day eye drops
- Novel once-a-day Brimonidine eye drops expected to take meaningful market share



Q. Given a choice, which of the following eye drops of Brimonidine would you prefer to prescribe? (n=30)

* Based on primary market research conducted on behalf of SPARC by third party in the US PDP – 716 = Brimonidine OD TID = Three times-a-day

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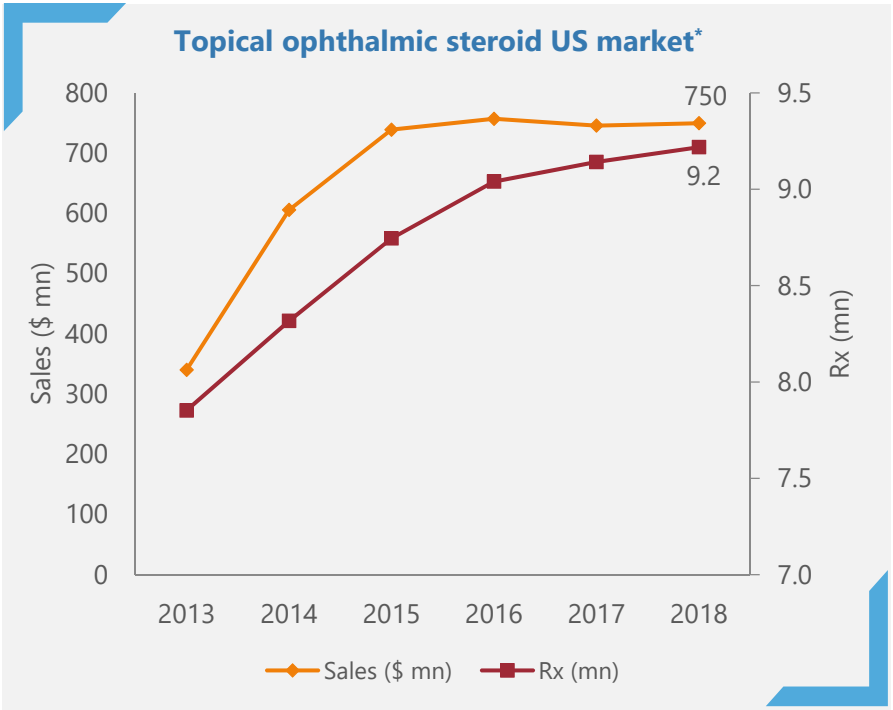
SDN – 037
US market opportunity

- Cataract causes half of all cases of blindness and affects more than 24 mn people in US with age 40 and older
- Topical steroids are standard of care for the treatment of pain & inflammation associated with cataract surgery
- US topical ocular steroid market valued at $ 750 mn with ~9 mn Rx dispensed annually*
- Currently marketed formulation cause blurring of vision and need to be dosed four times-a-day
- Novel improved steroid composition with BID dosing would provide significant compliance benefit



*IQVIA MAT June 2018 SDN – 037 = SDP – 037 BID = Two times-a-day

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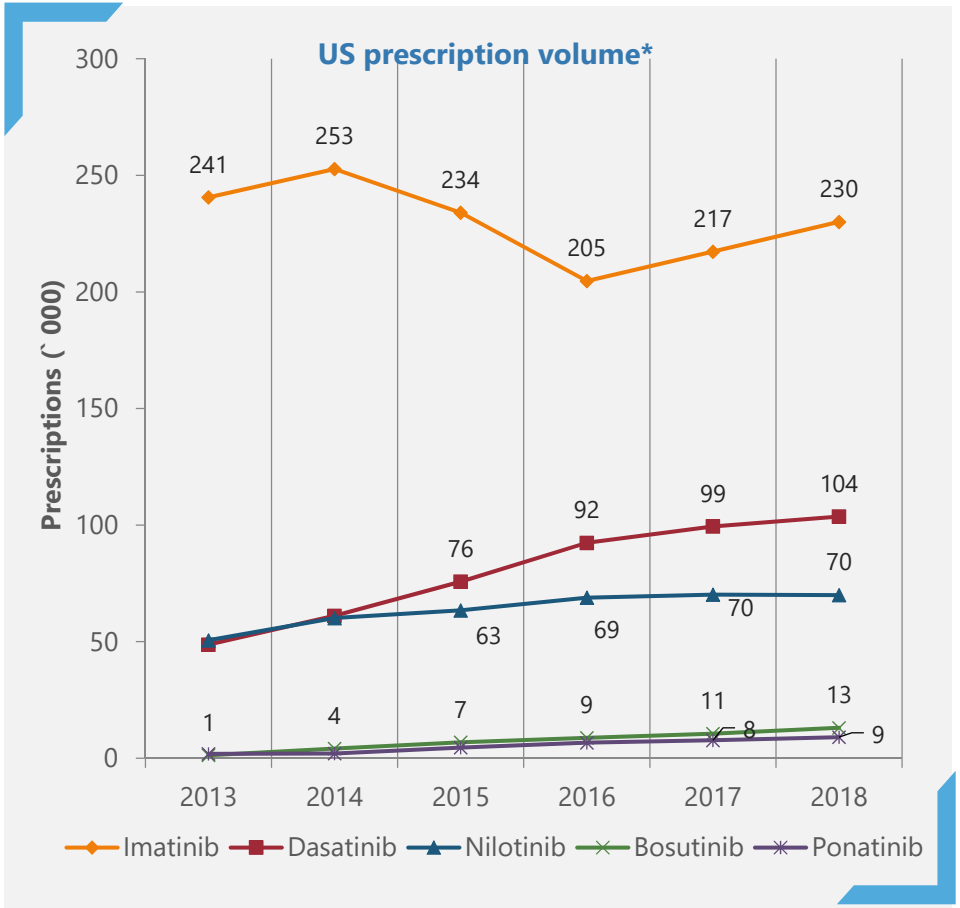
SCO – 088

Targeting treatment intolerance and resistance in CML

- Increasing usage of 2nd and 3rd generation TKIs
- Limited treatment options for 3rd line and beyond
- Physicians believe, the currently available therapies are inadequate for 3rd line treatment in CML#
- KOLs acknowledged the need for an agent with a reasonable toxicity profile for T315I mutation disease#



#Primary market research conducted on behalf of SPARC by third party in US. *IQVIA MAT June 2018. ^Internal Estimates, @Clin Cancer Res 2013;19:5828-5834. TKIs = Tyrosine Kinase Inhibitors CML = Chronic Myeloid Leukemia

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R&D Pipeline

COPD = Chronic Obstructive Pulmonary Disease CML = Chronic Myeloid Leukemia T2DM = Type 2 Diabetes Mellitus

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