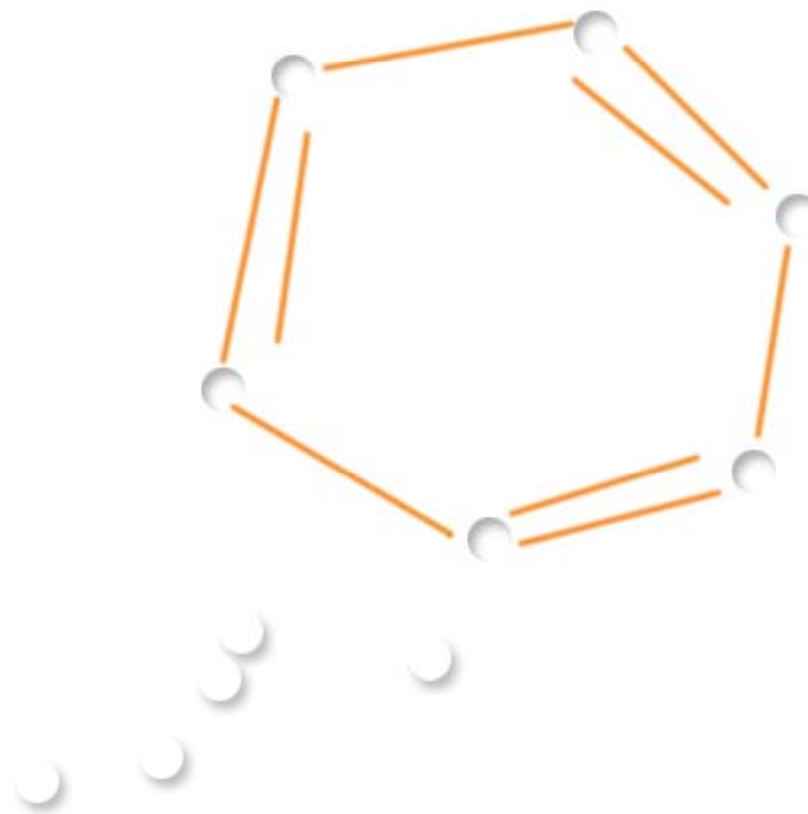




SUN PHARMA
ADVANCED RESEARCH
COMPANY LTD.

An Investor Update on *Innovation*

June 2011



BSE:532872 | NSE: SPARC | Bloomberg: SPADV@IN | Reuters: SPRC.BO

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Disclaimer



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SPARC – *Innovating, with measured risk.*



- A disciplined and systematic innovation process
- Focus on niche indications with predictable and sustainable market
- Develop products/technologies which solve unresolved problems and add meaningful value
- Early confirmation of the proof of concept
- Balanced resource allocation to projects of short and long gestation period

Key approaches to research at SPARC



NDDS Approach

- Improve patient compliance
- Enhance safety
- Reduced regulatory hurdles
- Expand product indications

NCE Approach

- Work on validated targets and biology
- Address limitations of current products
- Improve therapeutic index and product PK characteristics

Technology Platforms

Oral

- Gastro Retentive Innovative Device (GRID)
- Wrap Matrix System



Injectables

- Nano particulate formulations
- Biodegradable Depot Injections.



Topical

- Dry Powder Inhalers (DPI)
- SMM Technology for Ophthalmic Formulations
- GFR Technology for Once a Day Ophthalmic formulations
- Extended Release (ER) Microspheres for Topical Applications





**SUN PHARMA
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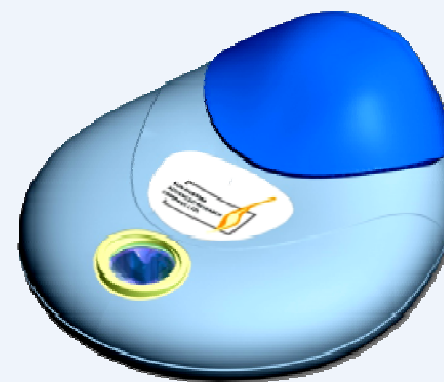
NDDS – Injectable and Topical Products

Dry Powder Inhaler



SPARC's DPI is a pre-metered, 60 dose, inhalation activated device for administration of combination of inhaled steroids and bronchodilator drugs

- Uniform dose delivery independent of inspiratory flow rate
- Consistently delivers higher amount of drug to lungs
- Eliminates double dosing and dose wastage
- Provides visual, audible and tactile feedback upon dose administration
- Glow-in-the-dark feature for easy night-time use
- Feature for assisting visually impaired, as reminder to refill device, when 8 doses remain
- Small and convenient for easy to carry.
- Compliant to the stringent USFDA and European requirements.



Equivalent clinical efficacy at “*half the dose*” of Seretide Accuhaler[®]



Randomized, Comparative, Active Controlled, Multi-Center Study in Asthma Patients in India

- Comparing
 - SPARC DPI containing Salmeterol **25mcg / Fluticasone 250mcg** (TEST) &
 - Seretide Accuhaler[®] –(Salmeterol 50mcg / Fluticasone 500mcg) (REFERENCE)
- Treatment duration = 4 weeks, N = 113

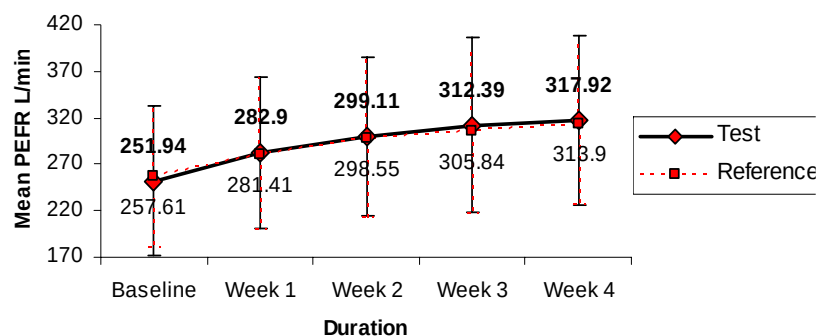
Study Outcome

- **Equivalent efficacy** to Seretide Accuhaler[®] on all primary and secondary end points
- SPARC's DPI demonstrated **statistically and clinically significant improvement vs. no treatment baseline in all efficacy parameters studied** (morning and evening PEFr and FEV1)
- Efficacy of SPARC's DPI in improving lung function demonstrated by :
 - Reduction in use of rescue medication
 - Day and night time asthma symptoms
 - Global impression of change rated by subjects and investigators

Equivalent efficacy at “*half the dose*” of Seretide Accuhaler[®]

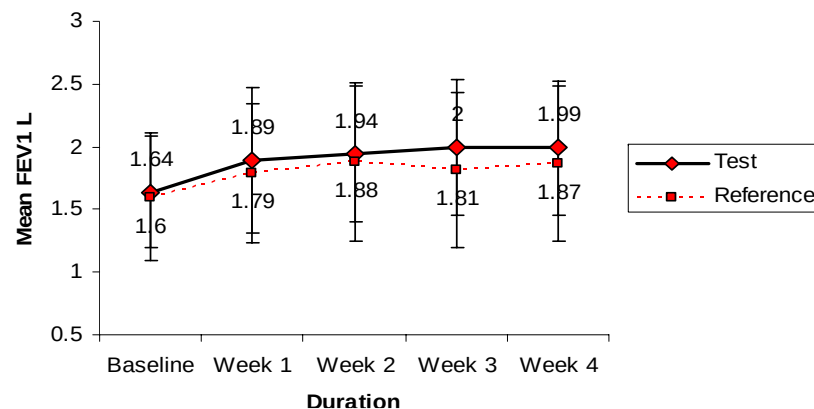


Average Morning PEFR by Treatment Group by Treatment Week (n = 107)



* $p < 0.0001$ for change from baseline

FEV1 from baseline to week 4 (n = 107)



* $p < 0.0001$ for change from baseline

- **TEST** = SPARC's DPI containing Fluticasone 250mcg/Salmeterol 25mcg
- **REF** = GSK's SERETIDE ACCUHALER[®] Fluticasone 500mcg/Salmeterol 50mcg

Future development plan



US -505(b)(2) route.

- Pre IND meeting completed.
 - IND filing in FY12
-

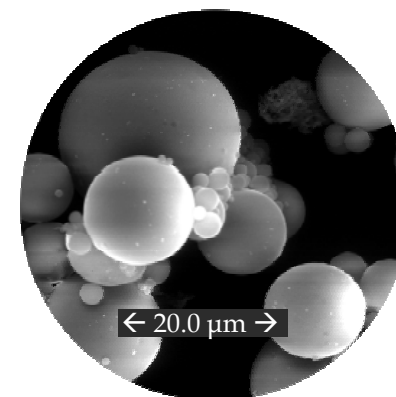
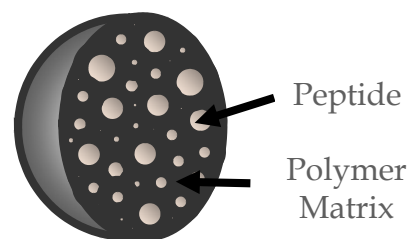
India

- Phase III study completed
 - To be launched in Q2FY12
-

Biodegradable Depot Injections and Implants

The Technology

- SPARC has developed a technology platform of biocompatible and biodegradable *micron-sized* polymer particles that contains drug molecule in its matrix for long-term systemic delivery of drugs.



Biodegradable Polymeric Microspheres

Key Advantages

- Simple injections by IM/SC route; requires no specialized training for administration
- Fine needles, low injectable volume, better patient acceptance.
- Rapid onset and Prolonged release (for months in a single shot)
- Uniform drug plasma concentration
- No peaks and valleys associated with daily and multiple doses - less toxic/adverse events
- Improves treatment adherence

Octreotide Depot Inj 1 M



Octreotide is a Somatostatin analogue used for the treatment of hormone dependant cancers. Somatostatin has a short half life and needs 3-4 injections daily

SPARC has developed Octreotide depot 1M Inj. capable of maintaining therapeutic plasma levels for one month following a single injection.

Octreotide depot Inj. (1 Month) has been developed at SPARC with biodegradable depot injection platform.

Based on clinical studies undertaken on Acromegaly patients, Octreotide depot inj. has been launched in India.

Octreotide 3 Month depot Inj. is currently under development at SPARC.

Future development plan



US

- Plan to file Octreotide Depot Inj IND in FY12
-

India

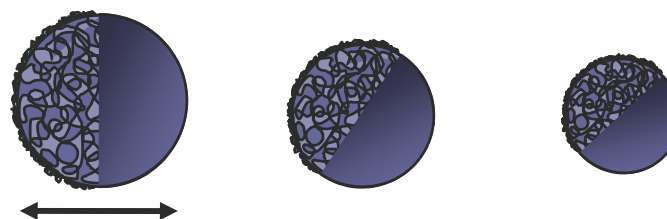
- One month product is already launched in India.
-

Nanoparticulate Formulations

The Technology

- Novel self-dispersing nano-particle technology platform for “difficult to formulate”, insoluble” anticancer drugs

Composite Nanoparticles Anticancer Drug + Polymer + Lipid



*Nanometer sized particles
i.e. 1/1000th of a human hair thickness*

Key Advantages

- Uses very safe excipient with no added toxicities
- Drug molecule remains the same; not covalently bound or altered.
- Low excipient to drug ratio.
- Delivers higher dose without increased adverse event profile.
- Eliminates the need of pre-medication, special infusion bags/bottles, and in-line filters

Paclitaxel Injection Concentrate for Nanodispersion (PICN)

Novel formulation of Paclitaxel using SPARC's proprietary nano particle platform technology

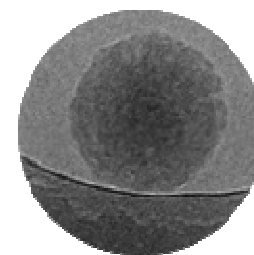
- Achieves 30% higher drug concentration in tumor tissues compared to conventional paclitaxel
- Unlike ABRAXANE®, quick and easy “one step” dilution and infusion preparation
- Shorter infusion time (30 min)
- Superior safety profile compared to ABRAXANE®, observed in Phase I clinical study in INDIA.



PICN as How Supplied



*PICN after
Reconstitution*



*Electron microscope
image of nano particle*

Safety established at high doses in Phase I clinical trial



Study enrolled 36 patients with metastatic breast cancer and who have progressed to at least one combination chemotherapy.

Key Findings from Safety

Data Analysis

- 28 patients exposed to PICN.
- Dose limiting toxicity was observed at 325mg/m²
- NO pre-medication with high dose corticosteroids, antihistamines or anti-emetics.
- NO hypersensitivity reactions in ANY patients
- Less neuropathy

Toxicity comparable to ABRAXANE®*

	PICN 260mg/m ² n= 9 , (%)	ABRAXANE® [†] 260mg/m ² n=229, (%)	TAXOL® [†] 175mg/m ² n=225 , (%)
Neutropenia <2.0 x 10 ⁹ /L	7 (77.78)	183 (80)	185 (82)
Neuropathy			
Any Symptoms	1 (11.11)	163 (71)	124 (56)
Severe Symptoms	0	23 (10)	7 (2)

*This comparison with large historical data of Abraxane and Taxol is for the purpose of interpreting PICN data. PICN safety remains to be established in large, randomized clinical trial

[†] ABRAXANE PI

Encouraging trend of efficacy in Phase I clinical study



Key Findings from Efficacy Data Analysis

- Overall response at all dose levels 45% (10 out of 22 patients).
- Efficacy of PICN is evaluated at MTD dose level 295mg/m² in 7 patients
 - 6 patients achieved partial response, and 1 had disease progression in the 295mg/m² group with ORR of ~86%.
- Phase II study is ongoing with 260 mg/m² and 295 mg/m² dose comparing with 260mg/m² Abraxane® in metastatic breast cancer

Trend of superior efficacy in Phase II clinical study continues...



Trend of superior efficacy compared to ABRAXANE® continues...*

PICN	PICN	ABRAXANE®
295mg/m ²	260mg/m ²	260mg/m ²
n= 22 , (%)	n=20, (%)	n=23 , (%)

Objective response rate (ORR)	59.1%	50.0%	34.8%
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We will look at early efficacy data with following understanding:

1. Data includes CT scan reports as available in Jan 2011 for Cycle 2 , Cycle 4 or Cycle 6.
2. The study is ongoing

Key Findings from Interim Efficacy Data Analysis

Efficacy and safety of PICN in subjects with metastatic breast cancer: Randomized open label active control comparator parallel group and multicentric study

- 118 out of 180 Enrolled, 65% enrollment complete
- Superior efficacy continues
- No pre-medication
- No hypersensitivity reactions
- Trend of less neuropathy continues

Trend of superior efficacy in Phase II clinical study continues...



Percentage Reduction in Tumor Size	PICN 295mg/m ² n= 12	PICN 260mg/m ² N=10	ABRAXANE [®] 260mg/m ² N=7
Percentage Reduction from baseline (Mean ± SD)	54.8 ± 26.0	46.3 ± 22.4	47.4 ± 24.4
(Median)	51.5	33.5	39.0
Number of Patients with Complete Response	2	1	1

These are early efficacy data for ongoing PICN phase 2/3 study. We will look at early efficacy data with following understanding:

1. Data includes interim analysis of data from CT scan reports as available in April 2011 for Cycle 2, Cycle 4 or Cycle 6.
2. The study is ongoing

Future development plan



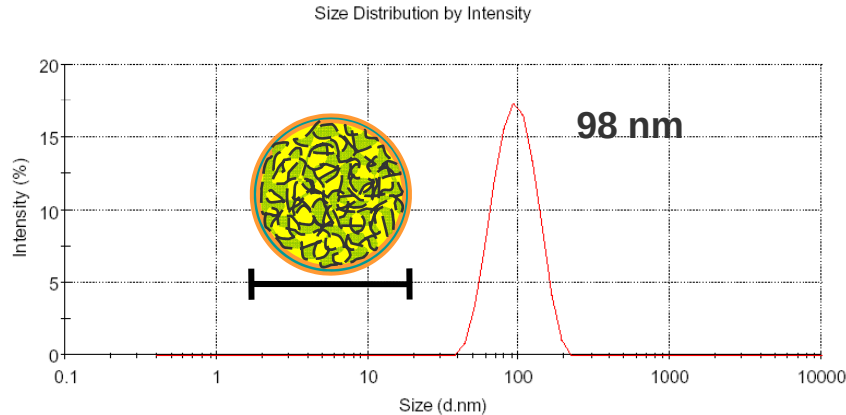
US -505(b)(2) route

- IND filing with USFDA completed and ethics committee approval obtained.
 - To initiate Phase I study of a combination chemotherapy of PICN with Carboplatin Q3 FY12.
-

India

- A phase II/III study in metastatic breast cancer is initiated in FY11. The study has completed 65% enrollment.
-

Docetaxel Injection Concentrate for Nanodispersion (DICN)

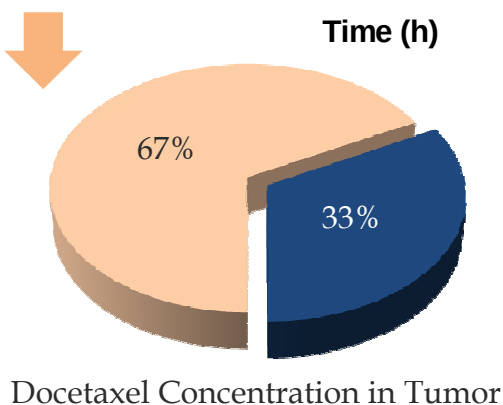
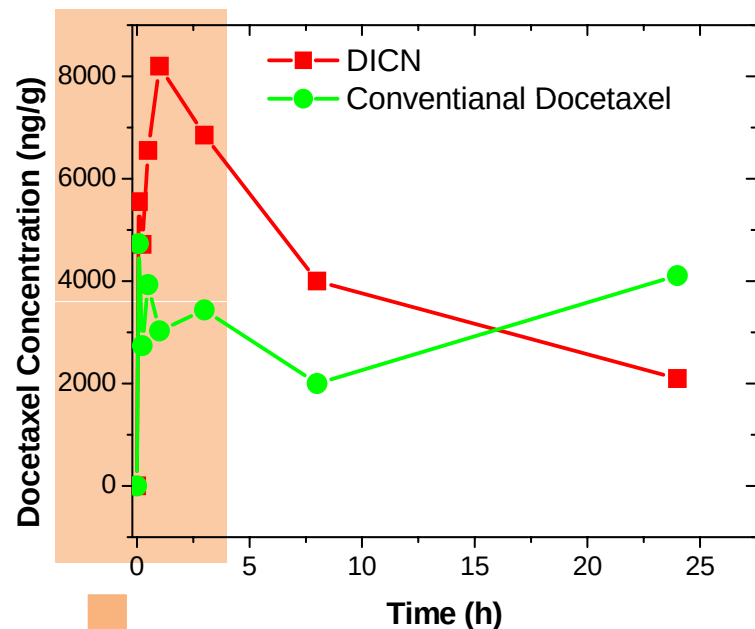


A typical histogram of Docetaxel nanodispersion showing z-average mean diameter of ~80-120 nm taken on a Malvern's Zetasizer.

A “self-dispersing” nano particle formulation of Docetaxel.

- DICN technology is on the same platform as PICN.
- Avoids “toxic” solvents used in conventional docetaxel formulations.
- Avoids limitations of specific bags and in-line filter use.
- Usage compliance: simple admixture in infusion bag.
- No premedication needed
- No hypersensitivity risk

Enhanced safety in preclinical studies



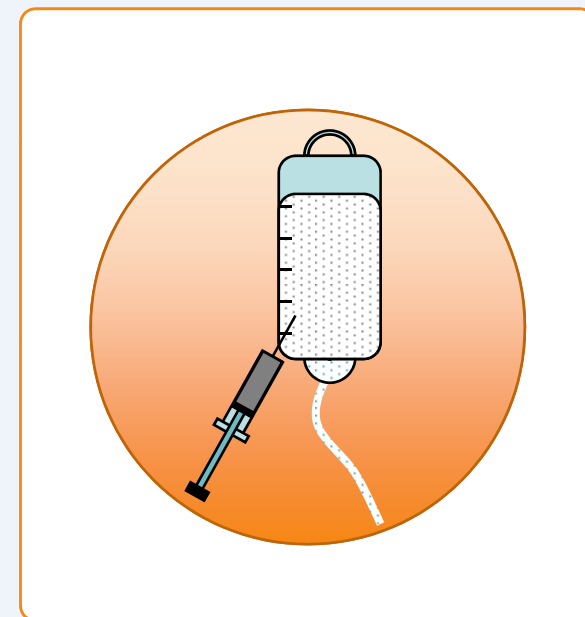
Key findings from preclinical studies

- DICN technology works on the same principles as PICN in preclinical trial
- Safe upto 7.5 times equivalent human dose, than the maximum approved Taxotere dose.
- Achieves 30% higher drug concentrations in tumor tissues compared to conventional Docetaxel and 200% higher in initial 8 hours.

Safety established at high doses in Phase I clinical trial

Key Findings from Safety Data Analysis

- Completed Phase I clinical trial in solid tumor patients
- Dose limiting toxicity was observed at 170 mg/m².
- MTD 150mg/m² which is ~50% higher than Taxotere.
- NO pre-medication with high dose corticosteroids, antihistamines or anti-emetics
- NO hypersensitivity reactions in ANY patients
- Dose linearity: enable to give higher doses with predictability.



DICN Future development plan



US -505(b)(2) route

- Pre-IND meeting with USFDA in FY12
-

India

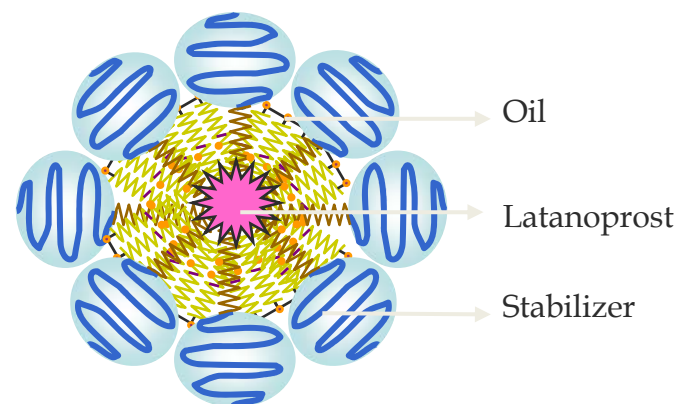
- Phase I study in solid tumor patients completed.
 - Phase II study in NSCLC patients planned in Q3 FY12
-

Swollen Micelle Microemulsion (SMM) Technology



The Technology

“Swollen micelle microemulsion” is a platform for solubilizing ophthalmic drugs with limited water solubility or completely insoluble ophthalmic drugs.



“Swollen Micelle microemulsion”

- SMM is a quaternary ammonium preservative/surfactant (BAK)-free solubilizing technology.
- Contains known ocular lubricant which fortifies the lipid layer in formation of tear film, and uncharged coating is soft to eye surface.
- Prevents drug from environmental temperature and light fluctuations.

Latanoprost “BAK Free” Ophthalmic Solution



- Reduced risk of ocular surface damage on chronic use
- Clear, colorless, BAK-free ophthalmic solution
- Non-infringing formulation to the market leader Xalatan® (Pfizer) with similar strength, dosing, administration and pack size
- Stable at Room Temp.; does not require refrigeration upon storage / transport
- Demonstrated improved safety profile and eye comfort characteristics in a phase III, randomized, active controlled clinical study in India in 104 patients

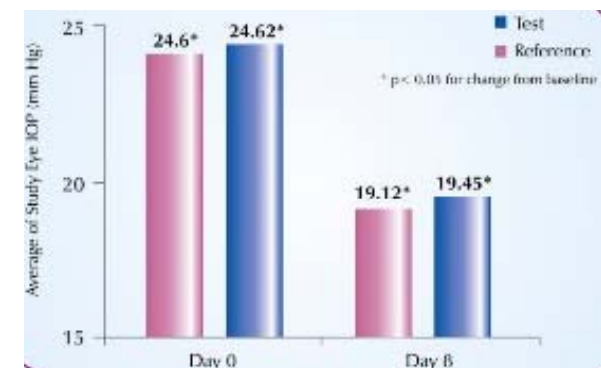


Trend of superior efficacy in Phase II clinical study continues...

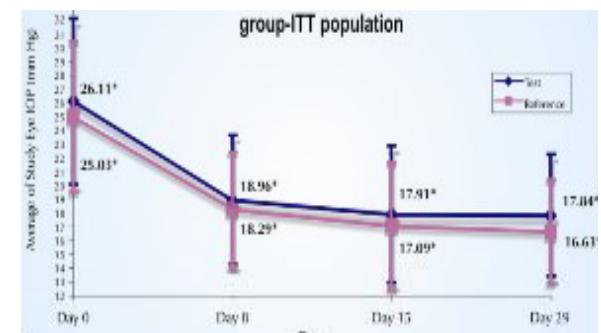
SPARC completed a 4 week, randomized, active controlled, multi-center, phase III study to compare safety and efficacy of SPARC's latanoprost with Xalatan[®]

- 104 subjects were enrolled in this study
- Clinically and statistically significant reductions in IOP was observed with SPARC's Latanoprost starting from 1 week and up to the 4 week study period
- Both efficacy and safety data were comparable to Xalatan[®]

IOP reduces within 1st week



IOP reduction maintained over study period



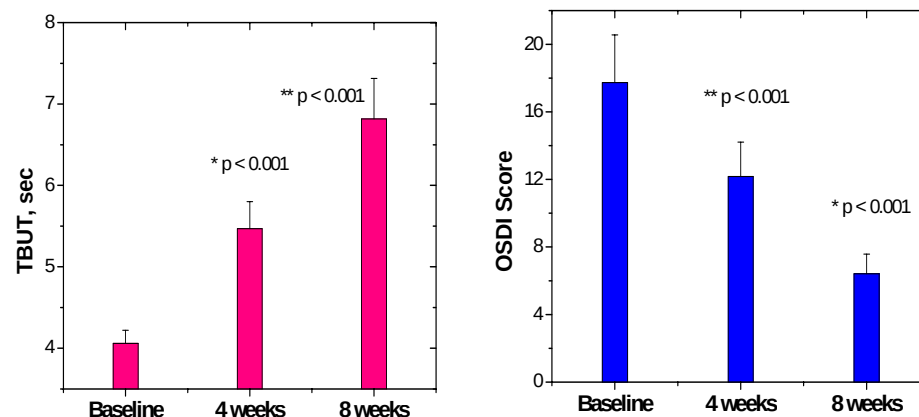
Pilot Safety Evaluation Study in India



SPARC completed a 8 week, pilot study to quantify changes in tear break-up time (TBUT), and ocular surface disease in subjects with primary open angle glaucoma or ocular hypertension after switching therapy from BAK containing Latanoprost to SPARC's formulation

- 25 subjects were enrolled in this study and 40 eyes were evaluated.
- Clinically and statistically significant increase in TBUT was observed within 4 weeks SPARC's Latanoprost starting from 4 week and up to the 8 week study period
- The % OSDI score reduction was statistically significant

Improvement in TBUT and OSDI



Future development plan



US -505(b)(2) route

- IND approved at USFDA
- USFDA requires 2 Phase III studies for possible product registration
 - An active controlled, non-inferiority, clinical study in 518 patients; patients enrolled till date 318
 - Open label extension safety study in 200 patients; patients enrolled till date 107
- Start date of the study: Q2 FY11
Target study completion date : Q3 2012.

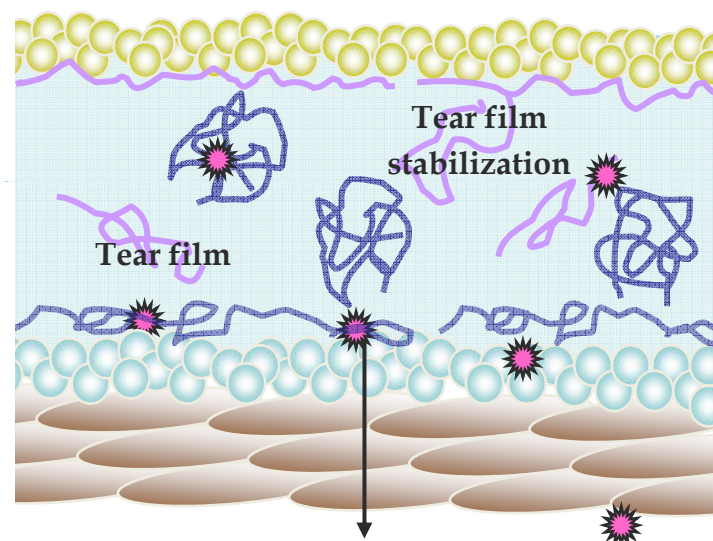
India

- Launched in India with excellent response.

Gel Free Reservoir (GFR) Technology

The Technology

- Gel Free Reservoir technology platform uses an unique polymer ratio that shows synergistic increase in viscosity without the loss of clarity and flow property.
- Stabilizes tear film and retain the active for prolonged periods
- Product with characteristics similar to natural tears.
- Can be successfully applied to many products
 - Timolol OD ophthalmic solution
 - NCE and other products are in development



Sustained Timolol transport across membrane

Future development plan



-
- Phase III clinical study completed in India for Timolol OD
 - Timolol OD launched in India
-

Challenge to deliver ophthalmic combination



The Challenge

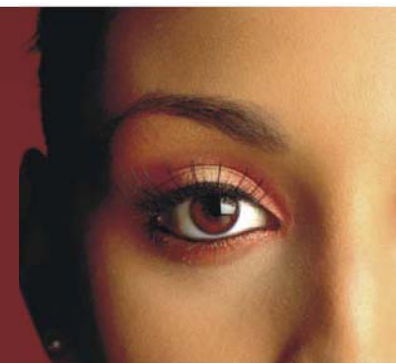
- Mixing water insoluble and water soluble drug

The Conventional Solution

- Use of toxic quaternary ammonium solubilizers

The Technology

*Latanoprost/Timolol
ophthalmic solution*



- Combination of essential elements of the two ophthalmic platforms
 - Self-preserving GFR technology
 - BAK-free and Surfactant free

Future development plan



-
- Preclinical studies completed
 - The Phase III efficacy and safety study is ongoing in India
 - Subsequently, SPARC will also be initiating Phase III, active controlled, non inferiority clinical study.
 - Offers a steady therapeutic level, avoids peaks & troughs
-



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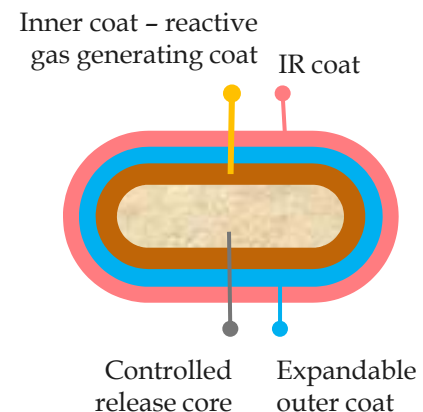
NDDS ORAL Products

Gastro Retentive Innovative Device (GRID)



The Technology

- Designed for retention in the stomach for longer time (~about 8 hours)
- Combination of mechanisms
 - Flotation
 - Size expansion
 - Mucoadhesion



Key Advantages

- Improves bioavailability of drugs with narrow zone of absorption in GI tract
- Floats instantaneously, Swells upto 8 times its initial volume
- Maintains physical integrity
- Flexible and soft
- Different types of release profiles possible (IR+ SR)
- Once - a day dosing improves patient compliance

Baclofen GRS Capsules

- Extended release capsule formulation of Baclofen with Proprietary Gastro Retentive Innovative Device (GRID) technology
- Once daily and recommended fed state do for optimal bioavailability and minimal se
- Baclofen GRS capsules will be available in strengths i.e., 10 / 20 / 30 / 40 / 50 / 60 m individualized dosing and greater dose flexibility
- Offers a study therapeutic level, avoids peaks & troughs



Baclofen GRS - Established Clinical Efficacy



Total of 388 healthy volunteers and 108 patients exposed to Baclofen GRS capsules

- 22 studies for comparative bioavailability and observation of food effect
- 11 pilot studies to optimize final formulation of Baclofen GRS capsules
- 11 studies to determine optimal dosing condition & time of administration
- PK study in spastic patients completed



" Summary of clinical studies in addition to PK evaluations"

- 4-Week Phase III clinical study in India in spastic patients
 - Successfully converted from Baclofen IR formulation to Baclofen GRS formulation
- 2 Gastroscopy studies in spastic patients confirmed that there is no accumulation of capsules in stomach after multiple dosing

Baclofen GRS Future Development Plan



US -505(b)(2) route

- Phase III, randomized, placebo-controlled efficacy study in 300 patients :
 - A special protocol assessment (SPA) was submitted to the US FDA in the fourth quarter of 2009 -10
 - SPARC initiated start up activity for Phase III clinical trials in Q1 2010-11
 - SPARC further decided to await SPA agreement and hence postponed the study commencement.
 - First patient expected to be in by Q3 2011-12
- One open label safety study in 100 patients
- 100 patients PD study to prove once a day dosing

India

- Baclofen GRS capsules are registered and marketed in India

Baclofen GRS Future Development Plan

Clinical study **To treat alcohol dependence**

- Clinical study planned in India for use of Baclofen GRS to treat Alcohol dependence
 - Randomized, double blind, placebo controlled, comparative, parallel groups, multi-centric study
 - Regulatory approval for clinical trial under way



Challenges in CR products with high solubility, high dose drugs

High solubility and high dose challenges

High excipient to drug ratio – bigger dosage form

Release control from dosage form

Initial dose dumping
Or a long lag time

Difficult to achieve

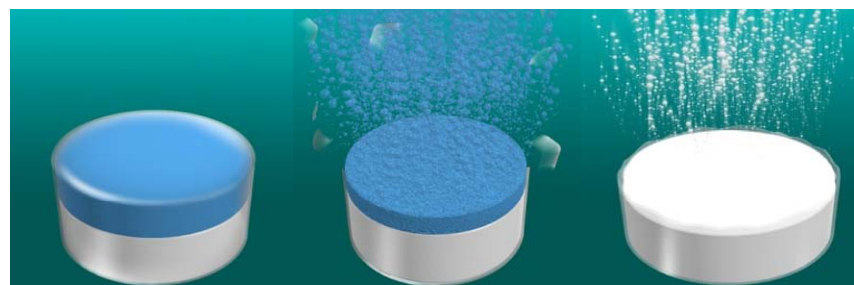
- Zero order release
- Combination of release patterns like IR+SR, IR+SR+IR

Significant variance in PK between fed & fasted dosing

Wrap Matrix System

The Technology

- Novel oral controlled drug delivery system based on pre-defined, precise and selective surface exposure



Key Advantages

- Once-a-day dosing
- Ability to handle products with larger daily dose
- Suitable for drugs with very high solubility
- No residual drug in dosage form on evacuation
- Minimal food effect
- Difficult to reproduce bioequivalence using any other formulation technology
 - Low risk of generics

Products with Wrap Matrix Technology



Levetiracetam - An Antiepileptic with high water solubility and very large dose

- Development of 1500 mg and 1000 mg once a day product completed.
- Bioequivalent product to Keppra XR 2 X 750 mg
- Completed Pivotal Pharmacokinetic studies
- Plan to file in US as 505(b)(2) in Q3 FY12

A Cardiovascular agent - high dose and high solubility

- Controlled release product developed with objective of reduced side effects.
- Pharmacokinetic studies ongoing; to be completed in Q3 FY12
- Combinations with various drugs with complementary mechanisms of action under development

A skeletal muscle relaxant with ultra short half-life

- Target Product profile includes better therapeutic action over repeat dose available IR product
- Target added benefit - less side effects due to reduced “peak and trough” plasma levels.
- Phase I studies initiated

Products with Wrap Matrix Technology



An Anticancer Agent combination with beneficial agent

- Phase I studies planned

CNS Agent : new indication

- Proof of Concept studies planned

CNS Agent with very high solubility

- Alternate approach under evaluation
- Pharmacokinetics studies are ongoing

ANDA

- ANDA product - Venlafaxine ER tablets approved in US & Europe
- additional products based on Wrap matrix technology filed as ANDA (by Sun Pharma)

Products Using Other Novel Technologies



Cardio-protective agent 1 – in new dosage form

- Formulated in new patient friendly dosage form
- Pre-NDA meeting with US FDA scheduled in Q2 2011-2012
- Phase II studies underway

Cardio-protective agent 2

- Formulated in new salt form
- Development studies underway



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NCEs

NCE candidates



SUN
1334H

SUN
597

SUN
09

SUN
44

SUN
K706

SUN-1334H Ophthalmic Solution

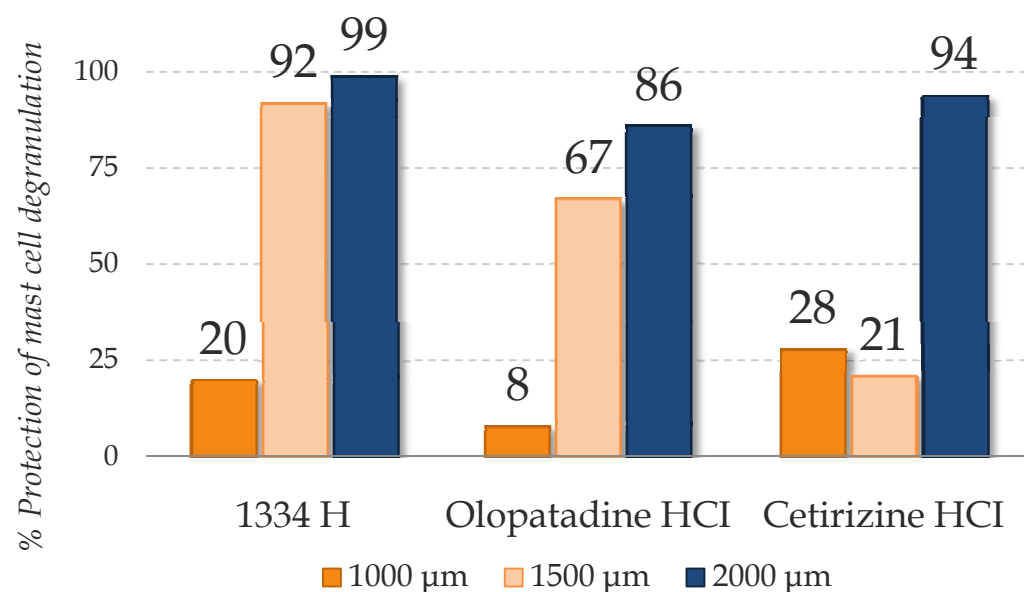


- Although oral antihistamines can cause reduction in symptoms of conjunctivitis, the topical administration gives advantage of quicker onset and better efficacy
- In preclinical studies, SUN-1334H 0.3% ophthalmic solution, shows good inhibition of allergen and histamine-induced conjunctivitis upon once-a-daily dosing

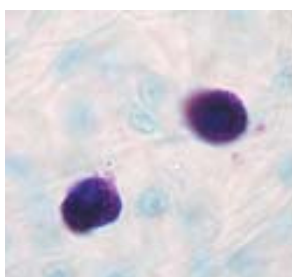
Treatment	Edema Scores*	
	0.5 hr	24 hr
Saline	0	0
Placebo	17.67	16.42
SUN-1334H ^a	3.75	3.42
Olopatadine ^b	3.83	4.25

* Sensitized Guinea Pig Model; ^a 0.3% solution; ^b 0.2% solution

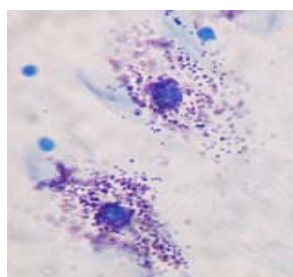
SUN-1334H Inhibition of Mast Cell Degranulation in Rats



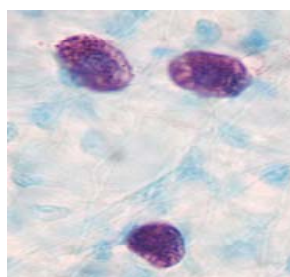
- In conjunctivitis, major cause of itching and inflammation of eyes is the release of inflammatory mediators due to “degranulation” of conjunctival mast cells.
- SUN-1334H causes mast cell stabilization inhibiting release of different mediators, which might help in reducing symptoms of conjunctivitis



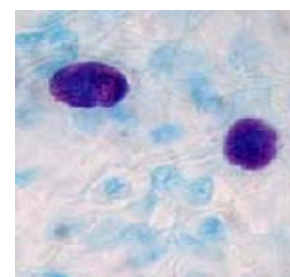
Negative control



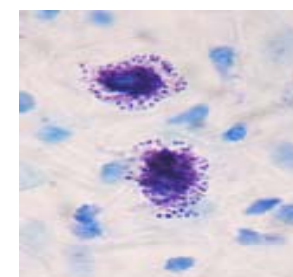
48/80 control



1334H (1500 μ M)



Olopatadine (1500 μ M)



Cetirizine (1500 μ M)

SUN-1334H Ophthalmic Solution- Phase I study (India)



Study Protocol

- A randomized, double-masked, placebo-controlled, parallel-groups, single day, dose escalation study
- Dose escalation from 0.09mg/ day (0.3%) once a day to 0.72mg/ day (0.6%) in 4 divided doses
- Total of 32 subjects exposed at escalating dose levels

Study Outcome

- No Dose Limiting Toxicity observed till 0.72 mg (0.6%) one drop in one eye four times a day dose.
- The drug is safe for further clinical development.

SUN 1334H Future Development Plan



SUN 1334H Ophthalmic

- Phase I clinical study completed in India : Q4FY11
- IND submitted in US; Phase II study ongoing

SUN 1334H Oral

- Chronic toxicity studies are ongoing
- Pilot cardiac safety studies are ongoing – completion by Q3FY12
- Renal safety study in human volunteers is planned

SUN-597 Superior Preclinical Profile



In vitro

- High binding affinity for human glucocorticoid receptor $K_i = 1.09\text{nM}$
- Good selectivity over other relevant sex hormone & mineralocorticoid receptors

In vivo

- Good potency, efficacy, and duration of effect in animal models of asthma and allergic rhinitis
- Low oral bioavailability and short half-life
- Very low liability to systemic side effects; thus providing a very high therapeutic index when compared with currently marketed corticosteroids

SUN-597 High Therapeutic Index in Asthma Model



Sephadex Lung Edema-ED50 (Rat) (mg/kg, intratracheal)

Treatment	Lung Edema	Thymus Inhibition
SUN-597	0.094	> 3*
Ciclesonide	0.388	3.13
Fluticasone propionate	0.086	0.36

* 30% inhibition of thymus

Liver Glycogen Deposition (Rat) Dose: 3 mg/kg, 3 days, intratracheal

Treatment	Glycogen deposition (mg/100 gm liver wt.)
SUN-597	11.0
Ciclesonide	175.0
Fluticasone propionate	1955.8

Therapeutic Index (Lung Inflammation Model)

SUN-597	>32
Ciclesonide:	8.07
Fluticasone:	4.19

SUN-597 Low Side Effect Potential



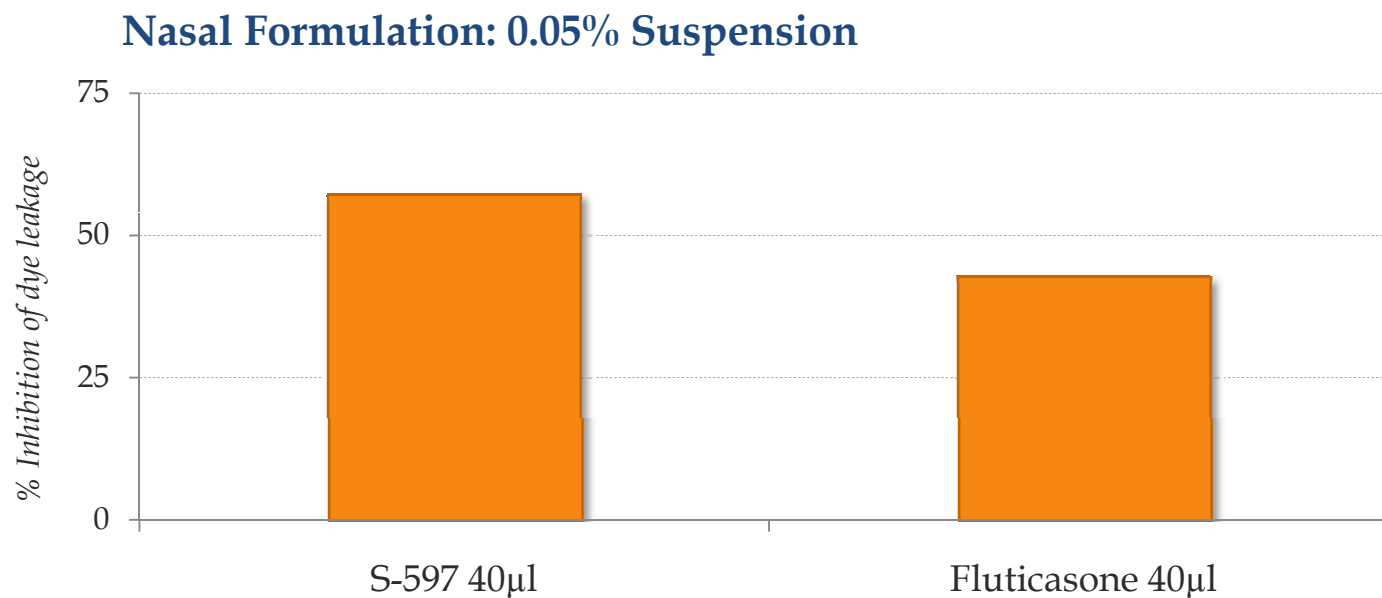
Safety on Oral Administration in Rats

Dose: 1 mg/kg x 7 days

Treatment	% Inhibition of Thymus	% Inhibition of Adrenal	% Inhibition of Body Weight Gain
SUN-597	0	7.7	0
Ciclesonide	29.5	28.7	2.7
Fluticasone propionate	50.3	21.2	49.2

- No effect in 30-day intranasal tox study in rats (NOAEL: 2.5 mg/kg/day)
- No effect on serum cortisol levels in 30-day intranasal toxicity study in dogs

SUN-597 Nasal Efficacy in Allergic Rhinitis Model



- SUN-597 as nasal formulation shows good potency and efficacy in preclinical in vivo models for allergic rhinitis

SUN-597 Nasal - Phase I study (India)



Study Protocol:

- A Randomized, double-blind, placebo-controlled, parallel-groups, intranasal single dose escalating study
- Study completed for all 5 escalating dose levels from 200 mcg once a day to 3200 mcg once a day.
- Total 40 subjects were exposed to escalating dose levels from 200 mcg once a day to 3200 mcg once a day.

Study Outcome:

- No Dose Limiting Toxicity have been observed till 3200 mcg once a day dose.
- The drug is safe for further clinical development.



SUN-597 Future development plan



SUN -597 Nasal

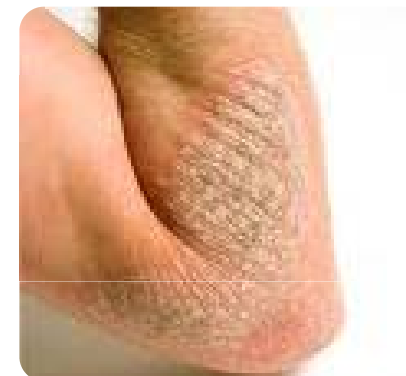
- Phase IB clinical trial ongoing; likely completion by Q2 FY12

SUN-597 Inhalation

- Preclinical toxicity is ongoing, completion by Q3 FY12
- IND filing by Q4 FY12 in India

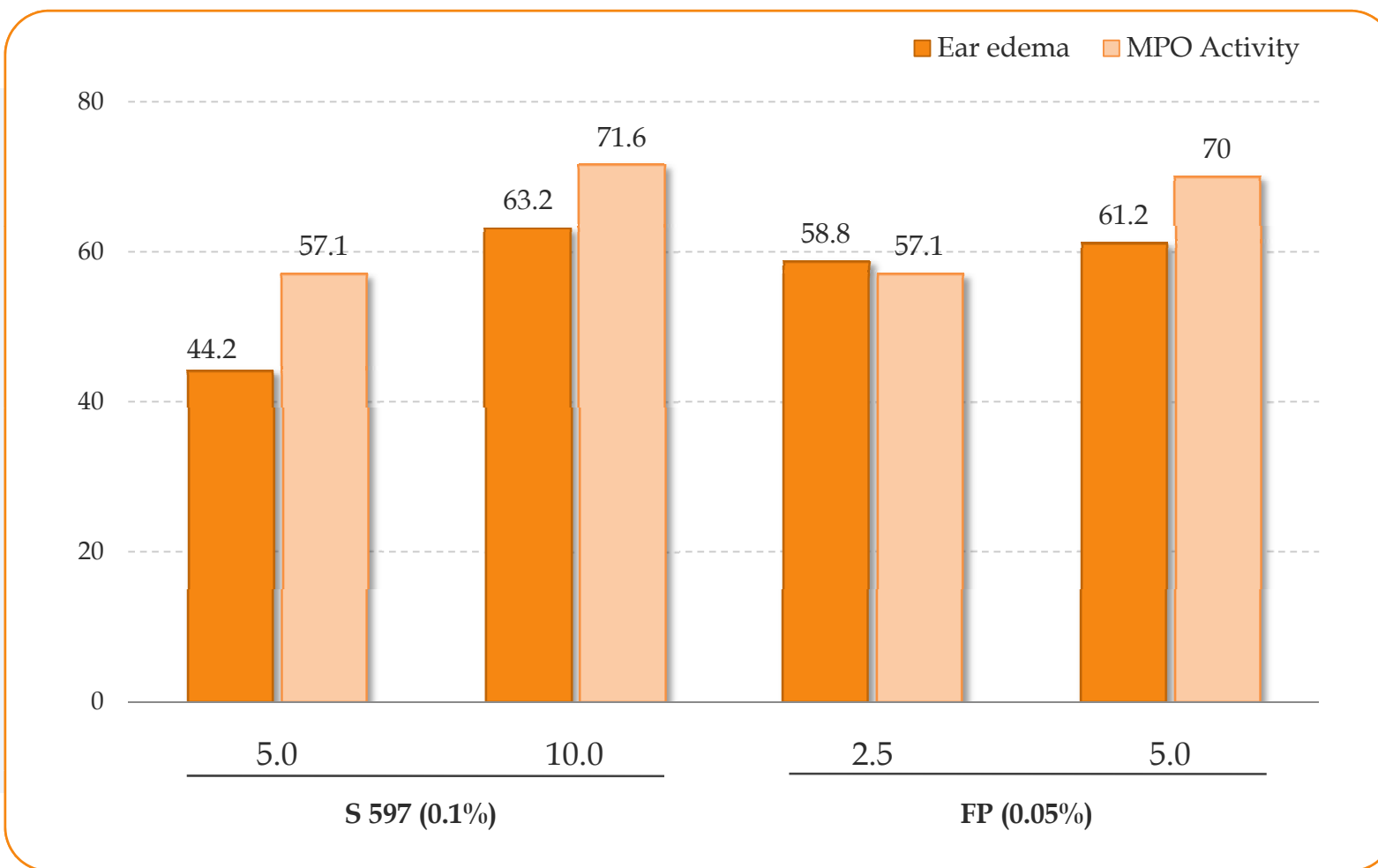
SUN-597 Topical Cream

- Topical corticosteroids are used for the treatment of inflammatory conditions of skin such as atopic dermatitis, psoriasis and vitiligo
- On prolonged use, topical corticosteroids can cause atrophy of the skin where steroid is applied. This is manifested as thinning of the skin and easy bruising
- SUN-597 has topical anti-inflammatory activity with a low potential for local and systemic side effects as assessed in the preclinical studies in rats



SUN-597 Topical cream efficacy in skin inflammation model

S 597 causes inhibition of dermal inflammation

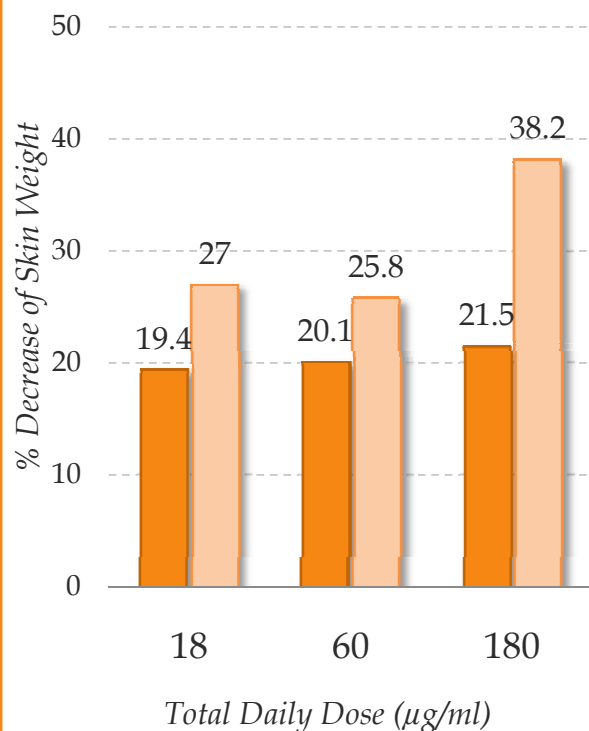


SUN-597 Topical cream shows low potential for side effects

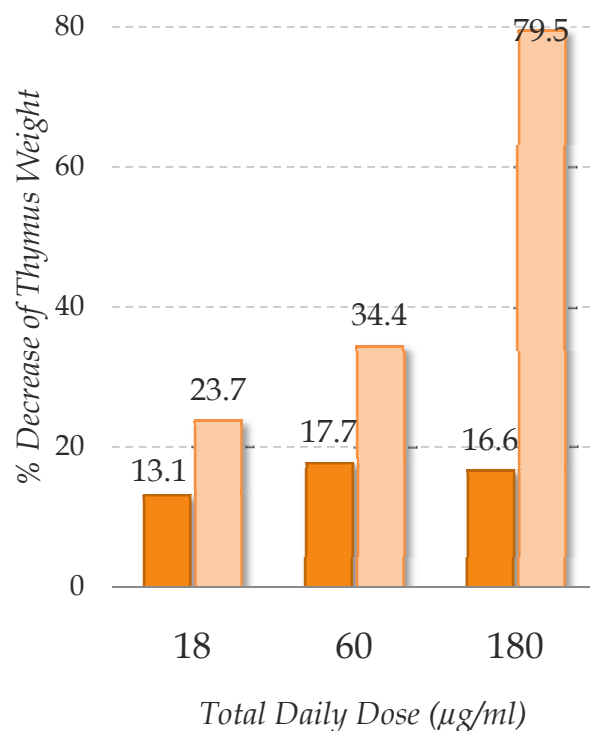


S 597 cream has low potential for local and systemic side effects

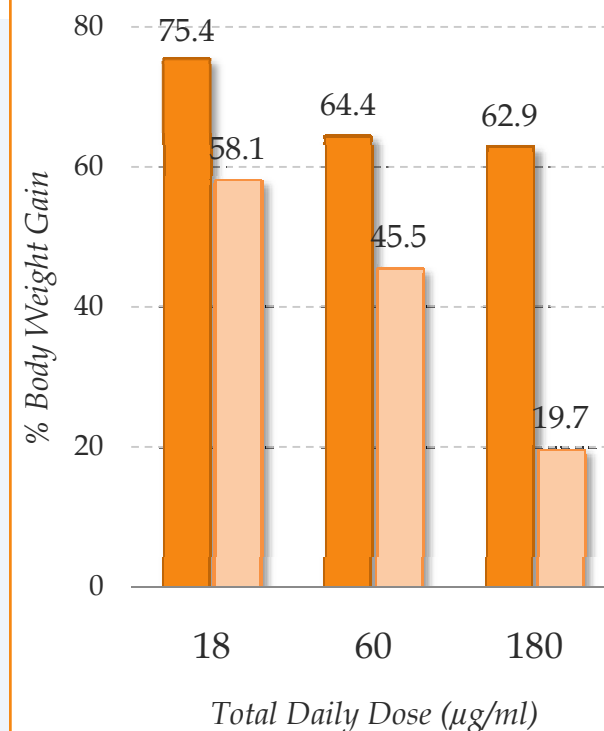
Skin Atrophy



Thymus Involution



Body Weight Gain

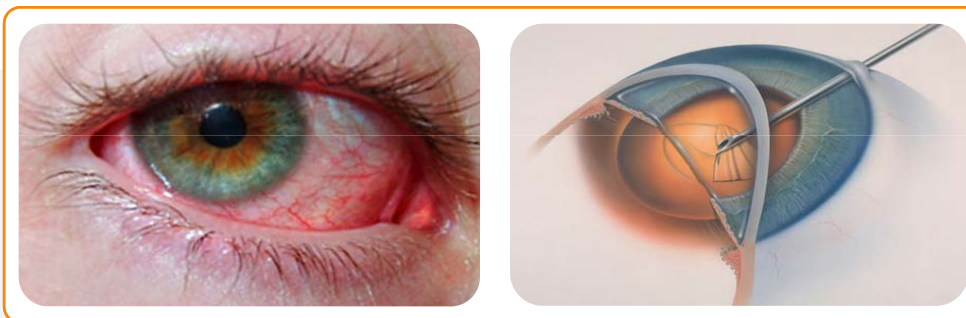


SUN-597 Topical future development plan



-
- Preclinical studies for selection of appropriate strength and formulation are ongoing
 - Formulation development by Q2 FY12
 - IND filing by Q4 FY12
-

SUN-597 Ophthalmic suspension

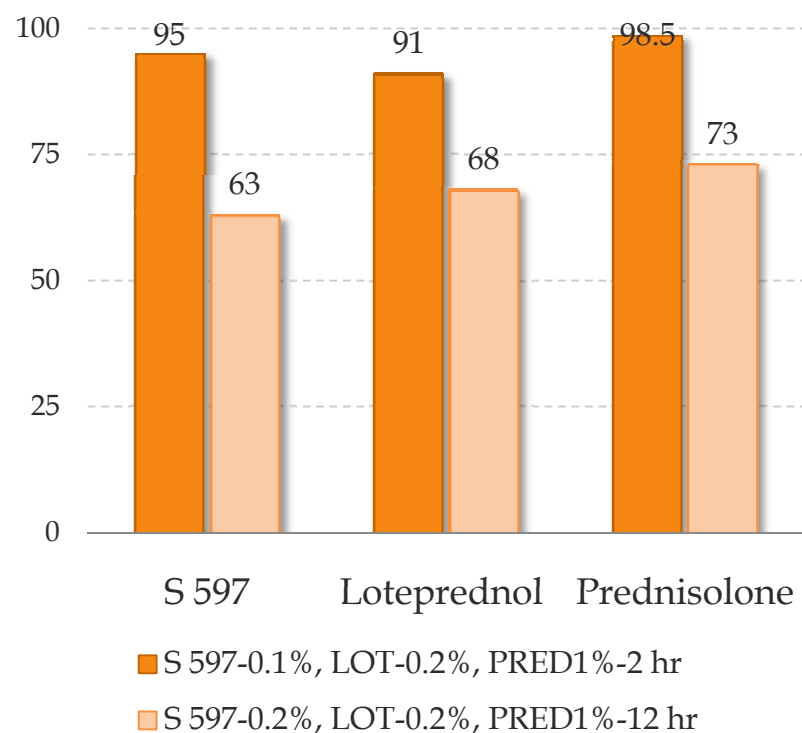


- Ophthalmic steroids are widely used in the treatment of post-operative inflammation and inflammatory conditions of eyes such as allergic conjunctivitis
- Topical application can achieve high concentration in ocular tissue leading to high efficacy and low systemic adverse effects-HPA axis suppression, osteoporosis, inhibition of growth etc
- However topical application of conventional steroids can induce various ocular side effects such as glaucoma and opportunistic infections of the eye
- SUN-597 reduces eye inflammation, however has negligible incidence of local side effects

SUN-597 Ophthalmic-Preclinical profile in ocular models

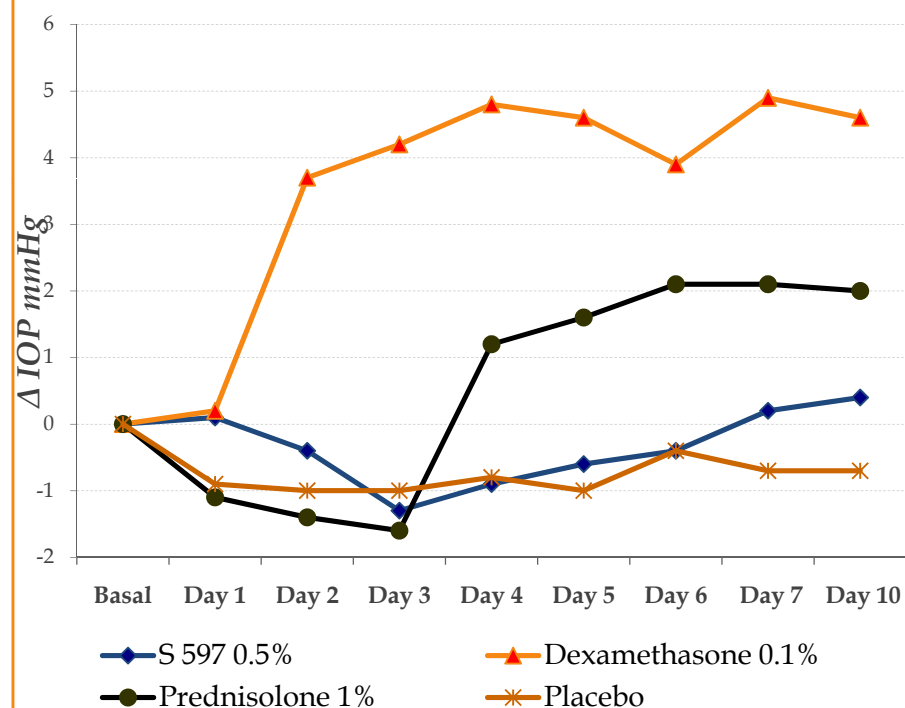


Inhibition of Allergen-Induced Conjunctival Vascular Permeability



S 597 causes inhibition of ocular inflammation induced by allergen in guinea pig model

Induction of Ocular Hypertension (Glaucoma)



S 597 has a low potential for induction of glaucoma in rabbit model

SUN-597 Ophthalmic future development plan



- Preclinical studies for selection of appropriate strength and formulation are ongoing
- Formulation development by Q2FY12
- IND filing by Q4FY12

SUN-09 Achieves Better Bioavailability of Baclofen



Dose: 20 mg/kg, intracolonic in rat

Treatment	AUC _{0-t} (μg.hr/ml)	Tmax (hr)
Baclofen	1.17	2.4
Baclofen released after SUN-09 administration	8.84	0.62

- In animal studies, intra-colonic administration of SUN-09 results in higher levels of baclofen compared to similar administration of baclofen
- Pharmacokinetic parameters viz. AUC is increased and Tmax is reduced indicating higher and quicker absorption

SUN-09 Significantly Superior Efficacy than Baclofen



- Oral administration of SUN-09 gives dose-dependent muscle relaxation with rapid onset of action in mice
- SUN-09 does not show additional safety concerns compared to baclofen in preclinical studies

Percentage Reduction of Rotarod Performance in Mice

Treatment	Dose (mg/kg, p.o.)	% Reduction
SUN-09	20.8	53.6
	31.2	81.2
	52.0	97.5
Baclofen	12.0	44.7
	18.0	47.0
	32.0	48.2

On a molar basis, doses of SUN-09 are equivalent to respective doses of baclofen

SUN-09 IR Tablet Phase I study (India)



Study Protocol:

- A Randomized, Double-Blind, Placebo- & Active-Controlled, Cross Over, Single Escalating Dose Study
- Study completed for escalating five dose levels from 4.334mg once a day to 52.005mg once a day
- Total 56 volunteers exposed to escalating dose levels from 4.334mg once a day to 52.005mg once a day

Study Outcome:

- No Dose Limiting Toxicity have been observed till 52 mg once a day dose
- Absorption of SUN-09 was rapid with dose related linearity of baclofen release
- PK profile similar to baclofen IR tablets

SUN-09 Future Development Plan



India

- Phase I clinical study using slow release SUN-09 tablets by Q3 FY12
-

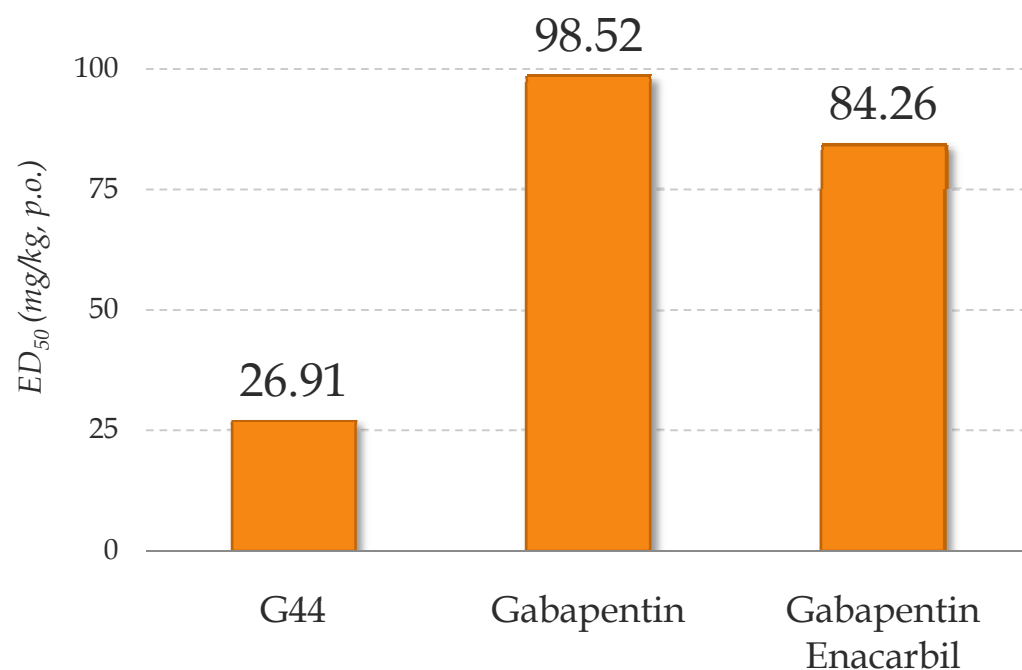
SUN-44 Superior to Gabapentin



- In animal model of epilepsy, SUN-44 shows better efficacy compared to gabapentin
- SUN-44 reduces the latency and incidence of tonic extensor and increases the protection from mortality

Treatment	Dose (mg/kg, p.o.) (Mice)	% Incidence of Tonic Extensor	% Protection from Mortality
SUN-44	35	37.5	40
	70	0.0	100
Gabapentin	35	75	0
	70	37.5	40

SUN-44 Activity in Neuropathic Pain Model



- Gabapentin is very commonly used in the treatment of neuropathic pain
- Compared to gabapentin or gabapentin enacarbil, SUN-44 shows better reduction of neuropathic pain in the rat model

SUN-44 Future Development Plan



- IND approved in INDIA
- Phase I to commence FY12

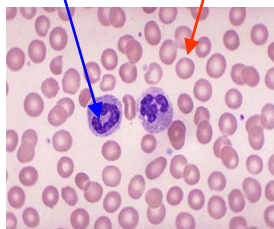


SUN-K706 Targeting resistance in Leukemia



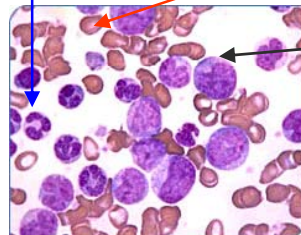
- Chronic myelogenous leukemia (CML) is a hematological malignancy (blood cancer) caused by a specific chromosomal aberration (genetic mutation) viz. t(9:22) in leukemic cells
- This chromosomal aberration t(9:22), results in Philadelphia chromosome (Ph) that encodes a chimeric protein Bcr-Abl (210 KDa) with constitutive tyrosine kinase activity
- This Bcr-Abl tyrosine kinase is responsible for uncontrolled proliferation and survival of the myeloid cells (WBC) in leukemia
- Inhibition of this aberrant Bcr-Abl kinase by a drug molecule can stop the uncontrolled proliferation of WBC
- Several Tyrosine kinase inhibitors are already in the market for the treatment of CML

White Cell Red Cell



Normal human blood

White Cell Red Cell



Blasts

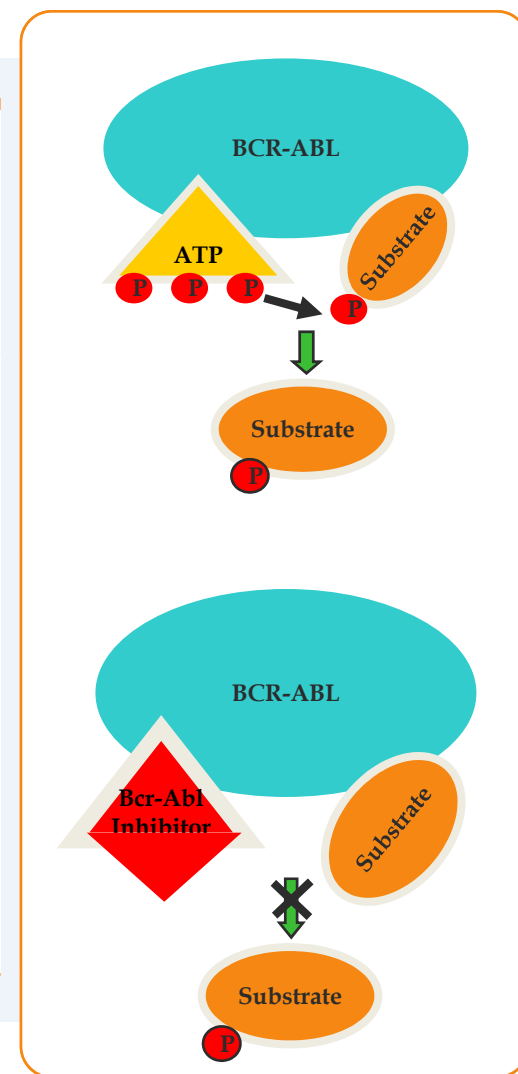
Blood with leukemia



SUN-K706 Targeting resistance in Leukemia



- The currently available drugs that are inhibitors of the Bcr-Abl tyrosine kinase are Imatinib (Gleevec®), Nilotinib (Tasigna®) and Dasatinib (Sprycel®).
- While these drugs are quite effective in the treatment of CML, they have certain shortcomings, viz.:
- Development of resistance predominately due to mutations in the Abl domain of the Bcr-Abl kinase
- None of these drugs are active on the most resistant mutation viz. T315I mutation, for which currently there is no approved therapy
- These drugs are known to produce side effects such as
 - QT prolongation (cardiac)
 - Myelosuppression
 - Hepatotoxicity,
 - Bleeding, electrolyte abnormalities & fluid retention



SUN-K706 A Novel Tyrosine kinase inhibitor from SPARC targeting T315I resistance



In-vitro kinase inhibition profile of SUN-K706

Kinase	IC ₅₀ (nM)			
	K 706	Ponatinib*	Dasatinib	Nilotinib
Abl	1.0	8.6	0.6	15.0
Abl-T315I	8.0	40.0	>10000	>5000
Abl-Q252H	0.8	0.44	ND	ND
Abl-Y253F	1.0	0.3	0.4	28.0
Abl-M351T	0.8	0.3	0.1	12.0
Abl-H396P	0.5	0.34	0.5	9.0
Lck	17.0	ND	ND	ND
Lyn	18.0	0.24	2.8	>5000

* Chem. Biol. Drug Des. (2011) 77 (1) 1-11

- SUN-K706 significantly inhibits Abl kinase as well as all the important mutants of Abl
- **Most importantly it inhibits the key resistant mutant viz. the T315I inhibition**
- SUN-K0706 shows more potent inhibition of T315I than Ponatinib, the T315I inhibitor under clinical development by Ariad

SUN-K706 Most potent and selective inhibitor of CML cells



- SUN-K706 shows highest potency for Abl expressing cells (K562 cells). To our knowledge, SUN-K706 is by far the most potent Abl-kinase inhibitor known to date in cell proliferation assay
- SUN-K706 is not active in Abl negative cells, indicating that it is specifically toxic to CML cells and not toxic to other cells

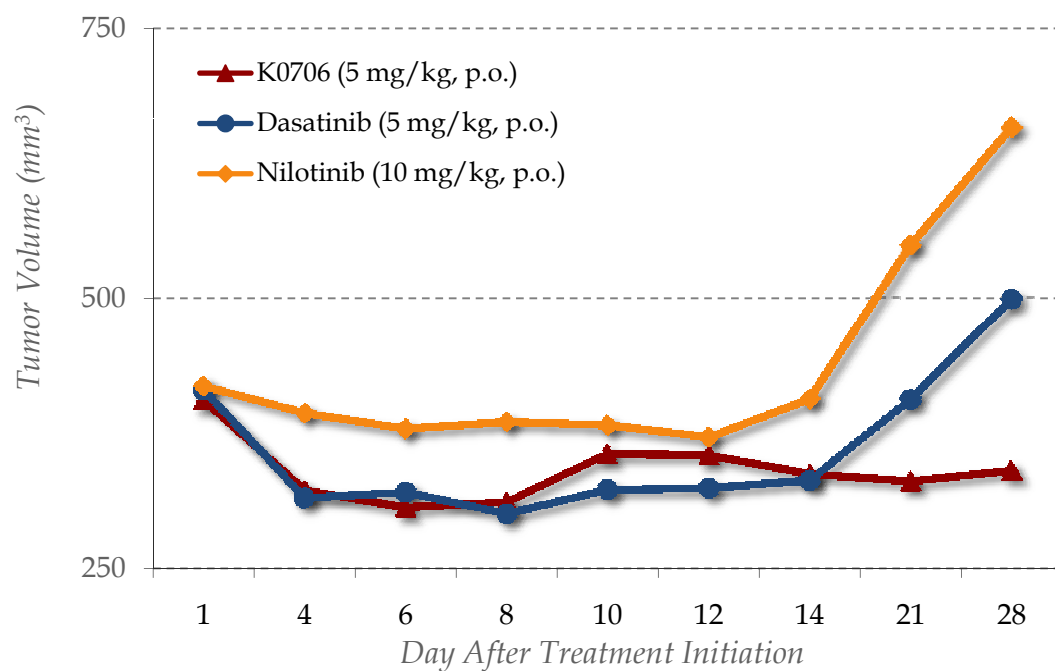
In-vitro c-Abl kinase inhibition profile (cellular assay)

Cell line	IC ₅₀ (nM)			
	SUN-K706	Ponatinib*	Dasatinib	Nilotinib
K562	0.0075	3.9	0.14	11.0
U937	Not active	Not active	Not active	Not active

* Chem. Biol. Drug Des. (2011) 77 (1) 1-11

SUN-K706 In vivo efficacy in K562 tumor xenograft model

Antitumor Activity of K0706 in K562 tumor xenograft Model



- K706 causes better inhibition of tumor in mice tumor xenograft model compared to other drugs

SUN-K706 Future Development Plan



-
- Toxicity studies required for IND Q4FY12
 - IND filing Q1FY13
-



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