

### Update on R&D pipeline

10<sup>th</sup> September 2020



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### **Presentation agenda**





Strategy overview

Anil Raghavan, CEO



#### **Clinical NCE assets**

SiuLong Yao, Head Clinical Development & Operations



#### **Clinical NDDS assets**

Nitin Dharmadhikari, Head Drug Delivery System



# Licensing update & competitive landscape

Michael Choi, Head Business Development



### Academic collaborations

Rajesh Ranganathan, Head Partnerships and Portfolio Strategy



#### Pre-clinical NCE assets

Vikram Ramanathan, Head Translational Development







Chetan Rajpara, CFO





### Strategy overview

#### Anil Raghavan



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### **On the hard road, together** Let's take a moment to reflect



#### **Broad Portfolio**

- 2 USFDA approved drugs (Xelpros, Elepsia)
- 3 NCEs in clinical development across 7 different indications
- 10+ NCE/NBE programs in the R&D pipeline covering 4 TAs



#### **Global Organization**

- 3 offices in two continents
- 160 labs; 120,000 sq. ft.
- 350+ scientists
- Internal R&D infrastructure
- Highly experienced senior management team

#### **Upcoming Catalysts**

- Approvals from late stage pipeline
- Vodobatinib CML registration trial readout
- Phase 2 readout of PROSEEK and SCD-044 studies
- Upcoming IND filings

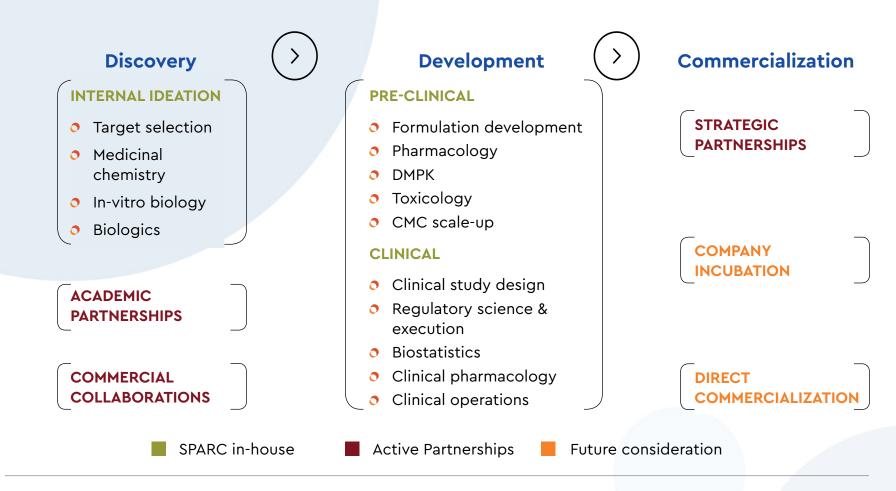


2007 2008 2009 2010	2011 2012 2013 2014	2015 2016 2017 2018	2019 2020
SPARC Spin Off –	Right's Issue 1 –	Right's Issue 2 –	Pref. Issue –
\$70m	\$34.3m	\$37.2m	\$74.2m

SPARC has evolved into a promising innovative products company with several high value opportunities at high capital efficiency

### Our operating model is fully built-up





SPARC's proposition – translational development engine with access to science, low cost of failure and flexible commercialization options

# First wave of innovation is nearing completion



Novel delivery systems through the 505(b)(2) pathway

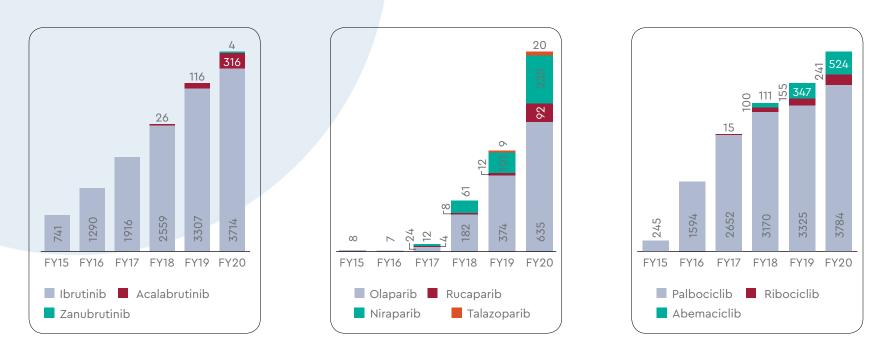
Technology Licensing	Liposomal Drug Delivery Technology	Oral Delivery Technologies	Liposomal Drug Delivery Technology – Sun Pharma (USA) Oral Delivery Technologies – Sun Pharma (India)
Approved Products	Xelpros BAK free	Elepsia XR	Xelpros – Sun Pharma (USA, India ), CMS (China) Elepsia – CMS (China)
Under Review	Taclantis		USA – Under USFDA review China – CMS India – Sun Pharma
Late Stage Clinical Trials	PDP-716	SDN-037	Pivotal studies of both programs expected to be read out in FY21 USA – Under discussions, China – CMS

Although these programs offered important validation for the operating model, incremental innovation opportunity spectrum has moderated considerably

## Market shifts towards real-value



#### Early movers garner a lion's share of value



- Significant market share advantages for early entrants across therapeutic areas and geographies
- Payors are reluctant to pay premiums when the demonstrated benefits are not attractive clinically, or limited in it's scope
- Difficult clinical development pathways for follow-on compounds High burden of evidence for the best-in-class strategy and
- Elevated risk profile of early stage innovation

Source | IQVIA MAT July 2019

## SPARC responded with a hard pivot



### To a mix of new biology and complex modalities

NDDS

Deprioritized

 Leveraging formulation capabilities, NDDS products were developed to offer incremental patient value:

Elepsia, Xelpros, PDP-716, SDN-037, Taclantis Best-in-Class for Validated Targets

Partnering

 Building on chemistry expertise, SPARC focused on optimizing NCEs for validated targets as it's first pivot into the NCE space:

c-Abl, S1PR1, ER Degrader

#### New Targets

Investing

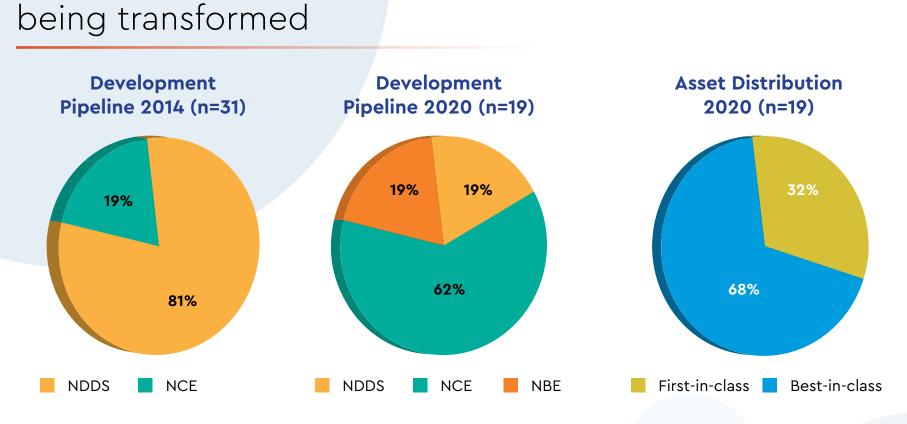
• SPARC is now focused on new targets and modalities:

Cancer metabolism, Precision oncology, Neurodegeneration, Bi-specific antibodies, Conjugated hybrids

# Setting up several near term catalysts sparc<sup>o</sup>

	Neuro- degenerative	$\langle \rangle$	<b>Vodobatinib PD</b> – Clinical proof-of-concept (PoC) by 2022 in Parkinson's Disease, first-in-class disease modifying opportunity.		
Diseases			Pilot study in Lewy Body Dementia in collaboration with Georgetown University is expected to be read out in 2022.		
	Cancer Resistance	$\langle \rangle$	<b>Vodobatinib CML</b> – Clinical PoC established, Pivotal study is recruiting. USFDA submission expected in FY23.	<b>SCO-120 HR+/ HER2- mBC –</b> Oral Selective Estrogen Receptor Degrader, IND completed in January	
			Orphan drug designation granted by USFDA.	2020. In early stage dose escalation.	
	Auto-immune Disorders	$\bigcirc$	<b>SCD-044</b> – SPARC bought Bioprojet's rights to SCD-044 in 2019. Phase 1 completed, leading to clinical validation of the hypothesis, Phase 2 studies in Psoriasis & Atopic Dermatitis are expected to start recruiting shortly. SCD-044 global license granted to Sun Pharma.		
	<b>Others</b>		<b>Phenobarbital for Neonatal Seizures –</b> Medium term NDA submission, Orph drug designation granted by USFDA.		
			Multiple near term IND opportunities.		

High value, multi-indication clinical portfolio nearing important milestones, setting up multiple cash events



**Building long term value** 

SPARC's early stage portfolio is

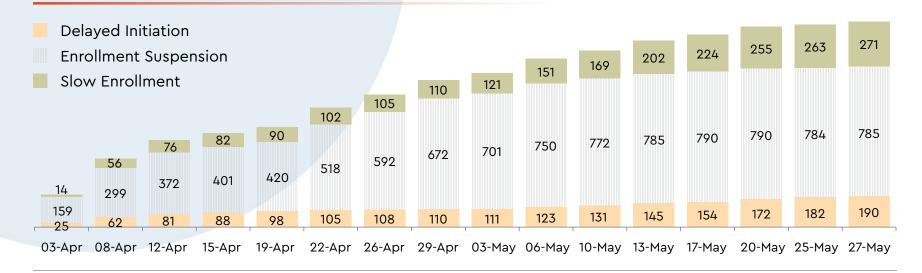


- Aggressive pruning to weed-out potentially unviable programs 0
- Increasing proportion of programs focusing on novel biology 0
- Investments in new modalities/complex platforms 0
- External innovation as a key tenet of strategy 0
- Discipline to stay within the identified therapeutic focus 0

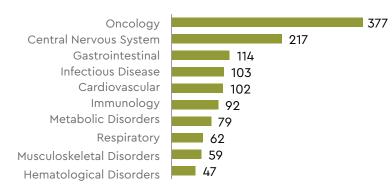
# Taking stock of COVID-19



### Eco-system is impacted significantly



#### **Disrupted Clinical Trials by Therapy Area**



#### Key tenets of SPARC's risk mitigation plan

- Sustain normal operations through a mix of on-site lab operations and robust WFH (70% office/lab based)
- Protect patients interest and data already in trials
- Build-up trial infrastructure aggressively so that we can pivot on normalization
- Geographic/regional expansion to de-risk accrual timelines and
- Aggressive virtualization

Source | Global Data, 27 May 2020

### **Expectations for next year**



### What to look for in the next 12 months

- Conclude and partner for commercialization first wave programs (PDP-716, SDN-037 & Taclantis)
- Aggressive accrual for on-going clinical studies
- Continued pre-clinical prioritization and build-up for additional INDs in FY22
- Build on the early success of strategic academic partnerships to add new programs to the portfolio
- Raise additional resources through a preferential issue to realize near term catalysts and graduate key pre-clinical programs to clinic





### **Clinical NCE assets**

SiuLong Yao



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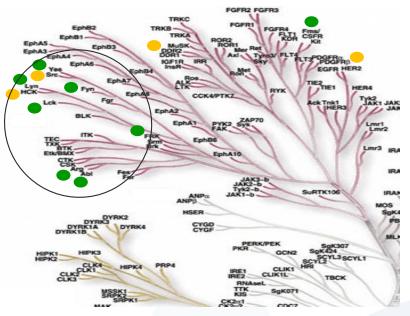
# Vodobatinib



# Highly selective ABL inhibitor with multiple applications

- Potent and highly selective BCR ABL TKI
- Good oral bioavailability in humans, crosses blood brain barrier
- Human PK established, moderate food effect
- No QT prolongation or other CV liability observed in Phase 1 studies

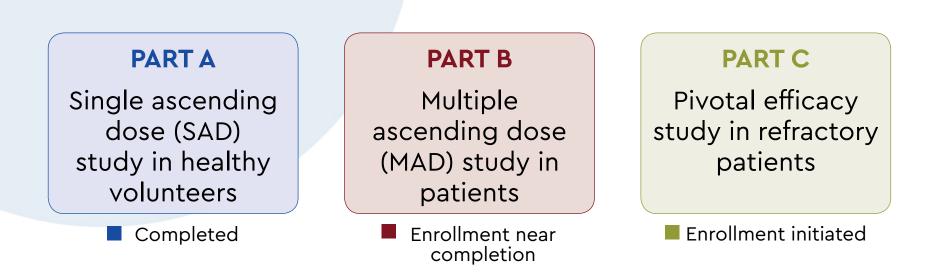
#### Kinome analysis revealing very limited off-target activity



TKI = tyrosine kinase inhibitor, CV = cardiovascular, PK = Pharmacokinetics



### Current clinical plan



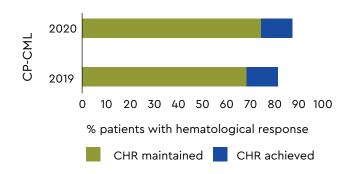




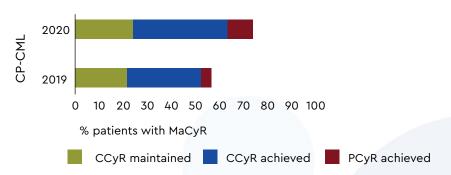
### Promising initial data persisting

- Phase 1 dose escalation study completed
- Anti-leukemic activity in CP-CML patients
  - 87% hematological response rate
  - 68% major cytogenetic response rate
  - 58% major cytogenetic response in patients failing ≥3 TKI therapies including ponatinib

#### **Hematological Response**



#### **Cytogenetic Response**



CML = chronic myelogenous Leukemia; CCyR = complete cytogenetic response; PCyR= partial cytogenetic response; TKI = tyrosine kinase inhibitor; MaCyR = major cytogenetic response; CP = chronic phase; CHR - Complete Hematological Response: 2019 data cutoff 17 August, n = 25. 2020 data cutoff 31 August. n = 31.



### Generally safe and well tolerated

- 2 serious adverse events related to Vodobatinib
- Mild to moderate GI disturbances and complaints of the musculo-skeletal system were most commonly observed
- No drug associated cardiac events reported

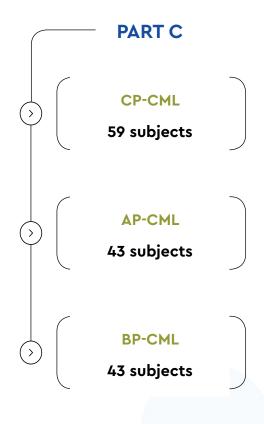


GI = Gastrointestinal



### Pivotal study plan

- Single arm study (Part C)
- Ph+ CML patients refractory and/or intolerant to ≥3 TKIs including ponatinib
- FPI Q4 FY20
- Participating countries
  - USA, Belgium, France, Italy, Spain, Romania, Hungary, Singapore, UK, Korea
- Topline results Q3 FY22



CML = chronic myelogenous leukemia, CP = chronic phase, AP = accelerated phase, BP = blast phase, Ph = Philadelphia chromosome, TKI = tyrosine kinase inhibitor, FPI = First patient in

# Vodobatinib for PD (SCC-138)



### First-in-class neuroprotective agent

#### **Pre-clinical**

- Enhances autophagic flux
- Decreases α-synuclein inclusions
- Efficacy against neurodegeneration demonstrated in multiple animal models

#### Clinical

- Human PK established
- Food effect study completed
- Single and multiple ascending dose studies completed
- Generally safe and well-tolerated
- Phase 2b PoC study ongoing (PROSEEK)

### Activation of tyrosine kinase c-Abl contributes to $\alpha$ -synuclein-induced neurodegeneration

Saurav Brahmacharl,<sup>12,3</sup> Preston Ge,<sup>12,3</sup> Su Hyun Lee,<sup>12</sup> Donghoon Kim,<sup>12,4</sup> Senthilkumar S. Karuppagounder,<sup>12,3</sup> Manoj Kumar,<sup>12,3</sup> Xiaobo Mao,<sup>12,3</sup> Yunjong Lee,<sup>12,3</sup> Olga Pletnikova,<sup>5</sup> Juan C. Troncoso,<sup>25</sup> Valina L. Dawson,<sup>12,3,6,7</sup> Ted M. Dawson,<sup>12,3,3,4</sup> and Han Seok Ko<sup>12,4</sup>

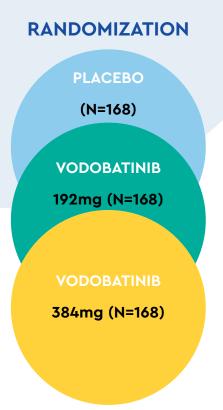
c-Abl phosphorylates  $\alpha$ -synuclein and regulates its degradation: implication for  $\alpha$ -synuclein clearance and contribution to the pathogenesis of Parkinson's disease

Anne-Laure Mahul-Mellier<sup>1</sup>, Bruno Fauvet<sup>1</sup>, Amanda Gysbers<sup>3</sup>, Igor Dikiy<sup>4</sup>, Abid Oueslati<sup>1</sup>, Sandrine Georgeon<sup>2</sup>, Allan J. Lamontanara<sup>2</sup>, Alejandro Bisquertt<sup>5</sup>, David Eliezer<sup>4</sup>, Eliezer Masliah<sup>5</sup>, Glenda Halliday<sup>3</sup>, Oliver Hantschel<sup>2</sup> and Hilal A. Lashuel<sup>1,\*</sup>





0



- Early stage subjects not on dopaminergic medication other than MAO-B inhibitors
- 88 sites in USA, Spain, Poland, Hungary, Slovakia, India
- Regulatory approval in all countries
- FPI
  - February, 2019 for USA
  - November, 2019 for EU
  - September, 2020 planned for India
- Expect to complete enrollment Q4 FY22







#### Advertising campaign

- Patient website
- Plan to extend pilot campaign to all sites
  - Search Engine Optimization
  - Traditional media (News papers, Radio, etc.)

#### **Complimentary approaches**

- Additional regions
  - Australia
  - UK and other European sites
- Increase protocol user-friendliness

# **Seeking Progress**

to Potentially Help Slow Disease Progression

#### A Clinical Research Study for People with Early-Stage Parkinson's

If you are over 50 and have been diagnosed with Parkinson's disease (PD) within the last 3 years, the PROSEEK Study may be an option. It is a clinical research study evaluating a once-daily, oral investigational drug designed to potentially help slow disease progression in people with early-stage PD.

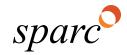
> Take our brief online questionnaire to see if you may be eligible to participate.

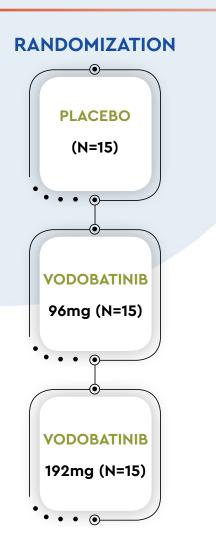
AM I ELIGIBLE?

Please note. the investigational drug is not approved by Health Authorities including The US Food and Drug Administration (FDA) for the treatment of Parkinson's disease or any other disease

PROSEEK = Phase 2 study of Abl tyrosine kinase inhibition with K0706 (SCC-138)

## Vodobatinib in Lewy Body Dementia





- Ongoing investigator-initiated trial in collaboration with Georgetown University
- 12 week study with primary outcome measure of safety
- Secondary outcome of CSF and bloodbased biomarkers
- Expected study completion by Q4 FY22



CSF = Cerebrospinal fluid





# Selective S1PR1 modulator for autoimmune diseases

- Novel, orally bioavailable, potent and selective S1PR1 agonist
- Fingolimod (first-in-class S1P receptor agonist) approved for multiple sclerosis is associated with serious bradycardia
- SCD-044 appears to have good balance between potentially efficacious doses & side effects
- SCD-044 under evaluation for psoriasis and atopic dermatitis



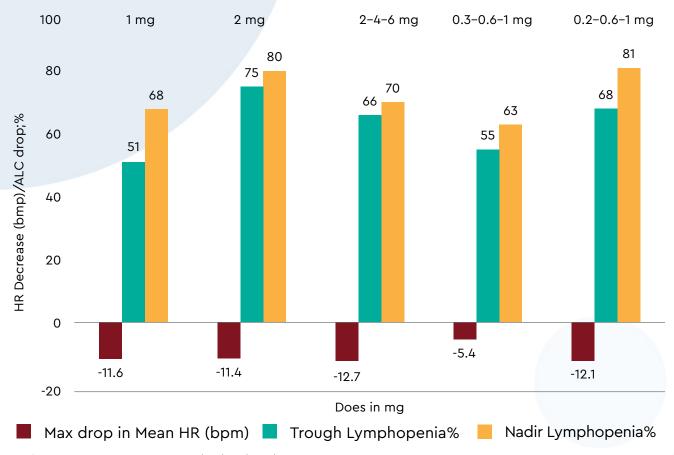
S1PR1 = Sphingosine 1-phosphate receptor 1

### SCD-044 therapeutic index



Efficacy and safety established in Phase 1 study

#### Heart Rate & Lymphocyte Counts following Multiple Doses



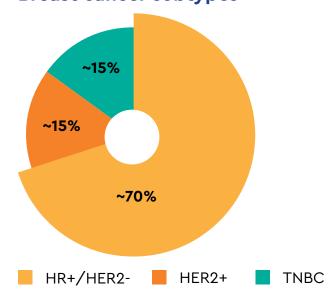
bmp = beats per minute, HR = Heart rate, ALC = Absolute lymphocyte count

### SCO-120

### Breast cancer SERD

- Hormonal therapy is SoC for ~70% of HR+/HER2- metastatic breast cancer patients<sup>1</sup>
- ERα mutations develop in 20–50% of patients with metastatic disease
- IM fulvestrant is the only approved SERD but it is poorly active against mutations
- SCO-120 is a novel orally-active selective ERα SERD for the treatment of HR+/HER2- breast cancer

#### Breast cancer subtypes<sup>2</sup>



ERα = estrogen receptor α, TNBC = triple negative breast cancer, SERD = selective estrogen receptor degrader, HER2 = human epidermal growth factor

receptor 2, HR = hormone receptor, SOC = standard of care, IM = intramuscular

<sup>1</sup> CancerMPact® Treatment Architecture U.S., Breast Cancer.. <sup>2</sup> JAMA. 2019 Jan 22;321(3):316. doi: 10.1001/jama.2018.20751.PMID: 30667503



SCO-120 Oral SERD



- US IND filed January, 2020
- SAD in healthy volunteers ongoing
- 50 mg & 100 mg cohort dosing completed
- Generally safe and well tolerated, no significant AEs
- Future studies
  - MAD in healthy volunteers, FPI Q4 FY21
  - Phase 2 PoC in patients, FPI Q2 FY23

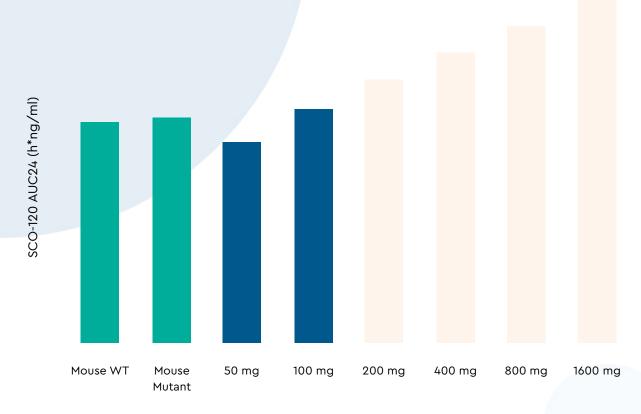


SERD = selective estrogen receptor degrader, SAD = single ascending dose, MAD = multiple ascending dose, AE = adverse event, FPI = First patient in, PoC = Proof of Concept





### Preliminary pharmacokinetics



📕 Efficacious Concentrations in Mice 📕 Concentrations in Humans 📕 Projected Concentrations in Humans

• Current exposures near those required for efficacy in preclinical studies

WT = wild type



## **Clinical NDDS assets**

Nitin Dharmadhikari



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# **Ophthalmology programs**



### Reaching the finish line

#### SDN-037

- Management of inflammation and pain post cataract surgery
- Phase 3 study completed
- Last patient out March, 2020
- Topline data expected September, 2020

#### PDP-716

- Treatment of glaucoma
- Futility analysis conducted October, 2019
  - 245 subjects
  - Exceeded statistical criteria to continue
- Ourrent status
  - Enrolment complete (N=681)
  - Last patient out November, 2020
  - Topline data expected by Q4 FY21



# Phenobarbital injection

# Preservative-free injection for neonatal seizure

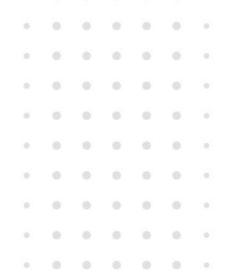
- Current standard of care for treatment of neonatal seizure
- Phenobarbital is an "unapproved drug" in USA; Approved before 1938 which did not require proof for safety and / or efficacy
- Existing marketed product is not approved by US FDA and contains benzyl alcohol as a preservative.
- Benzyl alcohol has been associated with "Gasping Syndrome" in neonates and low-birth weight infants
- IND approved in Q2 FY21; Human PK study ongoing







sparc





# Licensing update & competitive landscape

#### Michael Choi



### **Commercial partnerships**





#### **NOVEMBER 2019**

License deal with a subsidiary of China Medical System Holdings Limited (CMS) to develop and commercialize multiple products in Mainland China, Hong Kong, Macao and Taiwan

# bioprojet

#### **DECEMBER 2019**

License Agreement with Bioprojet to acquire exclusive rights for Investigational Medicinal Product, SCD-044



#### MAY 2020

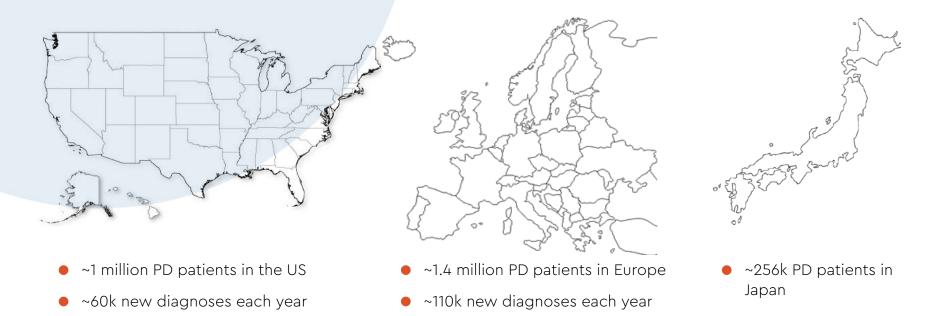
Worldwide license agreement with Sun Pharma for SCD-044, a potential treatment for atopic dermatitis, psoriasis and other auto-immune disorders



# **Epidemiology of Parkinson's Disease**



PD affects ~7M people globally; expected to grow above 14M by 2040\*

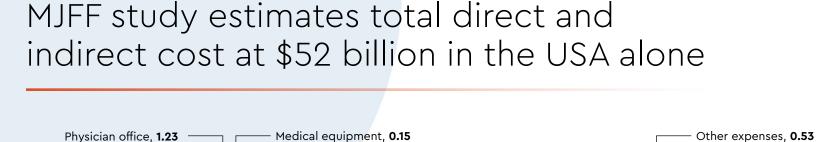


- Chronic and progressive nature of disease is a primary factor that is continuously adding to the current number of PD patients.
- Aging population and environmental factors further add to the global burden of the disease

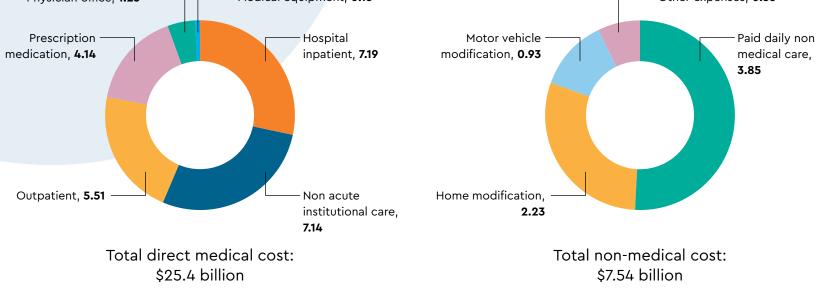
GBD 2016 Parkinson's Disease Collaborators. Lancet Neurol. 2018 Nov; 17(11):939–953. # Parkinson's Foundation – https://www.parkinson.org/ Understanding-Parkinsons/Statistics ^R. Balestrino et.al. Parkinson Disease, European Journal of Neurology, Oct 2019



spare



## Economic burden of PD



- Indirect cost consists of non-medical cost, missed work, lost wages, early forced retirement and family caregiver time
- Federal government spends nearly \$25 billion/year on patient care. Of that, \$2 billion is paid through social security, with the balance handled by Medicare

MJFF = Michael J. Fox Foundation

# Vodobatinib is a game changer in PD



As the 1<sup>st</sup> disease modifying therapy (DMT), Vodobatinib has the potential to address the enormous unmet need in PD

High

-evel of unmet needs

Lov

- ~70% of the PD patients to eligible to receive a DMT at diagnosis to delay the need of symptomatic treatment
- Physicians expect Vodobatinib to be used across all PD patients, including familial PD
- Payers perceive new MoA of Vodobatinib very promising and expect to reimburse accordingly
- Chronic therapy for a large patient population will not require exorbitant pricing for success
- Vodobatinib is the in the lead position vs. other potential DMTs in the pipeline and also offers a patient friendly oral formulation (vs. inj)
- Strong IP fencing with estimated expiry by 2040

Key unmet needs\* Lack of disease-modifying therapies to delay or slow down disease progression Symptomatic treatment efficacy wears off over time, therefore lack of effective treatment options as patient progresses Patient frustration on poly-

medication and titration as it may be hard to remember different dosage and dosing frequency

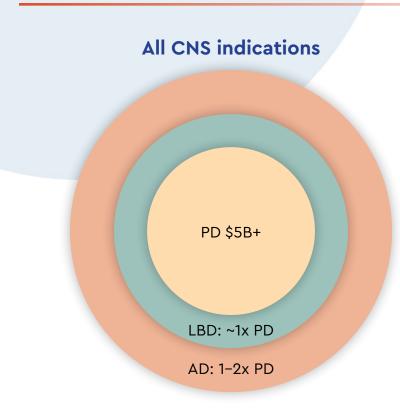
Lack of confirmatory diagnostic test, therefore difficult to diagnose early PD patients

\*Adapted from third party primary market research in the USA

### **Vodobatinib commercial potential**



### With successful development in PD, Vodobatinib has the potential to be SPARC's first blockbuster drug



- PD is the lead indication and current forecast in high single digit (\$B) validated by external third party research
- LBD indication has ~1.5x more patients than PD, but the overlap with PD is high
- AD indication has roughly 4x more patients than PD and the overlap with PD is low

CNS = central nervous system, PD = Parkinson's Disease, LBD = Lewy Body Dementia, AD = Alzheimer's Disease

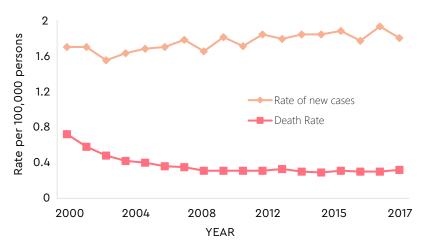
### CML market opportunity



# Long lifespan of patients have turned CML into a chronic relapsing disease

- With the advent of the Tyrosine Kinase Inhibitors (TKIs):
  - The annual mortality rate in CML has decreased by more than 50%
  - The 5 year relative survival has risen to ~70%
- The prevalence of CML is estimated to grow globally primarily attributed to prolonged survival and access to TKIs
- The increase in the CML prevalence has been consistent with the number of TKI sales (\$) reported

New cases and deaths per 100,000 (USA)#



### Estimated Global growth of prevalent cases 2018–2028\*

Region	Growth
North America	28%
Europe	16%
High-income Asia pacific	18%
Africa	29%
Lower-Income Aisa Pacific	30%
Latin America, Caribbean	36%

CML = Chronic Myeloid Leukemia, 'Global Impact of Tyrosine Kinase Inhibitors on Chronic Myeloid Leukemia Epidemiology Over the Next Ten Years (Journal of Global Oncology 2018)

- S. Tadwalkar and M. Hughes

\*SEER database Cancer Stat Facts: Leukemia — Chronic Myeloid Leukemia (CML)

### CML market opportunity



### 2<sup>nd</sup> and 3<sup>rd</sup> line agents have been successful even with generic Imatinib available

- The current TKI global market is approximately worth 6 billion USD
- Despite genericization of Gleevec, branded 2<sup>nd</sup> and 3<sup>rd</sup> gen TKIs retain commercial value due to the refractory nature of CML
- c-Abl TKIs have safety issues related to cardiovascular toxicity
- Vodobatinib was specifically designed to be a safer option for treatment of refractory patients
- We estimate global sales in line with the 3<sup>rd</sup> generation TKIs for the end of line indication with potential upside for 1st line indication

#### TKI Global Sales Data (\$M USD)\*

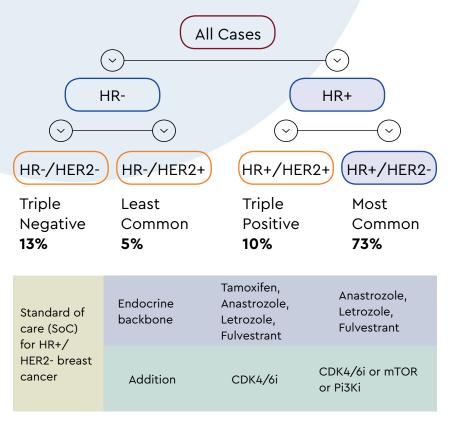


\*Sales as reported by respective companies TKI = Tyrosine Kinase Inhibitor, CML = Chronic Myeloid Leukemia

### SCO-120 market opportunity

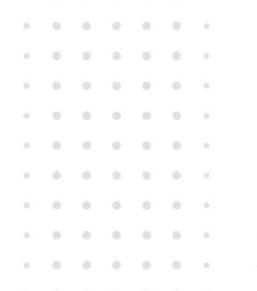


# A superior oral SERD which can address ERα mutations is much needed



- The HR+/ HER2- breast cancer affects over 230k patients per year<sup>#</sup>
- The current market value of the SoC is estimated to be \$5B in 2020\*
- CDK4/6 inhibitors has emerged as the new gold standard but require a endocrine backbone
- Fulvestrant is the only SERD available but is limited by poor bioavailability
- In addition, mutations in ERα cause resistance to current anti-estrogen therapies in 20–50% of patients
- A novel oral SERD like SCO-120 can address a significant unmet need in this large segment of breast cancer

<sup>\*</sup>IQVIA MAT June 2020, <sup>#</sup>Deduced from Kantar CancerMPact2019® US





# Academic collaborations

Rajesh Ranganathan

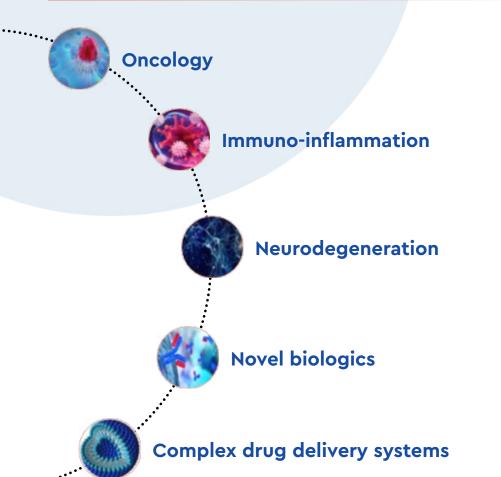


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## Diversify drug portfolio



By augmenting in-house expertise with strategic external partnerships



- Internal Strengths
  - Ideation: Nominate first-in-class drug targets in select therapeutic areas and engage in
- Exploratory programs
  - Augment capabilities to pursue new treatment modalities like novel biologics that may offer significant value proposition versus existing therapies
- Collaborations with external innovators
  - Partnerships with leading global researchers to source promising early-stage innovative science/biology
  - Focus continues to be on novel first-in-class or best-in-class opportunities as well as complex drug deliveryplatforms to address high unmet clinical needs

### **Expanding academic partnerships**



### ...to tap novel biology early on



UNIVERSITY OF MICHIGAN

- Novel drug delivery platform technology for targeted delivery of drugs for cancer and autoimmune disorders
- SPARC is currently conducting in vitro and in vivo studies to establish proof-of-concept
- SPARC has the option to exclusively license the technology on worldwide basis for further development & commercialization of the asset.

- Multi-year partnership to accelerate the discovery & development of new drugs
- SPARC shall provide up to a total of US\$ 10 Mn. in financial support and in-kind industry resources to advance development of promising drug discovery projects
- Focus on early-stage translational therapeutics in the areas of oncology, neurodegeneration and inflammation
- Separate joint research collaboration to leverage natural product compound libraries
- SPARC has the option to exclusively license the intellectual property on worldwide basis for further development & commercialization of the drug compounds



### **Pre-clinical NCE assets**

Vikram Ramanathan

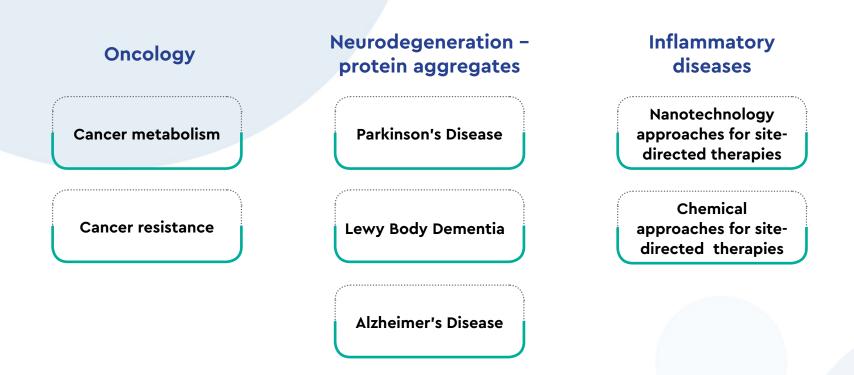


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### **Pre-clinical NCE overview**



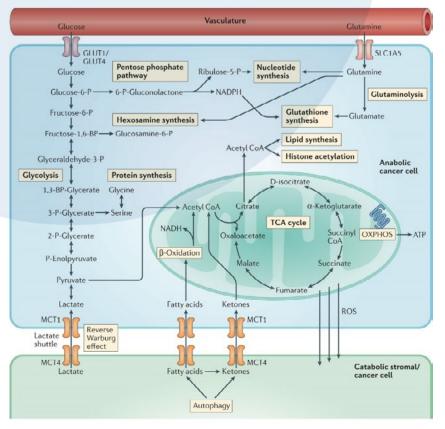
The preclinical NCE programs represent SPARC's transition to a truly innovative biopharma company with novel drugs for novel targets



## **Targeting cancer metabolism**



### Identifying the right molecular targets



Nature Reviews | Clinical Oncology

- Normal cells have a complex network of pathways and cycles to produce the required raw material for their growth (glucose, amino acids and proteins, lipids, nucleotides)
- Cancer cells grow fast by upregulating several metabolic pathways/cycles to meet their energy needs. They convert minor bypass pathways in healthy cells into major pathways
- Individual enzymes in these upregulated pathways in specific cancer-settings can be potential molecular targets. This is an area of active research

# Targeting of driver mutations in cancer



# Dominant mutations that drive cancer cell growth

- Only few of the many mutations that randomly occur in a patient are the drivers of the cellular changes that actually cause cancer growth. Certain random genetic transpositions are another form of drivers of cancer growth, for example BCR-Abl which is in our portfolio for clinical development
- "Driver mutations" confer growth advantage to the cancer cells and cause their proliferation. They outgrow normal cells
- Driver mutations are often predictive of clinical outcome. Allows genetic profiling of patient tumors to enable precision medicine

- First-generation and early therapies lose efficacy over time. The cancers develop resistance by acquiring resistant mutations in these growth drivers. About 90% of cancer deaths are attributed to drugresistance
- Our efforts are focused on targeting drug resistance in such driver mutations



# Targeting of driver mutations in cancer



# Example from our clinical portfolio and area of continued focus

#### SCO-120 (ER-α Degrader)

- Drug for resistant breast cancer where estrogen receptor target which drives cell proliferation (ER+) in tumors has undergone mutation to confer resistance to first-line therapies
- SCO-120 is designed to be active against such resistant mutations
- Our efforts focus on pursuing other oncology targets where similarly the target undergoes a genetic mutational change making them resistant to frontline line therapies

#### Mechanisms that can enable drug resistance in human cancer cells



Lodish et al. Molecular Cell Biology, 8th Edition, WH Freeman, 2016

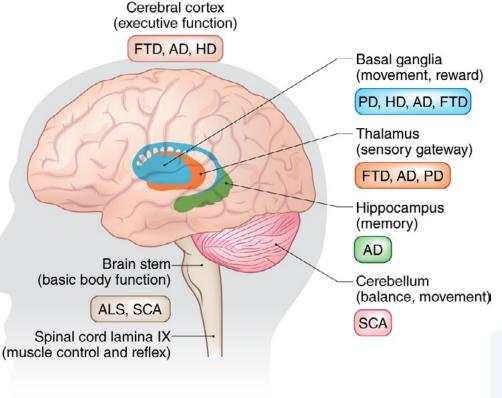
### **Neurodegenerative diseases**



### Different diseases manifest at different locations

- Different neurodegenerative diseases show abnormal brain pathology and atrophy of different regions of the brain, each disease with a specific regional pattern
- Accumulation of abnormal or misfolded protein aggregates in neurons is the common feature causing pathology across range of individual neurodegenerative diseases





AD Alzheimer's disease; FTD: frontotemporal dementia; HD Huntingtons' disease; SCA spinocerebellar ataxia

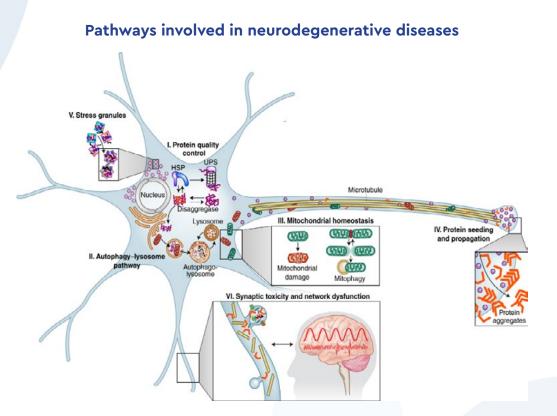
Gan et al. Nature Neurosci (2018)

### **Neurodegenerative diseases**



#### Cellular processes related to misfolded proteins

- Choking of normal pathways to clear misfolded proteins results in neuronal death and progressive brain atrophy which can manifest at some stage as dementia. Examples of such misfolded proteins are α-synuclein in Parkinson's disease and dementia of lewy bodies; amyloid β42 and tau in Alzheimer's disease; and huntingtin in Huntington's disease.
- Our focus is on identifying small molecules to enhance the misfolded protein clearance pathways in neurons, include ubiquitination (protein quality control), autophagy and interactions with heatshock proteins



### Inflammatory diseases



# Using platform technologies to address unmet medical needs

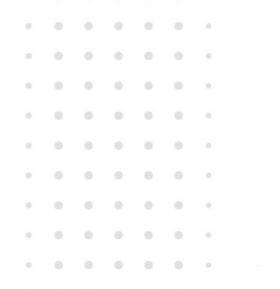
#### Nanotechnology approach for site-directed mAb therapy

- Collaboration with US academic who has world-class expertise in nanotechnology to deliver protein
- Using "molecular velcro" to localise to specific target organs and deliver one or more proteins simultaneously

#### Chemical approaches for site-directed therapies

• Using novel-linker technologies and moieties to design innovative ways to target immune cells in the vicinity of the target organs, and to access the lymphatic system







### **Biologics** Nitin Damle



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### **SPARC** biologics



- Current emphasis on bi-specific or multi-specific biologics
- Ideally suited for various disease indications in oncology and inflammation therapeutic areas
- Ease of combination with the existing standards of care
- Initial exploration emphasizing clinically validated molecular targets in cancer research
- Cancer cells and associated microenvironment
- Tumor-associated angiogenesis
- Immune check point functions

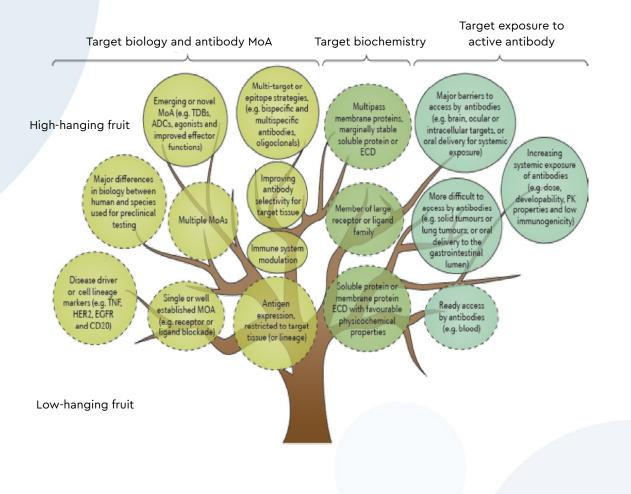


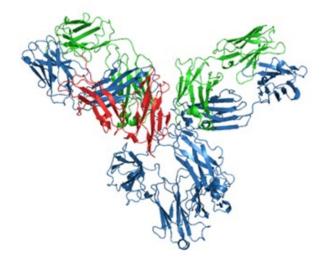
Image adapted from Next generation antibody drugs: pursuit of the 'high-hanging fruit'; Nature Reviews; Drug Discovery volume 17 March 2018; 197

### **SPARC biologics**

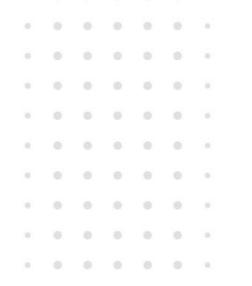


#### Capabilities established in-house

- Molecular biology / Recombinant DNA technology
- Purification and structural & functional characterization of recombinant proteins
- Antibody development and engineering
- Multifunctional immunofusion therapeutic proteins
- Antibody modifications for site-specific conjugation to fluorophores or cytotoxic drugs
- Tumor-targeted cytotoxic antibody-drug conjugates (ADC)









## **Financial update**

Chetan Rajpara



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### **Financial summary**



INR Mn	FY16	FY17	FY18	FY19	FY20	QI FY20	QI FY21
Total Income	1,642	1,947	832	1,964	866	210	1,861
Total Expenses	2,342	3,137	3,292	3,418	3,990	1,152	1,294
Exceptional Item	-	-	490	-	-	-	-
Profit (Loss) after Tax	-700	-1,190	-1,970	-1,454	-3,124	-942	567
USD Mn							
Total Income	25.1	29.0	12.9	28.1	12.2	3.0	24.5
Total Expenses	35.8	46.8	51.1	48.9	56.3	16.6	17.1
Exceptional Item	-	-	7.6	-	-	-	-
Profit (Loss) after Tax	-10.7	-17.7	-30.6	-20.8	-44.1	-13.5	7.5

Q1 FY21 includes receipt of upfront payment of \$20 Mn from SCD-044 licensing deal, which is a non-recurring item.

### Cash & liquidity

- Cash on hand INR 240 Mn (\$3.3 Mn) as on 7-Sep-20
- FY21 Budget ~60% spend for clinical expenses
- Several measures to control costs & to preserve cash
- Evaluating proposals to license certain late stage clinical assets, in order to reduce incremental spend and to create liquidity



- Plans to raise ~\$125-150 Mn by way of fresh equity issuance to meet expenses over next 3 years
- Line of Credit up to INR 2,000 Mn (~\$27.2 Mn) from holding company, of which INR 400 Mn (~\$5.4 Mn) is utilized



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## **Clinical pipeline**



NCE/NDDS	Asset	Indication		Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Registration
	Vodobatinib	Parkinson's Disease							
		Lewy Body Dementia							
	Vodobatinib	Refractory CML							
NCE	SCO-120	Metastatic Breast Cano	cer						
	SCD-044	Atopic Dermatitis							
		Psoriasis							
	Taclantis	Cancer							
	PDP-716	Glaucoma							
NDDS	SDN-037	Cataract Surgery							
	Phenobarbital	Neonatal Seizure							
	SDN-118	Depression							



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