

# Piper Jaffray 31<sup>st</sup> Annual Healthcare Conference

December 2019 AIM/Nasdaq: HCM



# CHI-MED

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Use of Non-GAAP Financial Measures - This presentation includes certain non-GAAP financial measures. Please see the appendix slides titled "Non-GAAP Financial Measures and Reconciliation" for further information relevant to the interpretation of these financial measures and reconciliations of these financial measures to the most comparable GAAP measures.



# Agenda

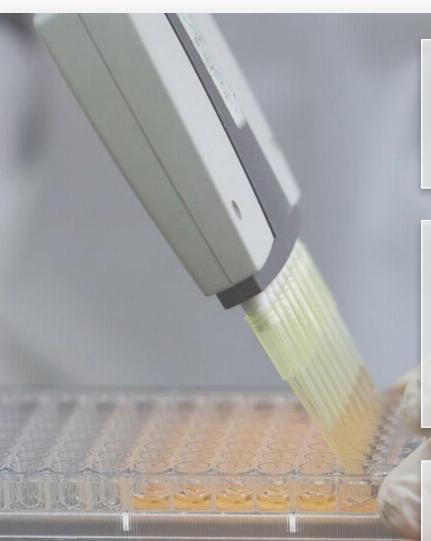
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Company Overview

# Building a global science-focused biopharma company from an established base in China...







## **Global Innovation**

- 5 clinical drug candidates in US/EU development
- Building global clinical development footprint
- World-class ~490-person scientific team

# **China Oncology**



- Major market potential driven by regulatory reforms & high unmet medical need in oncology
- Elunate® (fruquintinib capsules) first ever homegrown cancer drug launched in China<sup>[1]</sup>
- 8 oncology assets in China development



# **Existing China Business**

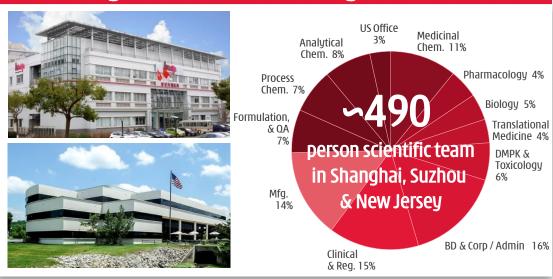
- Cash generative China Commercial Platform
- Platform for future innovative drug launches



# Proven innovation & commercial operations

M	anagement Team	Industry / (yea	
	Mr. CHRISTIAN HOGG, BSC, MBA Chief Executive Officer	P&G Procter & Gamble	30 / <b>19</b>
	Dr. WEIGUO SU, PhD EVP, Chief Scientific Officer	Pfizer	29 / 14
	Mr. JOHNNY CHENG, BEC, CA Chief Financial Officer	Bristol-Myers Squibb Nestle	30/11
	Dr. ZHOU JUN JIE, MD, MBA General Manager, SHPL	SANOFI	28 / 18
	Dr. MAREK KANIA, MD, MBA SVP, Chief Medical Officer, International	Lilly	25/1
	Dr. ZHENPING WU, PhD, MBA SVP, Pharmaceutical Sciences	Roche	25 / 11
	Mr. CHEN HONG, BSC, MBA SVP, Chief Commercial Officer	Bristol-Myers Squibb	21/9
	Dr. MAY WANG, PhD SVP, Bus. Dev. & Strategic Alliances	Lilly	25/ <b>9</b>
	Mr. ANDREW SHIH, Diplie, MBA SVP, HR - Org./Leadership Dev.	MERCK	23 / 1
1	Mr. MARK LEE, BEng, MBA SVP, Corp. Finance & Development	CREDIT SUISSE	20 / 10
4	Mr. ENRICO MAGNANELLI, BA, MBA Head of International Operations	<b>GILEAD</b>	20/1

## Integrated Innovation Organization [1]



## Commercial Team & Joint Ventures [1]

#### Commercial Team (subsidiaries):

**>200** staff covering:

- Drug distribution & marketing operations; &
- New Oncology Business Dept.

50/50 Joint Ventures:

>2,400 Rx medical sales reps.;

**∽900** person OTC sales team; &

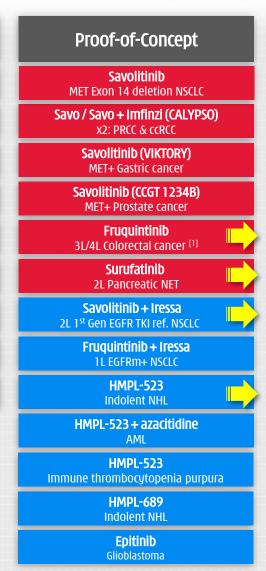
>1,500 staff in two major factories

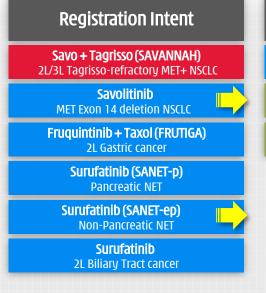
# Portfolio summary

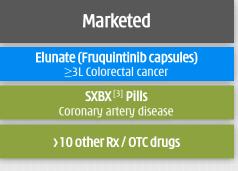
# Multiple waves of innovation - progressing rapidly



#### Dose Finding / Safety Run-In Fruquintinib + Tyvyt (PD-1) Solid Tumors [1] Surufatinib + Tuoyi (PD-1) Solid Tumors [1] HMPL-523 (Syk) Indolent NHL [2] HMPL-689 (PI3Kδ) Indolent NHL Fruquintinib + Tyvyt (PD-1) Solid tumors [1] Fruquintinib + genolimzumab (PD-1) Solid tumors Surufatinib + Tuoyi (PD-1) Solid tumors Surufatinib + Tyvyt (PD-1) Solid tumors HMPL-453 (FGFR1/2/3) Solid tumors













**Recent Operating Highlights** 

# **Recent Operating Highlights**



### **Surufatinib**



- Positive China Phase III and NDA accepted non-pancreatic NET un-blinded a year ahead of schedule;
- Initiated Phase IIb/III biliary tract cancer; & Phase I for PD-1 combos.

### Elunate® (fruquintinib capsules)

- Early progress on Elunate® 3L colorectal cancer in China;
- Cleared Phase III interim analysis 2L gastric cancer (FRUTIGA);
- Initiated Phase I for PD-1 combos.



#### Savolitinib





**Emerging signal for savolitinib/Imfinzi®** (PD-L1) combo – renal cell carcinoma.

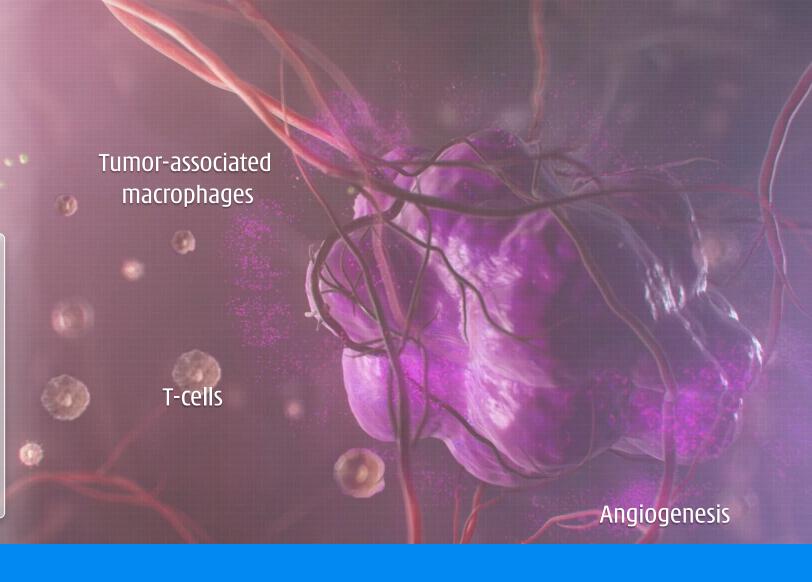




#### Mechanism of Action

Anti-angiogenesis: cut off blood flow to tumor (VEGFR/FGFR).

Immunotherapy: inhibit expression of tumor-associated macrophages which cloak cancer cells from T-cell attack (CSF-1R).





Surufatinib: angio-immuno kinase inhibitor

## Surufatinib

# Overview of NET - ~170,000 patients in the U.S. [1][2][3]



## What are neuroendocrine tumors ("NET")?

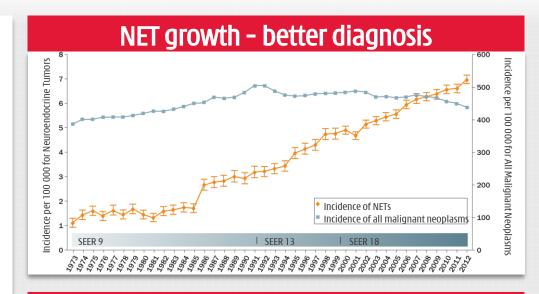
- ➤ ~2% of all malignancies.
- Tumor begins in the specialized cells of the body's neuroendocrine system. Cells have traits of both hormone-producing endocrine cells & nerve cells.
- Found throughout the **body's organs**. Most NETs take years to develop but some can grow fast.

## S Hormone-related symptoms [1]

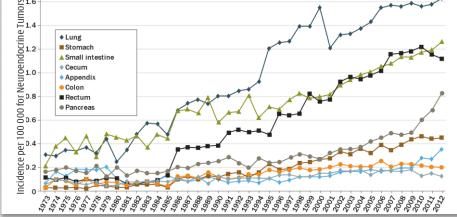
 Functional NETs (~8-35% of patients) release hormones / peptides causing symptoms like diarrhea & flushing; Non-functional NETs have no symptoms.

## S Differentiation & biomarkers for grading:

- Well differentiated: look like healthy cells grow slowly; Poorly differentiated: look less like healthy cells - grow quickly;
- Mitotic count Mitosis is process by which tumor cells grow & divide; Ki-67 index - Ki-67 a protein that increases as cells divide.



# NET epidemiology - highly fragmented



# High-level NET landscape

## Long-term disease - rapid deterioration in later stages [1][2][3]



## Grade 1 (G1) NET

Localized / Regional

~8-35% NET patients Functional NET Hormone related
symptoms:

94% flushing 78% diarrhea 53% heart plaque 51% cramping

Symptoms allow early diagnosis

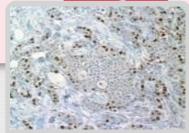
Somatostatin Analogue
Treatment - modulate/
control symptoms
related to hormone
overproduction & tumor
arowth:

Octreotide: \$1.6b revenue (2018) Lanreotide: \$1.0b revenue (2018)

### G1/2 - Advanced NET

Regional / Distant

> mOS: 8.3 yrs.



Moderately Differentiated

Ki-67 Index 3-20; Mitotic Count 2-20

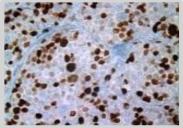
## G3 - NET/NEC

Distant

# No approved treatments

- exploring *I/O* [5]
- + TKI combos





Poorly Differentiated

Ki-67 Index >20; Mitotic Count >20



mos:

16.2 yrs.,

# G1/2 Advanced NET [1] (Ki-67 Index 0-20) Global opportunity in lung/other NETs & China wide-open



Site		est. %	Octreotide	Lanreotide	<sup>177</sup> Lu-Dotatate	Streptozocin	Sunitinib	Everolimus	Surufatinib
Disease status			Treatment naïve	Stable disease	Progressed in past 3 yrs.	Historical	Progressed in past 12 mo.	Progressed in past 6 mo.	Progressed in past 12 mo.
	Stomach	7%		CLARINET [2]	Historical Ph.II SSR over expression			RADIANT-4 <sup>[3]</sup>	SANET-ep
	Small bowel/ Appendix	9%	PROMID	CLARINET [2]	NETTER-1			RADIANT-4 [3]	SANET-ep
GI Tract	Colon & Rectum	31%		CLARINET [2]	Historical Ph.II SSR over expression			RADIANT-4 [3]	SANET-ep
	Pancreas	6%		CLARINET [2]	Historical Ph.II SSR over expression	Historical	PHASE III	RADIANT-3 [4]	SANET-p H1 2020 interim
	Lung	20%						RADIANT-4 [3]	SANET-ep
Other	Other	∽17%							SANET-ep
	Unknown 1°	∽10%						RADIANT-4 [3]	SANET-ep



# SANET-ep vs. RADIANT-4 – cannot compare SANET-ep broader range of tumor origins & later-stage patients



	Asia/China Extra- Pancreatic NET	SANET-ep (n=198) (surufatinib vs placebo)		U.S. Extra- Pancreatic NET	RADIANT-4 (n=302) (everolimus vs placebo)
Gastrointestinal Tract	Tsai et al. 2013 <b>58%</b>	47%	Gastrointestinal Tract	Yao et al. 2008 <b>50%</b>	58%
Rectum Stomach Small Intestine Other GI	30% 7% 19% 3%	27% 10% 8% 3%	Rectum Stomach Small Intestine Other Gr	33% 8% 6% 4%	13% 4% 34% 7%
Lung Other Organ Site Thymus Liver Mediastinum Adrenal Gland Other	22%	12% 28% 7% 6% 6% 2% 8%	Lung Thymus	21%	30%
Unknown Origin		14%	Unknown Origin		12%

#### SANET-ep

Enrolled more pts with poor prognosis.

			Survival Rate
Prir	nary Site	mos	@ 5-yr
R	ectum	2.8y	28%
St	:omach	2.4y	32%
Smal	I Intestine	8.6y	69%

#### **RADIANT-4**

**Did not enrol other extra-pancreatic NET organ sites** incl. but not limited to

Throat Thyroid
Kidney Ovary
Mediastinum Adrenal gland
Retroperitoneal Ampulla vater
Parathyroid gland Carotid body
Liver

**SANET-ep** 

Broader pt. coverage.

#### Pathology grade

**Tumor Origin** 

**ECOG PS 0:1** 

Prior systemic treatment

Multiple organ involvement

`	Grade 1		16%		65%	
	Grade 2		84%		35%	
	PS 0		60% (56% : 67%)		74% (73% : 75%)	
	(treatment : control)		00% (30% . 07%)		14% (15% . 15%)	
	PS 1		40% (44% : 33%)		26% (27% : 26%)	
	(treatment : control)		40% (44% . 55%)		20% (21% . 20%)	
	Any Prior Treatment		67%		61%	
	Chemotherapy		40%		25%	
	Targeted therapy		10%		none	
	Somatostatin Analogues		32%		none 55%	
		66% with multiple organ	involvement			
		76% had liver metastasis	S	79% had liver metastasis		
		47% had lymph nodes m	netastasis	43% had lymph nodes me	etastasis	
		33% had bone metastas	is	19% had bone metastasis		

#### **SANET-ep**

**Later-stage patients**, more heavily pretreated (incl. with targeted therapy) & weaker physical status.

Likely due to later diagnosis in China & availability of everolimus.

22% had lung metastasis

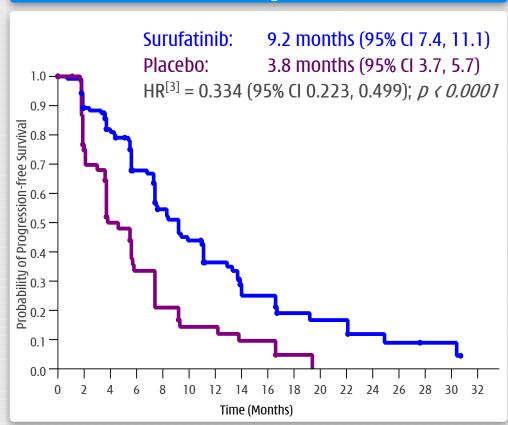
26% had lung metastasis

# G1/2 Advanced extra-pancreatic NET

Investigator assessed median PFS

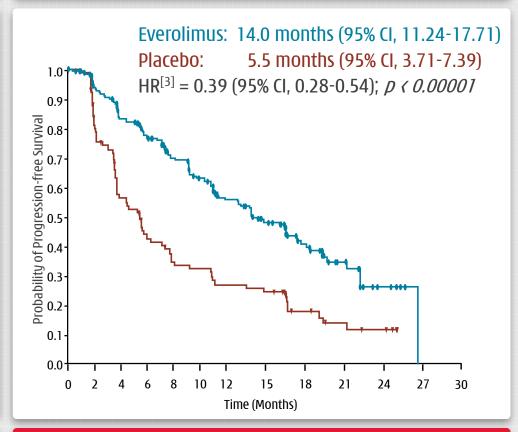


# **SANET-ep** [1] (n=198)



SANET-ep Primary (1°) endpoint was Investigator mPFS
BIIRC [4] mPFS for supportive analysis not 1° or 2°endpoint

# **RADIANT-4** [2] (n=302)



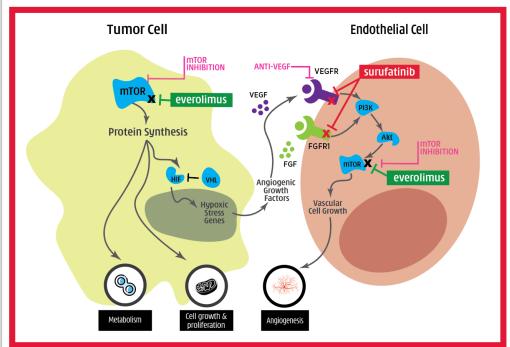
RADIANT-4 Primary (1°) endpoint was BIIRC [4] mPFS
Investigator mPFS not 1° or 2°endpoint

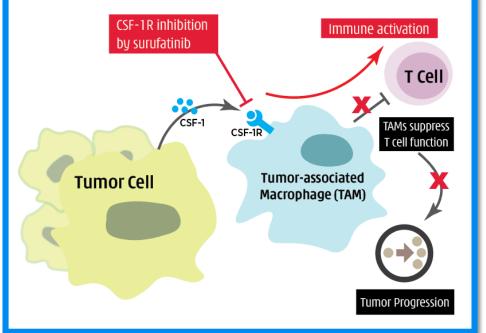


# Very different mechanism of action

**Everolimus** inhibits **mTOR** and blocks the effects caused by the loss of certain genes thereby reducing cell growth, proliferation, and angiogenesis.

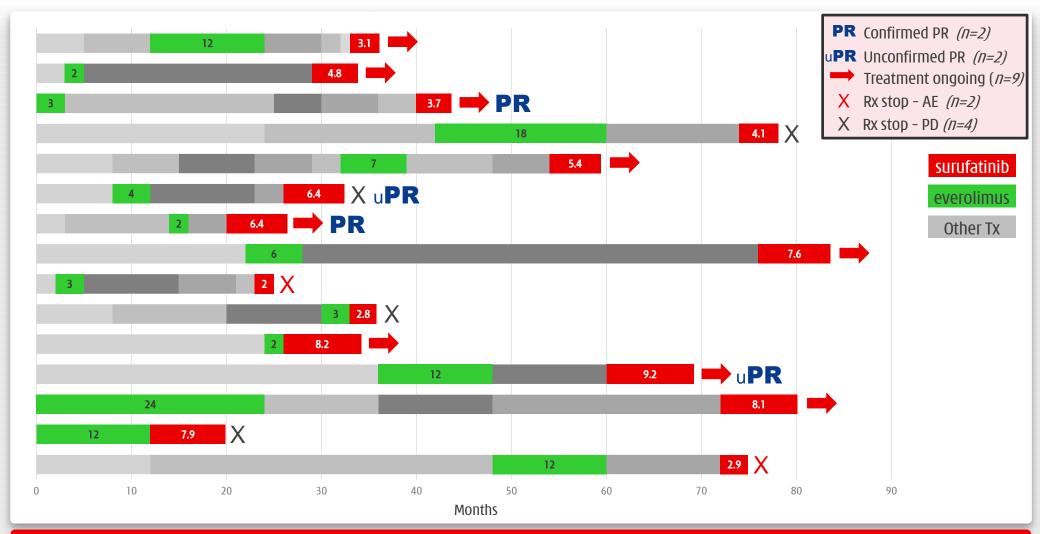
Surufatinib inhibits VEGFR1/2/3 and FGFR1 blocking vascular cell growth and angiogenesis; as well as CSF-1R which limits the production of TAMs which cloak the cancer cell from T-Cell attack.





# Surufatinib efficacy post everolimus failure U.S. Phase Ib (n=15) - pNET duration of treatment





Encouraging preliminary surufatinib efficacy post everolimus failure - different MOA[1]

# Surufatinib - China NET



Non-Pancreatic NET estimated to represent ∽80% of China NET

## **Epidemiology -** *China NET & BTC patient populations*

Potential First suru			Annual Incidence	Estimated Prevalence	mPFS	NRDL Pricing References
monotherapy indication Non-	China NET	100%	67,600	<b>~300,000</b> (Est. China ratio <sup>[1]</sup> )		
Two further surufatinib	Non-Pancreatic NET	<u>~80%</u>	<b>∽54,100</b>	~240,000 (Est. China ratio <sup>[1]</sup> )	<b>9.2 mo.</b> (SANET-ep Ph.III)	Sutent® (~US\$ 2,007/mo. <sup>[2]</sup> ) Afinitor®
registration- intent studies	Pancreatic NET	∽20%	<b>∽13,600</b>	<b>~30,000</b> (Est. China ratio <sup>[1]</sup> )	19.4 mo. (Ph.II) (SANET-p Ph.III TBD)	(∽US\$ 1,320/mo. <sup>[2]</sup> )
underway	Biliary Tract Cancer	100%	64,000		TBD	

NET is major unmet medical need in China – with long treatment duration

# Surufatinib - China NET



# NET potential ~\$100-120m/yr. - under treated/diagnosed

## Competitive landscape - China NET treatments [1]

Brand	Indication/s	Launched		2017	2018	Q1-2019
SUTENT®	Pancr. NET	2007	Sales (US\$ million)	27	24	7
<i>(sunitinib - VEGFR)</i> Pfizer	(& GIST/RCC)		List Price (US\$/month)	4,455	NRDL Oct-18	2,007
AFINITOR®	Pancr. NET	2013	Sales (US\$ million)	9	13	3
<i>(everolimus - mTOR)</i> Novartis	(& 2L RCC)		List Price (US\$/month)	NRDL Jul-17	1,320	1,320
SANDOSTATIN LAR®	GEP-NENS [3]	2003	Sales (US\$ million)	14	15	5
<i>(octreotide - SSA<sup>[2]</sup>)</i> Novartis			List Price (US\$/month)	1,169	NRDL Oct-18	835

Pancreatic-NET market est. ∽\$10-15m/yr. - Non-Pancreatic NET market ∽5-10X

# Surufatinib

# CHI-MED

# Potentially our first un-partnered oncology drug launch

#### Two Phase III neuroendocrine tumor ("NET") registration studies... Data presentation at ESMO 2019 25 China sites. SANET-ep Surufatinib Non-pancreatic NET Met all efficacy endpoints 1° endpoint: median PFS. (Actual N=198) Placebo Well tolerated 2:1 2° endpoints: ORR, DCR, SANET-D DOR, TTR, OS. Surufatinib **SANET-p Interim Analysis Pancreatic NET** R in (H1 2020. (Planned N=195) Placebo

2:1

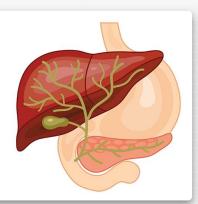
#### ...preparing for our first China launch... 2019 2020 Est. Late 2020 04'19 -Sep 29, '19 - SANET-ep Jun 14. '19 - SANET-ed **Interim Analysis** Presentation at ESMO China launch NDA Accepted Study stopped early, a year • mPFS primary endpoint Tumor control secondary ahead of schedule. **Building out Oncology Full China** Current endpoints • Pre-NDA meeting with CDE. Sales, Mkt., & Med. Aff. Org. ^70 ppl. coverage Placebo control

# Surufatinib Other ongoing trials



#### Phase IIb/III study in 2L BTC

- First patient dosed in March 2019;
- Nearly all planned sites now activated;
- Interim analysis mid-2020, based on first 80 patients;
- Total enrollment ~300 patients.



#### PD-1 collaborations

- With Junshi (Tuoyi®): Dose expansion in multiple tumor types to begin Q4 2019;
- With Innovent (Tyvyt®): Global studies in planning.



Junshi Biosciences

#### Ex-China development

- U.S. Phase Ib/II in P-NET & BTC initiated July 2018 NET enrollment complete;
- FDA End of Phase II meeting targeted for Q4 2019;
- U.S. & Europe Phase III registration study expected to initiate in Q1 2020.





**2b** 

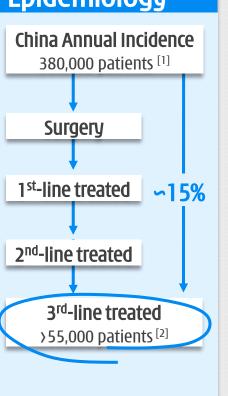
Elunate® (fruquintinib capsules)



# 3<sup>rd</sup>-line colorectal cancer ("CRC")



# **Epidemiology**



## Launch pricing [3]

#### Launch pricing (OOP [4])

~US\$ 3,260 per cycle (RMB 21,966 per cycle) (one cycle 4 weeks)

#### **Patient Access Program**

Cycle 1: ~US\$ 3,260

Cycle 2: ~US\$ 3,260

Cycle 3: Free (PAP<sup>[5]</sup>)

Cycle 4: Free (PAP<sup>[5]</sup>)

Cycle 5: ~US\$ 3,260

Cycle 6 onwards: Free (PAP<sup>[5]</sup>

#### Total OOP cost to patients

~US\$ 9,800 (RMB 65,880)

#### Average Usage

∽Avg 5 mths / 5.5 cycles (to progression; 3.7 mo. mPFS [6] )

### National Reimbursed Drug List (NRDL)

#### 2019 NRDL released by China's National Healthcare Security Administration ("NHSA")

- Announced Nov. 28, 2019; effective Jan. 1, 2019
- 8 newly listed oncology drugs, including Elunate®
- Reimburse 50-70% of patient costs under urban scheme

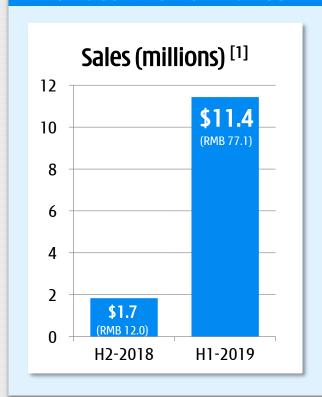
OOP costs for 3 per cycle	3L CRC Patients	Urban Med. Insur. Scheme (UMI)	Non-UMI
Population % China		317m <i>23%</i>	1,053m <i>77%</i>
Elunate® (fruquintinib)	Pre-NRDL Post-NRDL <b>3L CRC Pts OOP</b>	RMB21,966 7.938 <b>2,381~3,969</b>	RMB21,966 7.938 <b>7,938</b>
Stivarga® (regorafenib)	Pre-NRDL Post-NRDL <b>3L CRC Pts OOP</b>	RMB30,240 16,464 <b>4,939~8,232</b>	RMB30,240 16,464 16,464

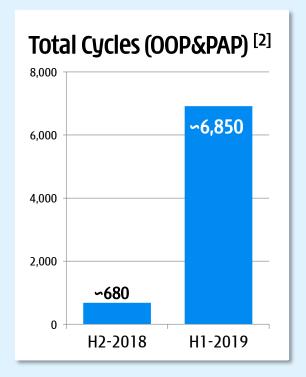


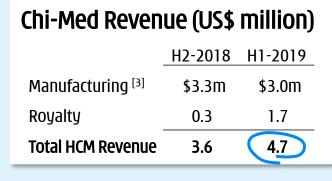
# H1 2019 performance



### Elunate® Performance









## Elunate® early progress - PAP working but NRDL will provide greater access

[1] Royalties to Chi-Med in H2 2018 and H1 2019 of \$0.261m and \$1.715m, respectively; at the lowest tier royalty rate of 15%, this implies net sales from third parties to Lilly of \$1.7m and \$11.4m, respectively; at RMB:US\$ exchange rate of 6.87:1 and 6.74:1, respectively, this implies RMB sales of 12m and 77m, respectively; [2] Treatment cycle = 28 day, i.e. assume three x 7 capsule 5mg packs per cycle or five x 21 capsule 1mg packs per cycle; OOP = Out of pocket payment; PAP = Patient access program; [3] Sales of Elunate manufactured by Chi-Med to Eli Lilly.





## Competitive landscape - small molecule VEGFR TKIS

Brand	Indication/s	Launch		2011	2012	2013	2014	2015	2016	2017	2018	01-2019
STIVARGA®	3L CRC /2L GIST	_	Sales (US\$ million) [1]							5	21	20
<i>(regorafenib)</i> Bayer AG	2L HCC	Mar 2018	List Price (US\$/mo.)							4,368	NRDL Oct-18	2,352
NEXAVAR®	Unres. RCC & HCC		Sales (US\$ million) [1]	80	96	96	93	91	97	108	130	50
<i>(sorafenib)</i> Bayer AG	Diff. Thyroid can.		List Price (US\$/mo.)						7,250	NRDL Jul-17	3,610	3,610
SUTENT®	RCC, GIST, pNET	2007	Sales (US\$ million) [1]	9	33	41	21	26	29	27	24	7
<i>(sunitinib)</i> Pfizer			List Price (US\$/mo.) [4]							5,544	NRDL Oct-18	2,498
INLYTA®	2L adv. RCC	2015	Sales (US\$ million) [1]					3	12	16	13	5
<i>(axitinib)</i> Pfizer			List Price (US\$/mo.)							5,957	NRDL Oct-18	1,787
VOTRIENT®	RCC	2017	Sales (US\$ million) [1]							5	12	5
<i>(pazopanib)</i> Novartis			List Price (US\$/mo.)							7,891	NRDL Oct-18	2,348
AITAN®	3L Gastric can.	Dec 2014	Sales (US\$ million) [2]					<b>∽4</b> 5	∽126	219	258	~82
<i>(apatinib)</i> Hengrui			List Price (US\$/mo.)						2,870	NRDL Jul-17	1,810	1,810
FOCUSV®	3L NSCLC	June 2018	Sales (US\$ million) [3]								∽190	~83
<i>(anlotinib)</i> Sino Biopharn	n		List Price (US\$/mo.)								NRDL Oct-18	981

Elunate® first 6 mo. sales progressing... relative to all MNC VEGFRi China launch sales [5]

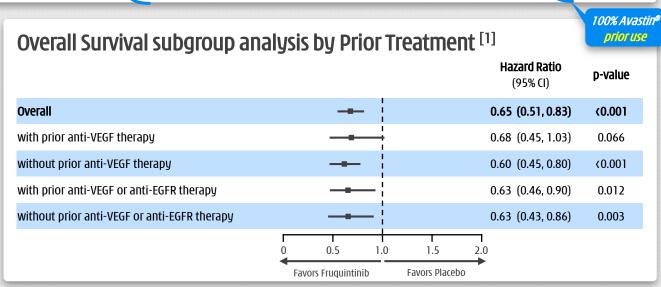


# 3<sup>rd</sup>-line CRC efficacy advantage



	FRESCO [1]  Mainland China		CONC	UR	CONC	:UR	CORRECT		
Third-Line Metastatic Colorectal cancer			Chinese Patients (Mainland China, Hong Kong, Taiwan) <sup>[2]</sup>		Mainland China, Hong Kong, Taiwan, Vietnam, South Korea		Global		
Treatment arms	<b>Elunate</b> ®	Placebo	Stivarga®	Placebo	Stivarga®	Placebo	Stivarga®	Placebo	
Patients (n)	278	138	112	60	136	68	505	255	
Objective Response Rate, n (%)	4.7%	0.0%	3.6%	0.0%	4.4%	0.0%	1.0%	0.4%	
Disease Control Rate, n (%)	62.2%) +4	9.9 12.3%	45.5% +38	.8 6.7%	51.5% +44	.1 7.4%	41.0% +2	6.1 14.9%	
Median Progression-Free Survival (mPFS) (mo.)	3.7 +1	<mark>.9 1.8</mark>	2.0 +0.	3 1.7	3.2 +1.	1.7	1.9 +0	.2 1.7	
Median Overall Survival (mOS) (mo.)	9.3 +	2.7 6.6	8.4 +2.	2 6.2	8.8 +2.	6.3	6.4 +1	.4 5.0	

- Advantage for Elunate® efficacy vs.
  Stivarga® in Chinese metastatic
  CRC patients;
- Advantage for Elunate® post VEGF/EGFR targeted therapy
  - mOS: 7.69 mo. vs. 5.98 mo. placebo (HR 0.63 & p-value 0.012)
  - mPFS: 3.65 mo. vs. 1.84 mo. placebo (HR 0.24 & p-value <0.001)





# Toxicity limitations of Stivarga®



	ELUNATE® Fruquintinib Capsules	Stivarga® (regorafenib) tablets
BIOCHEMICAL ACTIVITY	IC <sub>so</sub> (nmol/L)	IC <sub>so</sub> (nmol/L)
On-Target Kinases:		
VEGFR1	33	13
VEGFR2	35	4.2
VEGFR3	0.5	46
Off-Target Kinases:		
Ret	128	1.5
FGFR1	181	202
c-kit	458	7
PDGFRβ	>10,000	22
RAF-1	>10,000	2.5
B-RAF	>10,000	28
B-RAF <sup>V600E</sup>	>10,000	19

#### Stivarga® liver toxicity black-box warning:

Increased liver function test monitoring (weekly if elevated) & remedial dose interruption.

STIVARGA (regorafenib) tablets, oral Initial U.S. Approval: 2012

#### WARNING: HEPATOTOXICITY

See full prescribing information for complete boxed warning.

- Severe and sometimes fatal hepatotoxicity has been observed in clinical
- Monitor hepatic function prior to and during treatment. (5.1)
- Interrupt and then reduce or discontinue Stivarga for hepatotoxicity as manifested by elevated liver function tests or hepatocellular necrosis, depending upon severity and persistence. (2.2)

	ELU	NATE®	Stiva (regorafenib)	
3 <sup>rd</sup> -Line Metastatic Colorectal cancer	FRESCO Mainland		CONCUR (Mainland China	
Treatment arms	<b>Elunate</b> ®	Placebo	<b>Stivarga</b> ®	Placebo
Patients (n)	278	138	112	60
≥G3 AE (Safety population)	61.1%	19.7%	69.6%	46.7%
SAE (Safety population)	15.5%	5.8%	31.3%	26.7%
VEGFR on-target related AEs:				
Hypertension ≥G3	21.2%	2.2%	12.5%	8.3%
Hand-Foot Syndrome (Palmar-plantar), ≥G3	10.8%	0.0%	17.0%	0.0%
Off-target (i.e. non-VEGFR) related AEs:				
Hypophosphatemia, ≥G3	0.0%	0.0%	8.0%	0.0%
Hypokalemia, ≥G3	0.7%	0.7%	6.3%	0.0%
Rash/desquamation, ≥G3	0.0%	0.0%	4.4%	0.0%
Lipase increase, ≥G3	0.0%	0.0%	6.3%	1.7%
Hepatic function (Liver function) AEs:				
ALT increased, ≥G3	0.7%	1.5%	7.1%	3.3%
AST increased, ≥G3	0.4%	0.7%	8.9%	0.0%
Blood bilirubin increased, ≥G3	1.4%	1.5%	8.9%	8.3%
Tolerability:				
AE Leading to dose interruption	35.3%	10.2%	68.8%	25.0%
AE Leading to dose reduction	24.1%	4.4%	23.2%	0.0%
AE Leading to treatment discontinuation	15.1%	5.8%	14.3%	6.7%

## Elunate® superior safety - advantage especially for liver mets patients





# Ongoing trials

## Phase III in 2L gastric cancer (FRUTIGA)

- Passed first interim analysis by IDMC, trials continuing per IDMC recommendation;
- On track to complete enrollment Q2 2020.



#### PD-1 collaborations

- With Innovent (Tyvyt®): dose/regimen finding ongoing;
- With Genor (genolimzumab): dose escalation ongoing;
- Dose expansion expected to kick off starting Q4 2019.





## Phase II in 1L NSCLC (in combination with Iressa®)

Study complete and to submit data for presentation at an upcoming scientific conference.





2c Savolitinib

# Savolitinib

## Biggest opportunity is MET+ NSCLC



#### **Primary NSCLC** Resistance-driven EGFRm+ NSCLC All Iressa/Tarceva patients relapse Median PFS 9-10 months. 1.8 million NSCLC MET+ MET+ patients per year ∽10% Other **∽6%** (T790M-) MET+ **EGFRM** 790M+ **~30%** MET+ **~30%** SCLC/ **IRESSA®** Unknown 1<sup>st</sup> Line 3<sup>rd</sup> Line 2<sup>nd</sup> Line gefitinib Tarceva Treatment Iressa/Tarceva Tagrisso T790M+ **~45%** naïve resistant[1] resistant ErbB2 TAGRISSC ErbB2 XALKORI KRAS **TAGRISS** PI3Kca O ZYKADIA ErbB **EGFR** ALUNBRIC

	Target	Launch	2018 (\$m) <sup>[3]</sup>
Iressa	EGFRM	2003	\$518m
Tarceva	EGFRM	2004	550
Tagrisso	EGFRm / T790M	2015	1,860
Xalkori	ALK / ROS1 / MET	2011	524
Zykadia	ALK	2015	Not disc.
Alecensa	ALK	2015	650
Total Sales			→ 4.1b

Launch	2016	2017	2018	9M 2019	
					Est. global sales
Dec-15	423	955	1,860	2,305 (+82%)	of ¢4 Chn
					of ∽\$4-5 bn
					osimertinib by 2022 <sup>[2]</sup> .

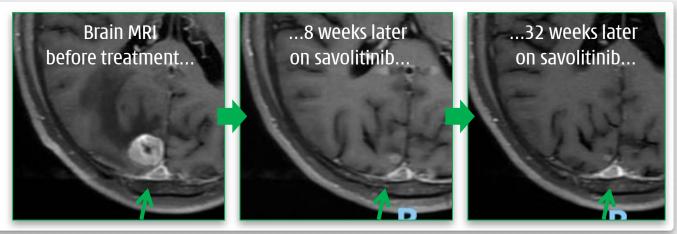
All **Tagrisso** patients relapse 2L Median **PFS 9-10 months**.

# Savolitinib - MET Exon 14 deletion NSCLC [1]

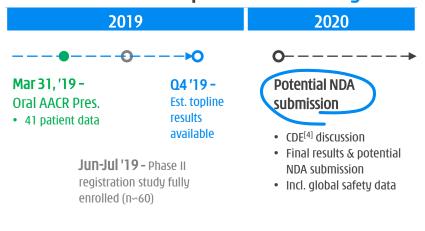
## Potential China NDA submission in 2020 [2]



- 4. Encouraging MET Exon14d NSCLC study China data at AACR 2019 [3]
- 41 pts; 31 pts efficacy evaluable.
- 💙 Promising antitumor activity.
- Rapid, durable tumor response observed.
- Anti-tumor activity observed in brain mets.
- Savolitinib generally well tolerated; most related 1 TEAEs were grade 1 or 2.



#### 5. MET Exon14d NSCLC potential NDA filing 2020 [2]



#### 6. Savolitinib monotherapy China market opportunity

		Annual Incidence	Estimated mPFS	Pricing Reference	Potential
Non-small Cell Lung Cancer <sup>[4]</sup>	100%	737,400			<u>first</u> savo monotherapy indication MET
MET Exon 14d NSCLC	2%	14,700	TBD	Tagrisso® China NRDL	Exon14d NSCLC
MET gene ampl. NSCLC	2-4%	14,700 - 29,000			
Gastric Cancer	100%	442,300	drive	ırther MET- en patient	
MET gene ampl. Gastric Cancer	4-10%	18,000 - 44,000		tions – savo otherapy	

[1] The trial is focused on patients with MET Exon 14 mutation who have failed prior systemic therapy, or are unable to receive chemotherapy, however the target patient population is intended to be all MET Exon 14 mutation patients; [2] We expect that the Phase II study of savolitinib in MET Exon 14d NSCLC would, if successful, be sufficient to support NDA submission; [3] Data cut-off Feb. 26, 2019. Lu S et al, CT031 - Preliminary efficacy and safety results of savolitinib treating patients with pulmonary sarcomatoid carcinoma (PSC) and other types of non-small cell lung cancer (NSCLC) harboring MET Exon 14 skipping mutations. Presented at American Association of Cancer Research Annual Meeting 2019, Atlanta, GA, Mar. 31, 2019; [4] Center for Drug Evaluation of the National Medicinal Products Administration of China.

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# TATTON B & D data - efficacy

# Tagrisso® + savolitinib in EGFR TKI refractory NSCLC



	(	TATTON Part D osimertinib 80 mg + savolitinib 300 mg		
	Part B1 (n=69) Prior third-generation EGFR-TKI	Part B2 (n=51)  No prior third-generation  EGFR-TKI  (T790M negative)	Part B3 (n=18)  No prior third-generation  EGFR-TKI  (T790M positive)	Part D (n=36)  No prior third-generation  EGFR-TKI  (T790M negative)
<b>Objective response rate</b> ,* % [95% CI] Complete response, % Partial response, %	<b>30%</b> [20, 43] 0 30%	65% [50. 78] 0 65%	<b>67%</b> [41, 87] 0 67%	64% [46. 79] 0 64%
Non-response, % Stable disease (≥ 6 weeks) Progressive disease Not evaluable	45% 10% 14%	24% 6% 6%	33% 0 0	28% 3% 6%
Disease control rate, #% [95% CI]	<b>75%</b> [64, 85]	<b>88%</b> [76, 96]	<b>100%</b> [81, 100]	<b>92%</b> [78, 98]
Median DoR, months [95% CI]	<b>7.9</b> [4.0, 10.5]	<b>9.0</b> [6.1, 22.7]	<b>12.4</b> [2.8, NR]	<b>8.0</b> [4.5, NR]
Median PFS, months [95% CI]	<b>5.4</b> [4.1, 8.0]	<b>9.0</b> [5. <u>5</u> , 11.9]	<b>11.0</b> [4.0, NR]	<b>9.1</b> [5.4, 12.9]

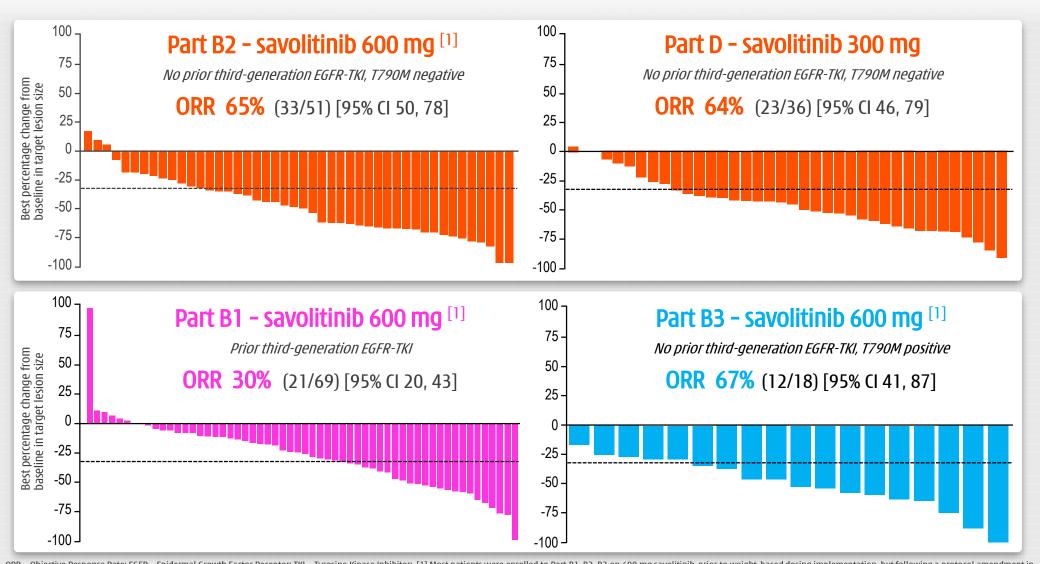
## No reduction in efficacy with 300mg savo - SAVANNAH converted to 300mg dose

[1] Most patients were enrolled to Part B1, B2, B3 on 600 mg savolitinib, prior to weight-based dosing implementation, but following a protocol amendment in response to a safety signal of hypersensitivity, the final 21 patients enrolled in Part B were dosed with savolitinib by body weight as follows: patients who weighed ≤55 kg (n=8) received 300 mg daily and those weighing >55 kg (n=13) received 600 mg daily; Best response data are for patients who had an opportunity to have two follow-up scans.; \*Complete or partial response confirmed at ≥4 weeks. \*Disease control rate = confirmed complete response + stable disease at ≥5 weeks.; CI, confidence interval; NR, not reached.

## TATTON B & D data - ORR

# Tagrisso® + savolitinib in EGFR TKI refractory NSCLC

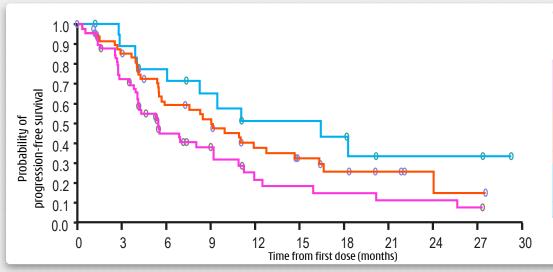




## TATTON B & D data - PFS

# Tagrisso® + savolitinib in EGFR TKI refractory NSCLC

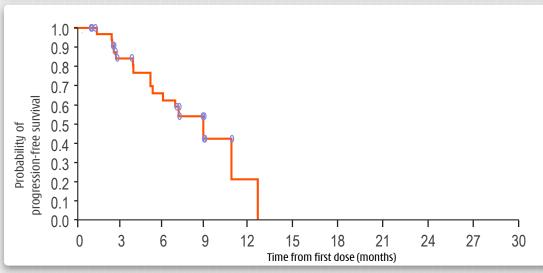




	Median PFS, months [95% CI]	Median (range) duration of follow-up in censored patients, months
Part B1 Prior third-generation EGFR-TKI; (600 mg [1]; n=69)	<b>5.4</b> [4.1, 8.0]	<b>2.6</b> [0.0-27.3]
Part B2 No prior third-generation EGFR-TKI, T790M negative; (600 mg [1]; n=51)	<b>9.0</b> [5.5, 11.9]	<b>10.1</b> [0.0-27.5]
<b>Part B3</b> No prior third-generation EGFR-TKI, T790M positive; (600 mg <sup>[1]</sup> ; n=18)	<b>11.0</b> [4.0, NR]	<b>14.7</b> [1.2-29.3]

#### Progression data had a maturity of 62%.

Patients who had not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST assessment. Circles indicate censored observations.



	Median PFS, months [95% Cl]	Median (range) duration of follow-up in censored patients, months
Part D No prior third-generation EGFR-TKI, T790M negative; (300 mg; n=42)	<b>9.1</b> [5.4, 12.9]	<b>3.0</b> [0.0-11.0]

#### Progression data had a maturity of 40%.

Patients who had not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST assessment. Circles indicate censored observations.

# TATTON B & D data - AEs & tolerability

# Tagrisso® + savolitinib in EGFR TKI refractory NSCLC



Event, n (%)	All Part B (n=138)	Part D (n=42)
Any AE	135 (98)	39 (93)
Any AE possibly related to savolitinib	115 (83)	25 (60)
AE grade ≥3	79 (57)	16 (38)
AE possibly causally related to study treatment leading to discontinuation of:		
Savolitinib	38 (28)	9 (21)
Osimertinib	14 (10)	2 (5)
Any AE leading to death	6 (4)	2 (5)
Any SAE	62 (45)	11 (26)

Part D data are preliminary, therefore, for osimertinib, the mean actual treatment exposure was 8.5 months for Parts B and D, respectively, and 7.1 months for savolitinib, for Parts B and D, respectively Han J. et al, "TATTON expansion cohorts: a Phase Ib study of osimertinib plus savolitinib in patients with EGFR-mutant, MET-amplified NSCLC following disease progression on a prior EGFR-TKI", #LBA, ESMO Asia, Singapore, November 23, 2019;

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# TATTON B & D data - AES & SAES Most common AEs<sup>[1]</sup> independent of causality & SAEs (≥3%)<sup>[2]</sup>



AF* p (0/)	All Part B	(n=138)	Part D (n=42)	
AE*, n (%)	All grades	Grade ≥3	All grades	Grade ≥3
Nausea	67 (49%)	4 (3%)	13 (31%)	0
Fatigue	48 (35)	6 (4)	4 (10)	0
Decreased appetite	47 (34)	5 (4)	6 (14)	1 (2)
Vomiting	46 (33)	6 (4)	5 (12)	0
Oedema peripheral	44 (32)	3 (2)	8 (19)	0
Diarrhoea	39 (28)	4 (3)	8 (19)	2 (5)
Paronychia	30 (22)	3 (2)	7 (17)	0
Pyrexia	29 (21)	1 (1)	6 (14)	0

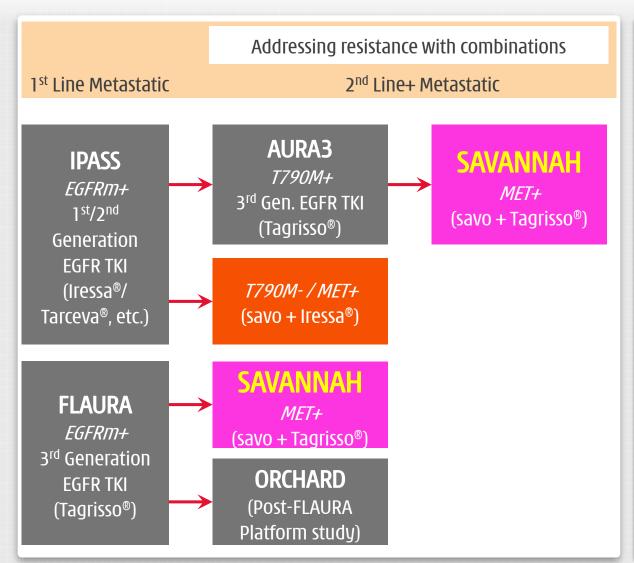
ΛΓ* n (9/)	All Part B	(n=138)	Part D (n=42)	
AE*, n (%)	All grades	Grade ≥3	All grades	Grade ≥3
Rash	26 (19%)	3 (2%)	8 (19%)	0
Stomatitis	26 (19)	0	4 (10)	0
Constipation	26 (19)	0	3 (7)	0
Pruritus	24 (17)	1 (1)	5 (12)	0
Headache	23 (17)	0	3 (7)	0
Myalgia	22 (16)	3 (2)	6 (14)	1 (2)
Cough	22 (16)	0	4 (10)	1 (2)
AST increased	21 (15)	9 (7)	2 (5)	0
Pneumonia	15 (11)	7 (5)	7 (17)	5 (12)

SAE**, n (%)	All Part B (n=138)	Part D (n=42)
Pneumonia	5 (4%)	4 (10%)
Anaphylactic reaction	6 (4)	1 (2)
Pneumothorax	6 (4)	1 (2)
Pyrexia#	5 (4)	0
Dyspnoea	5 (4)	0
Drug hypersensitivity	4 (3)	1 (2)
Diarrhoea	4 (3)	1 (2)
Back pain	4 (3)	0
Pulmonary embolism	3 (2)	2 (5)

# **SAVANNAH Study**

#### Encouraging TATTON data - led to the initiation of SAVANNAH





#### **SAVANNAH** (*NCT03778229*)

#### **S** Phase II single-arm study:

- ➤ Global N. & S. America, Eur., & Asia.
- > Primary endpoint ORR.
- Secondary endpoints: PFS, OS, DoR & percent change in tumor size.
- > Primary data completion est. 2021.

#### **S** Weight-based dosing regimen:

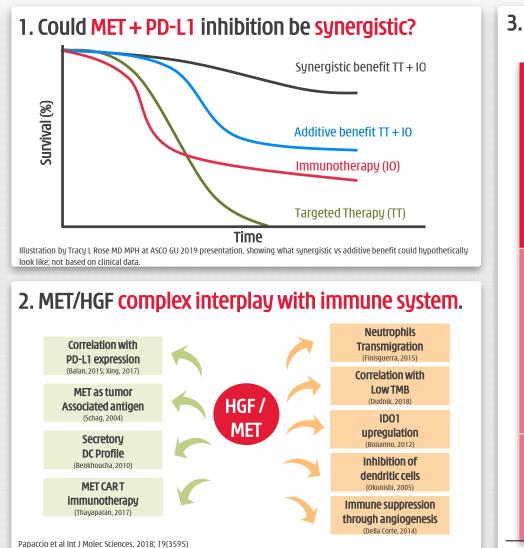
- ➤ TATTON D exploring lower savo dose in order to maximize long-term tolerability for combo.
- > TATTON D enrollment complete.

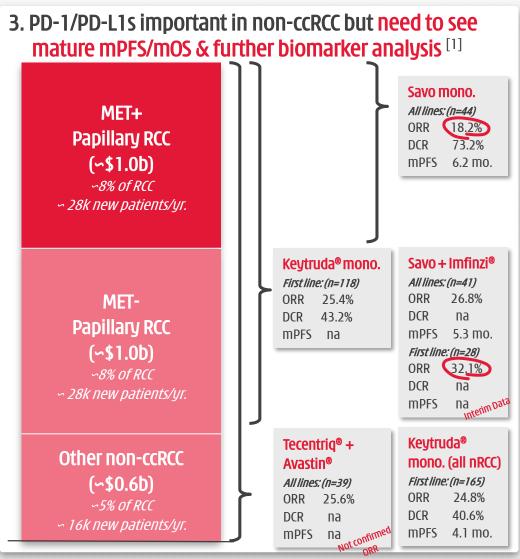
#### S ORCHARD study:

- Post FLAURA Platform study offering targeted treatments for all patients expect high enrollment.
- MET+ patients prioritize to SAVANNAH.

# Savolitinib + Imfinzi® combination









**2d** 

Other Recent Operating Highlights



## Other Recent Operating Highlights

#### B-cell malignancies / non-Hodgkin's lymphoma

- HMPL-523 (Syk) >150 patients dosed in China/Australia Phase I/Ib; to guide registration strategy in late 2019;
- HMPL-689 (PI3K $\delta$ ) Phase II dose selected in China & expansion underway;
- **US/EU Phase I 1<sup>st</sup> patient dosed** for both HMPL-523 & HMPL-689.

#### **Organization**

- Accelerating expansion of New Jersey-based international C&R operations;
- Establishing China oncology commercial team ∽70 commercial staff in place, focused on medical affairs & preparation for potential surufatinib launch.

#### **Discovery**

IND submission on HMPL-306 – an isocitrate dehydrogenase (IDH) 1/2 inhibitor.

## What is next from discovery?

## Differentiated assets against multiple targets

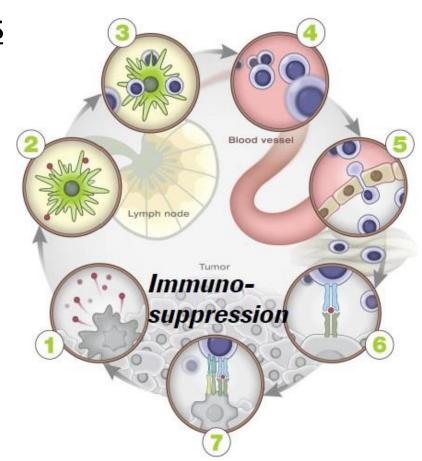


#### **Priming & activations**

- a0X40
- 4-1BB

#### Antigen release

- MET (savolitinib)
- EGFR (epitinib/theliatinib)
- Syk (HMPL-523)
- PI3Kδ (HMPL-689)
- FGFR (HMPL-453)
- IDH 1/2 (HMPL-306)
- ERK
- RIP1K



#### **Anti-angiogenesis**

- VEGFR (fruquintinib)
- VEGFR/FGFR (surufatinib)
- FGFR (HMPL-453)

#### Negative regulators

- Treg (HMPL-689)
- CSF-1R (surufatinib)
- IDOi
- AhRi
- TIM3
- TCBs
  - Pre-clinical small molecule
  - Pre-clinical antibody

Creating highest-quality range of assets against novel targets for use in combos



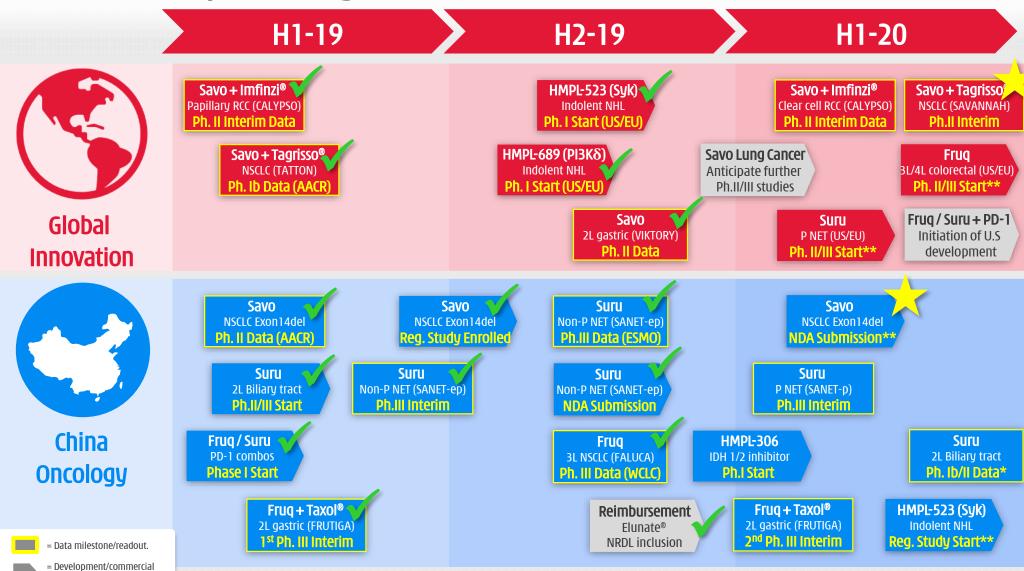


**Potential Upcoming Events** 

# Potential upcoming events

progress.





\* submission to scientific conference; \*\* subject to supportive data; Targets: Savolitinib = MET; Fruquintinib = VEGFR1/2/3; Surufatinib = VEGFR1/2/3 / FGFR1 / CSF-1R; HMPL-523 = Syk; HMPL-689 = PI3Kδ; Indications: NHL = Non-Hodgkin's Lymphoma; NET = Neuroendocrine tumors; RCC = Renal cell carcinoma; NSCLC = Non-small cell lung cancer.



H1 2019 Financial Results, Cash & Guidance

## H1 2019 Financial results R&D expense accelerated to \$74.5m in first 6 months







	2018	H1-18	H1-19	Growth	at CER [2] (Non-GAAP)
GROUP REVENUES  Unconsolidated JV Revenues	<b>214.1</b> <i>491.5</i>	102.2 271.7	102.2 276.9	<b>-</b> +2%	<b>+5%</b> +8%
SEGMENT NET INCOME/(LOSS) [1]					
INNOVATION PLATFORM	(102.4)	(52.9)	(63.8)	-21%	-29%
COMMERCIAL PLATFORM	41.4	26.9	27.7	+3%	+9%
Prescription Drugs Business Consumer Health Business	32.1 9.3	20.8 6.1	21.8 5.9	+5% -4%	+11% +2%
Chi-Med Group Costs	(13.8)	(6.7)	(9.3)	-39%	-39%
GROUP NET LOSS [1]  EPS Attrib. to Ord. S-H (Basic) (US\$)	<b>(74.8)</b> <i>(0.11)</i>	(32.7) (0.05)	(45.4) (0.07)	-39%	-48%

[1] Net Income / (Loss) attributable to Chi-Med; [2] at CER = at Constant Exchange Rate, which is a non-GAAP financial measure used to present period-to-period comparisons without the effects of currency movements by retranslating the current period's performance at the previous period's foreign currency exchange rates. Please refer to the slides titled "Non-GAAP Financial Measures and Reconciliation" for more information and a reconciliation of these measures to the most comparable GAAP measure.

# Cash position & 2019 Guidance

## \$384 million in available cash resources [1]



#### **Cash Position**

(at end June 2019)

- \$237 million cash / cash equiv. / Short term inv. [2]
- \$147 million additional unutilized banking facilities [3]
- \$64 million additional cash in JVs
- \$0 million in bank borrowings



(US\$ millions)	2019 Previous Guidance	2019 Current Guidance
Research & Development Expenses	(160) - (200)	(130) - (170)
Adj. (non-GAAP) Group Net Cash Flows [4]	(120) - (150)	(90) - (120)

- Research & Development Expense savings:
  - > RMB weaker; & global suru/fruq Ph.IIb/III 2020.
- Flexibility on timing of future financing activity:
  - Sufficient resources to advance pipeline through multiple major value inflection points;
  - ➤ Non-dilutive finance from non-core CP divest. [5]



5 Summary

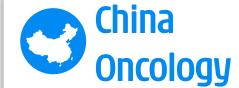






## Global Innovation

- NDA submission for savolitinib combo with Tagrisso®
- Expand savo. Exon14 deletion development global
- 2 compounds to enter registration studies in 2020, surufatinib & fruquintinib
- Proof-of-concept achieved on both Syk & PI3Kδ compounds



- Establish Elunate® as best-in-class VEGFR TKI in >\$5bn market by 2026<sup>[1]</sup>
- 2 new NDAs in '19/'20, suru.
   ep-NET & savo. Exon14d NSCLC
- 2 more compounds into registration trials in 2020, Syk & PI3K $\delta$
- Expanded life cycle development on all assets, incl. PD-1 combos



- Cash generative China Commercial Platform
- Platform for future innovative drug launches

[1] Frost & Sullivan.

### Chi-Med in short



## 19-year track record of achievement & discipline

- In-house discovery excellence world-class scientific talent & strategy discovery platform that has created all clinical assets internally;
- **Proven development** the first China company to bring home-grown asset to market<sup>[1]</sup>;
- **Commercial excellence** deep knowhow & infrastructure in China profitable.

## Risk-balanced - non-binary biotech

- Multiple shots-on-goal 9 novel drug candidates<sup>[2]</sup> two proven through pivotal studies<sup>[3]</sup>;
- World-class partnerships AstraZeneca & Eli Lilly as well as wholly-owned assets.

### Ambition

Building a global science-focused biopharma company from an established base in China.





HUTCHISON CHINA MEDITECH

Thank you