



HUTCHISON CHINA MEDITECH

## CLSA Investors' Forum

September 2019

AIM/Nasdaq: HCM

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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 ~440-person scientific team



## China Oncology

- Major market potential driven by regulatory reforms & high unmet medical need in oncology
- Elunate® (fruquintinib capsules) first ever home-grown 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

[1] China-discovered novel oncology drug to receive unconditional NDA approval in China.

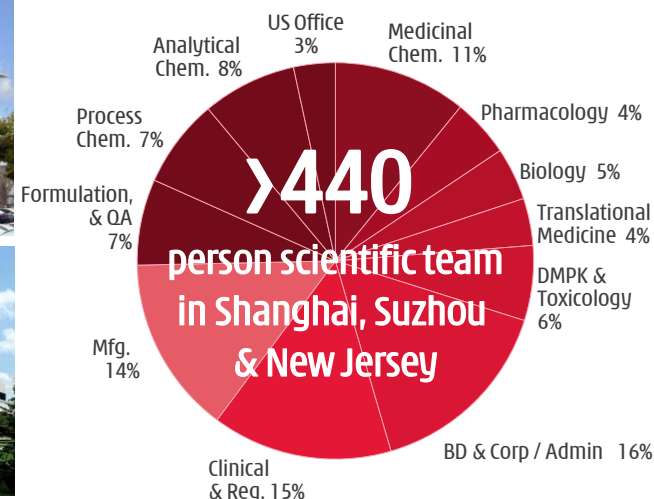
# Proven innovation & commercial operations

## Management Team

Industry / Chi-Med  
(years)

	<b>Mr. CHRISTIAN HOGG, BSc, MBA</b> Chief Executive Officer		30 / 19
	<b>Dr. WEIGUO SU, PhD</b> EVP, Chief Scientific Officer		29 / 14
	<b>Mr. JOHNNY CHENG, BEC, CA</b> Chief Financial Officer	  	30 / 11
	<b>Dr. ZHOU JUN JIE, MD, MBA</b> General Manager, SHPL		28 / 18
	<b>Dr. MAREK KANIA, MD, MBA</b> SVP, Chief Medical Officer, US		25 / 1
	<b>Dr. ZHENPING WU, PhD, MBA</b> SVP, Pharmaceutical Sciences	 	25 / 11
	<b>Mr. CHEN HONG, BSc, MBA</b> SVP, Chief Commercial Officer		21 / 9
	<b>Dr. MAY WANG, PhD</b> SVP, Bus. Dev. & Strategic Alliances		25 / 9
	<b>Mr. ANDREW SHIH, DiplIE, MBA</b> SVP, HR - Org./Leadership Dev.		23 / 1
	<b>Mr. MARK LEE, BEng, MBA</b> SVP, Corp. Finance & Development		20 / 10
	<b>Mr. ENRICO MAGNANELLI, BA, MBA</b> Head of International Operations		20 / 1

## Integrated Innovation Organization <sup>[1]</sup>



## Commercial Team & Joint Ventures <sup>[1]</sup>

### 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



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## Operating Highlights – H1 2019

# Main H1 2019 Operating Highlights

## Surufatinib



- 🌐 **Positive China Phase III** - 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



- 🌐 **Reached enrollment goal on Phase II registration study** - MET Exon 14 del. NSCLC;
- 🌐 AstraZeneca collaboration **leading global position in EGFR-TKI resistant NSCLC**;
- 🌐 **Emerging signal for savolitinib/Imfinzi®** (PD-L1) combo - renal cell carcinoma.



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### *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).

Tumor-associated  
macrophages

T-cells

Angiogenesis

2a Surufatinib: angio-immuno kinase inhibitor

# Surufatinib

## Overview of NET - ~140,000 patients in the U.S. [1][2]

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

- 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.

### Hormone-related symptoms [1]

- **Functional NETs** (~40% of patients) release hormones / peptides that **cause symptoms like diarrhea & flushing**; Non-functional NETs have no symptoms.

### 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.

## U.S. NET epidemiology - highly fragmented

55~75%



**Gastroenteropancreatic** [3]

10%~20%



**Other/  
unknown**

25%~30%



**Lung /  
Bronchus**

✓ **Sandostatin®** (*functional only ~40% of patients*)

✓ **Afinitor®** (*non-functional only ~60% of patients*)



**Pancreatic  
(pNET)**



**Other Gastro  
Intestinal NET**

Incidence

1,215

5Yr Survival

56%

Prevalence

8,995

% of all NET

6.4%

9,762

58%

72,237

51.4%

✓ **Somatostatin analogues** (*early disease ~50% of patients*)

✓ **Sutent®, Afinitor®, Lutathera®, cytotoxic chemos** (*advanced disease ~50% of patients*)

✓ **Somatostatin analogues** (*early disease ~50% of patients*)

✓ **Afinitor®** (*non-functional advanced disease only ~30% of patients*), **Lutathera®, cytotoxic chemos** (*advanced disease 50% of patients*)

[1] Dasari A, et al.: Trends in the Incidence, Prevalence, & Survival Outcomes in Patients With Neuroendocrine Tumors in the U.S.. JAMA Oncol. 2017;3(10):1335-1342;

[2] [www.cancer.net](http://www.cancer.net) (patient information from ASCO) - NET is a subtype of neuroendocrine neoplasms, NENS; [3] Gastroenteropancreatic neuroendocrine tumors = GEP NETs.

# Surufatinib

## Existing U.S. NET treatment landscape - also highly fragmented



	Somatostatin Based Therapies			Kinase Inhibitor Therapies				
	Sandostatin® LAR (octreotide)	Somatuline Depot® (lanreotide)	Lutathera® ( <sup>177</sup> Lu-Dotatate)	Afinitor® (everolimus)	Sutent® (sunitinib)	Surufatinib (preparing China NDA)		
2018 Sales	\$1.6bn	\$1.0bn	\$0.17bn	\$1.6bn	\$1.0bn	-		
MOA <sup>[1]</sup>	Somatostatin analogue	Somatostatin analogue	Somatostatin receptor targeting radiotherapy	mTOR inhibition	Inhibits multiple receptor tyrosine kinases	VEGFR/FGFR1 & CSF-1R inhibition		
Admin.	Subcutaneous or intramuscular inj. (LAR)	Subcutaneous injection	Subcutaneous injections (radio-qualified physicians).	Oral tablet	Oral capsules	Oral capsules		
Shelf-life	3 years	2 years	72 hours	3 years	3 years	2+ years <sup>[3]</sup>		
Dosage	2 wks: Sando. inj. 0.1-0.6mg per day; then 2 months Sando. LAR 20mg per 4 wks.	120mg inj. every 4 wks.	7.4GBq (one ~25ml vial) inj. every 8 wks - 4 doses total.	10mg orally once daily.	37.5mg taken orally once daily.	300mg orally once daily.		
NET indication /s	<ul style="list-style-type: none"><li>LT treatment of severe diarrhea &amp; flushing from meta. carcinoid tumors.</li></ul>	<ul style="list-style-type: none"><li>GEP-NETs: unresectable, well or moderately diff., (locally adv. or meta) GEP-NETs to improve PFS.</li><li>Carcinoid Syndrome: to reduce frequency of short-acting somatostatin rescue therapy.</li></ul>	<ul style="list-style-type: none"><li>Somatostatin receptor-positive GEP-NETs.</li></ul>	<ul style="list-style-type: none"><li>pNET: progressive pNET (unresectable, locally adv. or meta).</li><li>GI-NET or Lung NET: progressive, well-diff., non-functional/NET (unresectable, locally adv. or meta). Not for functional carcinoid tumors.<sup>[2]</sup></li></ul>	<ul style="list-style-type: none"><li>pNET: Progressive, well-differentiated pNETs (unresectable locally adv. or meta).</li></ul>	<ul style="list-style-type: none"><li>Non-pNET: SANET-ep study was in low- or intermediate-grade adv. non-pancreatic NET.</li><li>pNET: Phase III ongoing.</li></ul>		
Estimate % of total NET population	~40-50% (functional / early disease)	~40-50% (functional / early disease)	~30% (advanced disease - GEP-NET)	~35-40% (advanced disease - non-functional )	<5% (advanced disease - p-NET)	to be determined		
Non-NET indication/s	<ul style="list-style-type: none"><li>Acromegaly; watery diarrhea from VIPomas.</li></ul>	<ul style="list-style-type: none"><li>Acromegaly.</li></ul>		<ul style="list-style-type: none"><li>Adv. HR+ HER2-n breast cancer; adv. 2L RCC; renal angiomyolipoma and TSC.</li></ul>	<ul style="list-style-type: none"><li>2L GIST; adv. RCC; high risk of recurrent RCC.</li></ul>			
	Sandostatin® / Placebo	Somatuline Depot® / Placebo	Lutathera® + Sando. LAR / Sando. LAR	Afinitor® / Placebo		Sutent® / Placebo	Surufatinib / Placebo (undisclosed)	
mPFS (mo.)	14.3 / 6.0	NR / 18.0	NR / 8.5	pNET 11.0 / 4.6	Lung & GI NET 11.0 / 3.9	pNET: 11.4 / 5.5	Ph II pNET 19.4	Ph II, non-pNET 13.4
HR	0.34	0.47	0.21	0.35	0.48	0.42	Ph III	Ph III not
(p-value)	0.000072	<0.001	<0.0001	<0.001	<0.001	<0.001	Ongoing	yet disclosed
ORR	2% / 2%	NR	18% / 3%	5% / 2%	2% / 1%	9% / 0%	17% (Ph II)	15% (Ph II)
DCR	69% / 40%	NR	95% / 76%	73% / 51%	81% / 64%	72% / 60%	90% (Ph II)	93% (Ph II)
Pivotal Trial	PROMID	CLARINET	NETTER-1	RADIANT-3	RADIANT-4	A6181111	SANET-p	SANET-ep

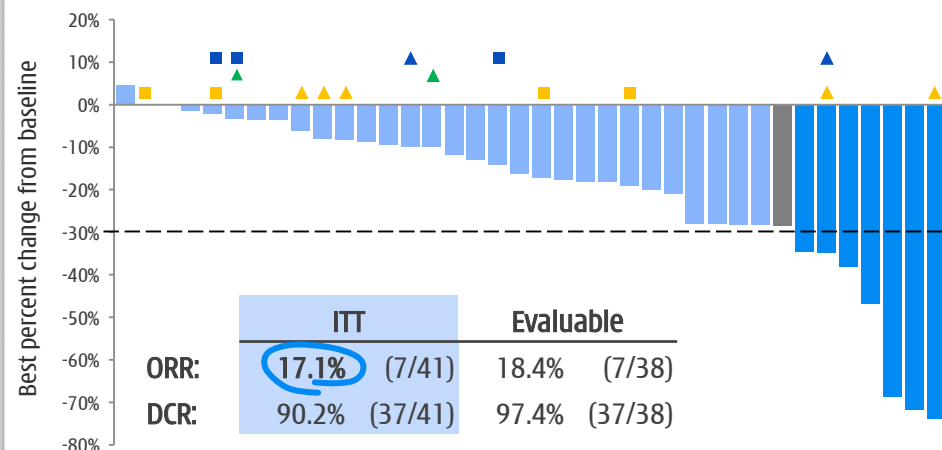
[1] MOA = Mechanism of Action; [2] Afinitor is only approved for pancreatic neuroendocrine tumors in China; [3] 2-year stability studies completed so far; [4] Phase II data - Phase III SANET-ep trial Phase III trial SANET-p is ongoing; mPFS = median progression-free survival; HR = Hazard Ratio; ORR = objective response rate; DCR = Disease control rate.

# Surufatinib - China NET - Phase II data <sup>[1]</sup>

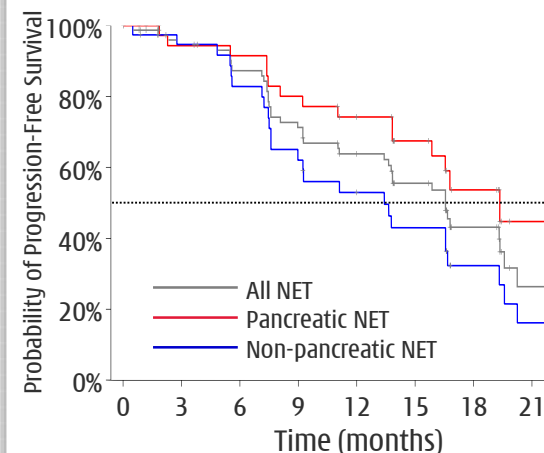
Broad spectrum NET efficacy **incl. Sutent®/Afinitor® failure ptnts.**



## Phase II: Pancreatic NET



## Phase II: Progression-Free Survival (PFS)

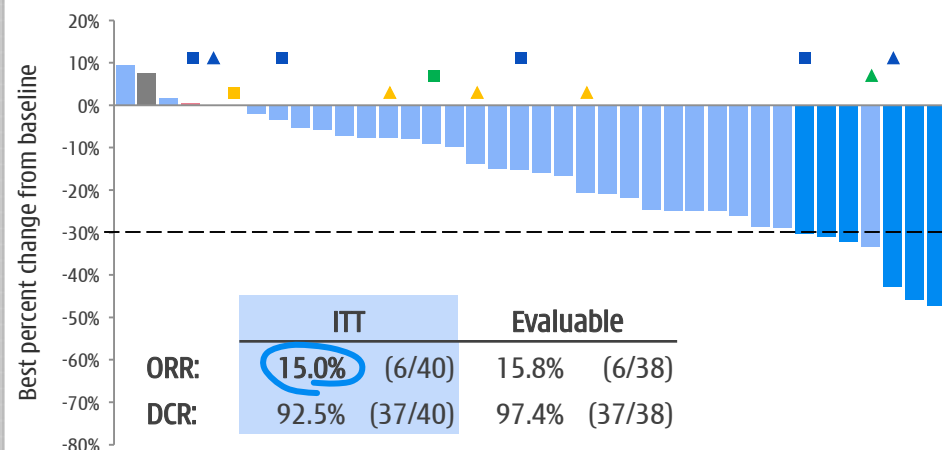


	Median PFS (months)	PDS or Deaths (% pts)
All NET (n=81)	16.6m (13.4, 19.4)	51.9% (42/81)
P-NET (n=41)	19.4m (13.8, 22.1)	39.0% (16/41)
Non-P NET (n=40)	13.4m (7.6, 16.7)	65.0% (26/40)

Data has yet to reach maturity - data cut-off as of Jan 20, 2017.

Partial Response Stable Disease Progressive disease Prior Sutent® Prior Fatinib (VEGFR) Prior Afinitor® Progressive Disease on Prior TKI

## Phase II: Non-Pancreatic NET



## Phase II: Safety - Well tolerated - Adverse Events manageable.

	Grade ≥3 (≥4pts) n (%)	Adverse Events ("AEs") - Regardless of causality	N=81 n (%)
Hypertension	25 (30.9)	Any AE	81 (100.0)
Proteinuria	11 (13.6)	Grade ≥3 AE	63 (77.8)
Hyperuricemia	8 (9.9)	Any SAE	21 (25.9)
Hypertriglyceridemia	7 (8.6)	Any drug-related AE	81 (100)
Diarrhea	6 (7.4)	Any drug-related grade ≥3 AE	58 (71.6)
ALT increased	5 (6.2)	Any drug related SAE	10 (12.3)
Anemia	4 (4.9)	Drug related AE leading to:	
Hypokalemia	4 (4.9)	dose interruption	40 (49.4)
Hepatic function abnormal	4 (4.9)	dose reduction	20 (24.7)
		drug withdrawal	7 (8.6)



# Surufatinib - China NET

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



## Epidemiology - China NET & BTC patient populations

Potential  
First suru  
monotherapy  
indication Non-  
pancreatic NET

Two further  
surufatinib  
registration-  
intent studies  
underway

		Annual Incidence	Estimated Prevalence	mPFS	NRDL Pricing References
China NET	100%	67,600	~300,000 (Est. China ratio <sup>[1]</sup> )		<b>Sutent®</b> (~US\$ 2,007/mo. <sup>[2]</sup> ) <b>Afinitor®</b> (~US\$ 1,320/mo. <sup>[2]</sup> )
Non-Pancreatic NET	~80%	~54,100	~240,000 (Est. China ratio <sup>[1]</sup> )	13.4 mo. (Ph.II) (SANET-ep Ph.III -- TBD)	
Pancreatic NET	~20%	~13,500	~60,000 (Est. China ratio <sup>[1]</sup> )	19.4 mo. (Ph.II) (SANET-p Ph.III -- TBD)	
Biliary Tract Cancer	100%	64,000		TBD	

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

[1] Current estimated Prevalence to Incidence ratio in China at 4.4, lower than U.S. 7.4 ratio due to lower access to treatment options.

[2] NRDL pricing references calculations assume exchange rate of RMB6.74 per US\$1.

# Surufatinib - China NET

All NET est. ~\$100-120m/yr. - currently under treated/diagnosed



## Competitive landscape - China NET treatments<sup>[1]</sup>

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

Pancreatic-NET market est. ~\$20m/yr. - Non-Pancreatic NET market ~4-5X

# Surufatinib

Potentially our first un-partnered oncology drug launch



## 2 Phase III NET registration studies...

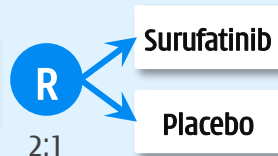
25 China sites.

1° endpoint:  
median PFS.

2° endpoints:  
ORR, DCR, DoR,  
TTR, OS.

### SANET-ep

Non-pancreatic NET  
(Planned N=273)



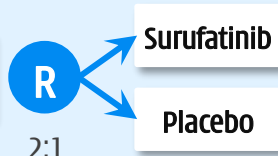
**SANET-ep Interim Analysis June 2019** - study early termination - already met mPFS endpoint;



Data presentation at conference in **H2 2019**. ✓

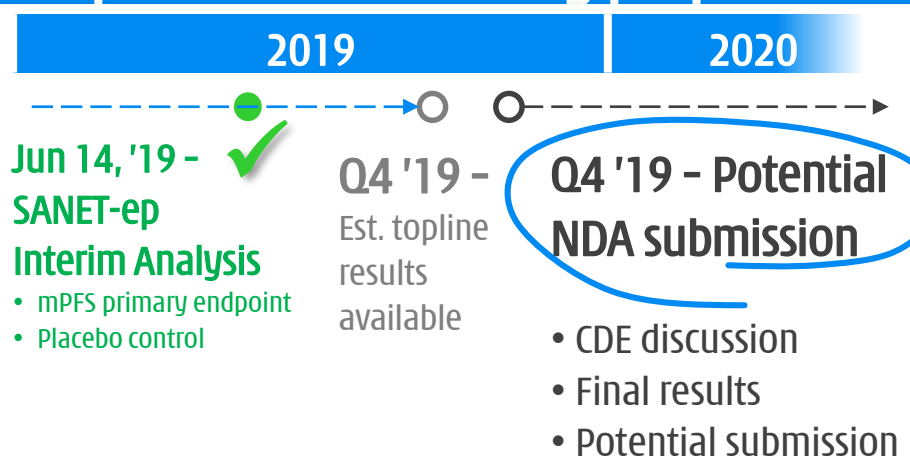
### SANET-p

Pancreatic NET  
(Planned N=195)



SANET-p Interim Analysis in **H1 2020**.

## ...potential NDA being prepared...



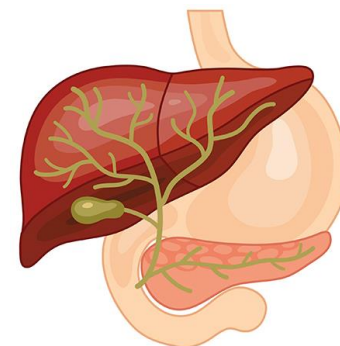
# Surufatinib

## 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 escalation near completion;
- Dose expansion in multiple tumor types to begin Q4 2019.



### 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.





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100  
hmp  
Hutchison Medi Pharma  
Lilly

Fruquintinib Capsules

ELUNATE®

5mg



Hutchison Medi Pharma

Lilly

2b

Elunate® (fruquintinib capsules)

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

## Epidemiology

**China Annual Incidence**  
380,000 patients <sup>[1]</sup>

**Surgery**

**1<sup>st</sup>-line treated**

~15%

**2<sup>nd</sup>-line treated**

**3<sup>rd</sup>-line treated**

>55,000 patients <sup>[2]</sup>

## Launch pricing <sup>[3]</sup>

**Launch pricing (OOP <sup>[4]</sup>)**

~US\$ 3,260 per cycle  
(RMB 21,960 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<sup>[6]</sup>)

## Shanghai PRDL – effective June 10, 2019

**Population covered by Shanghai PRDL <sup>[7]</sup>**

15.0 million or 62% of total 24.2 million population <sup>[8]</sup>

**Shanghai PRDL inclusion**

- -2% discount from Launch pricing
- PAP continuation for all patients in Shanghai
- Shanghai PRDL to reimburse 60% of patient costs

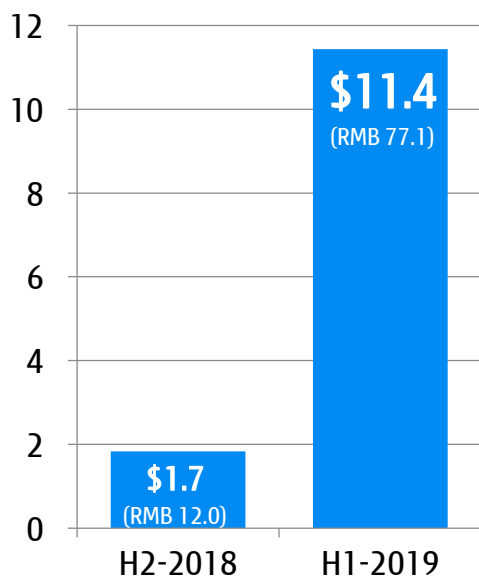
**Total net OOP cost to patients**

~US\$ 3,800 (RMB 25,740) <sup>[9]</sup> for unlimited Elunate<sup>®</sup> treatment

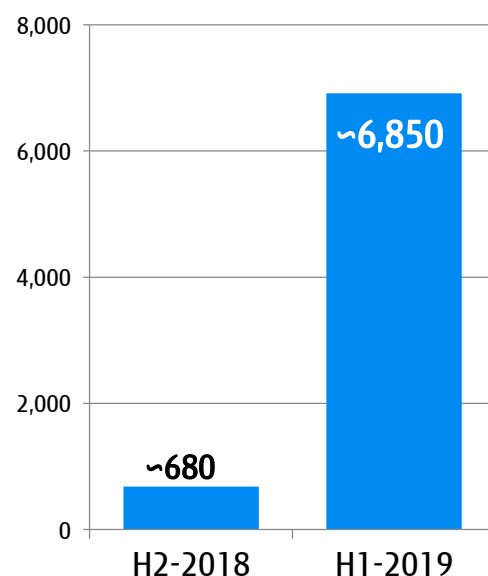


## Elunate® Performance

**Sales (millions) [1]**



**Total Cycles (OOP&PAP) [2]**



**Chi-Med Revenue (US\$ million)**

	H2-2018	H1-2019
Manufacturing [3]	\$3.3m	\$3.0m
Royalty	0.3	1.7
<b>Total HCM Revenue</b>	<b>3.6</b>	<b>4.7</b>



**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.

# China VEGFR landscape

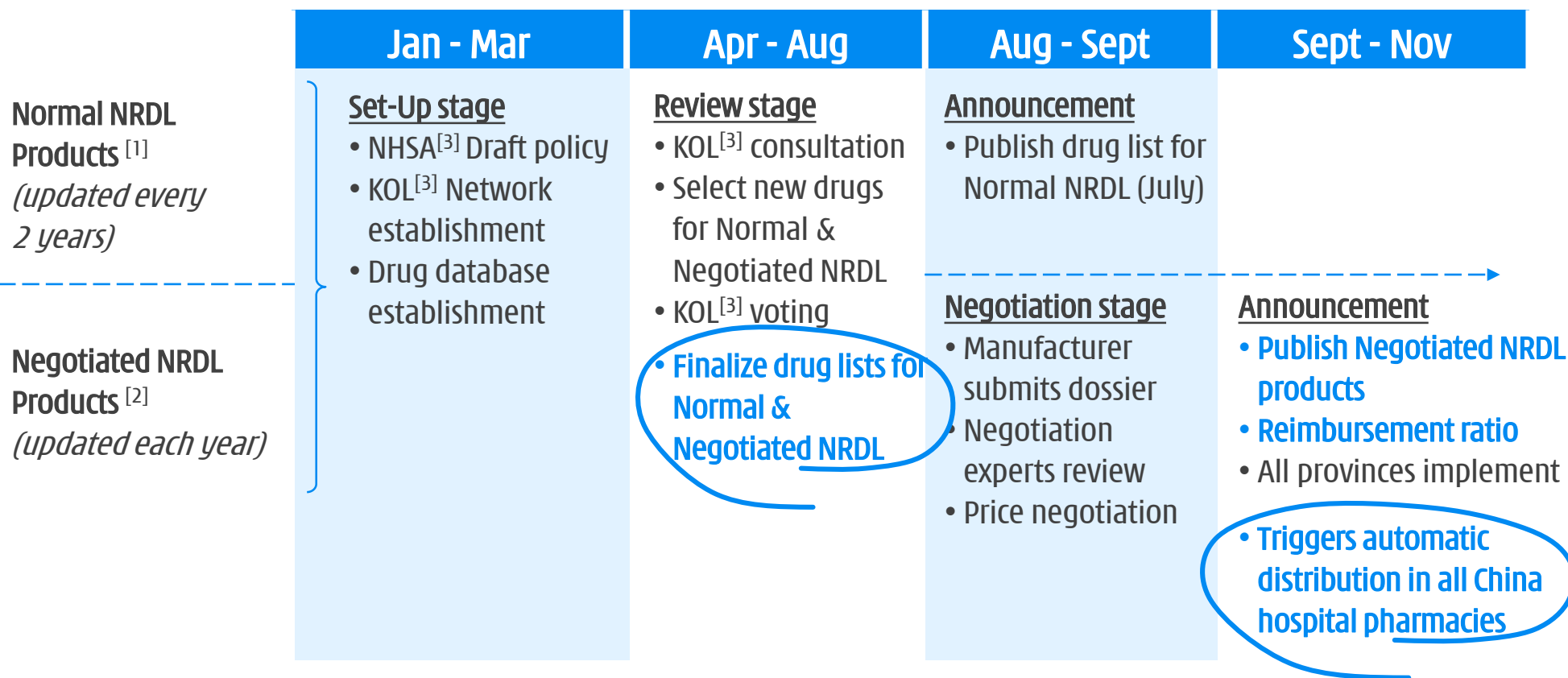
## Competitive landscape – *small molecule VEGFR TKIs*

Brand	Indication/s	Launch	2011	2012	2013	2014	2015	2016	2017	2018	Q1-2019
<b>STIVARGA®</b> (regorafenib) Bayer AG	<b>3L CRC</b> /2L GIST 2L HCC	May 2017 Mar 2018	Sales (US\$ million) <sup>[1]</sup>						5	21	20
			List Price (US\$/mo.)						4,368	NRDL Oct-18	2,352
<b>NEXAVAR®</b> (sorafenib) Bayer AG	Unres. RCC & HCC Diff. Thyroid can.	2006	Sales (US\$ million) <sup>[1]</sup>						108	130	50
			List Price (US\$/mo.)						7,250	NRDL Jul-17	3,610
<b>SUTENT®</b> (sunitinib) Pfizer	RCC, GIST, pNET	2007	Sales (US\$ million) <sup>[1]</sup>						27	24	7
			List Price (US\$/mo.) <sup>[4]</sup>						5,544	NRDL Oct-18	2,498
<b>INLYTA®</b> (axitinib) Pfizer	2L adv. RCC	2015	Sales (US\$ million) <sup>[1]</sup>						16	13	5
			List Price (US\$/mo.)						5,957	NRDL Oct-18	1,787
<b>VOTRIENT®</b> (pazopanib) Novartis	RCC	2017	Sales (US\$ million) <sup>[1]</sup>						5	12	5
			List Price (US\$/mo.)						7,891	NRDL Oct-18	2,348
<b>AITAN®</b> (apatinib) Hengrui	3L Gastric can.	Dec 2014	Sales (US\$ million) <sup>[2]</sup>						219	258	~82
			List Price (US\$/mo.)						2,870	NRDL Jul-17	1,810
<b>FOCUSV®</b> (anlotinib) Sino Biopharm	3L NSCLC	June 2018	Sales (US\$ million) <sup>[3]</sup>							~190	~83
			List Price (US\$/mo.)							NRDL Oct-18	981

**Elunate® first 6 mo. sales progressing ... relative to all MNC VEGFRi China launch sales <sup>[5]</sup>**



## 2019 China NRDL update - *High-level process*



**Elunate<sup>®</sup> reimbursement – Discussions underway for NRDL inclusion Q4 2019**

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

Third-Line Metastatic Colorectal cancer	FRESCO <sup>[1]</sup>		CONCUR		CONCUR		CORRECT	
	Mainland China		Chinese Patients (Mainland China, Hong Kong, Taiwan) <sup>[2]</sup>		Mainland China, Hong Kong, Taiwan, Vietnam, South Korea		Global	
Treatment arms	Elunate <sup>®</sup>	Placebo	Stivarga <sup>®</sup>	Placebo	Stivarga <sup>®</sup>	Placebo	Stivarga <sup>®</sup>	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% +49.9	12.3%	45.5% +38.8	6.7%	51.5% +44.1	7.4%	41.0% +26.1	14.9%
Median Progression-Free Survival (mPFS) (mo.)	3.7 +1.9	1.8	2.0 +0.3	1.7	3.2 +1.5	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 +2.5	6.3	6.4 +1.4	5.0



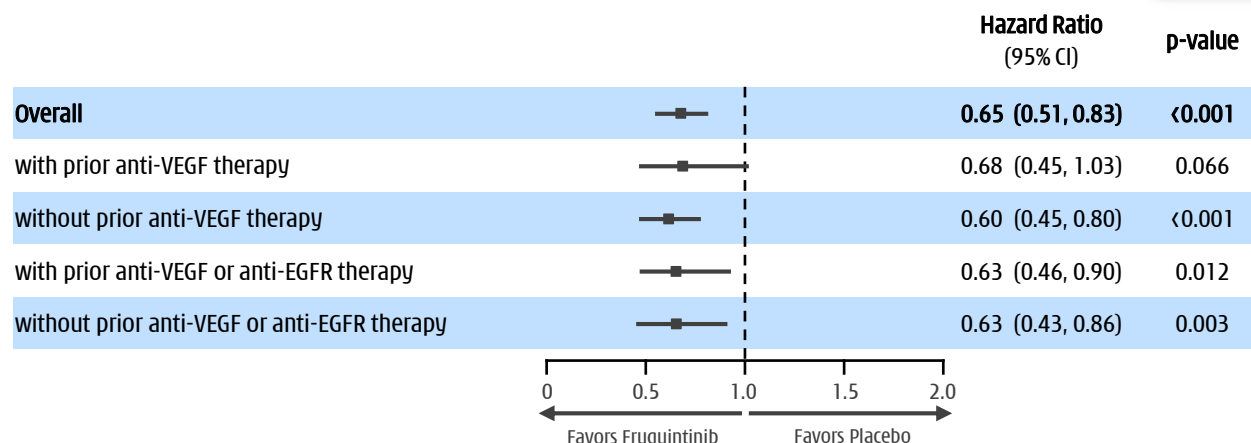
**Advantage for Elunate<sup>®</sup> efficacy vs. Stivarga<sup>®</sup> in Chinese metastatic CRC patients;**



**Advantage for Elunate<sup>®</sup> 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)

## Overall Survival subgroup analysis by Prior Treatment <sup>[1]</sup>



100% Avastin<sup>®</sup>  
prior use

BIOCHEMICAL ACTIVITY	IC <sub>50</sub> (nmol/L)	IC <sub>50</sub> (nmol/L)
<b>On-Target Kinases:</b>		
VEGFR1	33	13
VEGFR2	35	4.2
VEGFR3	0.5	46
<b>Off-Target Kinases:</b>		
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 trials. (5.1)
- 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)

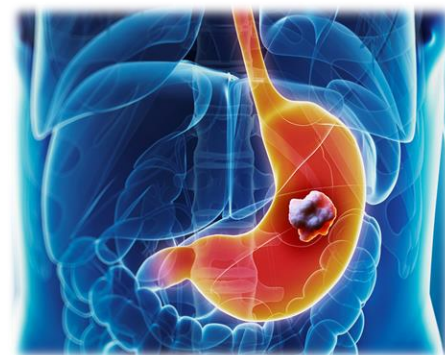
3 <sup>rd</sup> -Line Metastatic Colorectal cancer	FRESCO Study Mainland China [1]		CONCUR Study (Mainland China, HK, Taiwan) [2]	
Treatment arms	Elunate®	Placebo	Stivarga®	Placebo
Patients (n)	278	138	112	60
≥G3 AE (Safety population)	61.1%	19.7%	69.6%	46.7%
SAE (Safety population)	15.5%	5.8%	31.3%	26.7%
<b>VEGFR on-target related AEs:</b>				
Hypertension ≥G3	21.2%	2.2%	12.5%	8.3%
Hand-Foot Syndrome (Palmar-plantar), ≥G3	10.8%	0.0%	17.0%	0.0%
<b>Off-target (i.e. non-VEGFR) related AEs:</b>				
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%
<b>Hepatic function (Liver function) AEs:</b>				
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%
<b>Tolerability:</b>				
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<sup>®</sup>): dose/regimen finding ongoing;
- With Genor (genolimzumab): dose escalation ongoing;
- Dose expansion expected to kick off starting Q4 2019.

**Innovent**  
Innovent Biologics


**嘉和生物药业**  
Genor Biopharma

## Phase II in 1L NSCLC (in combination with Iressa<sup>®</sup>)

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

**IRESSA<sup>®</sup>**  
gefitinib



An abstract, artistic representation of a DNA double helix and various organic, cellular-like structures in shades of purple, yellow, and red, serving as a background for the upper portion of the slide.

# *AstraZeneca and Chi-Med*

Harnessing the power of Chinese Innovation



Savolitinib

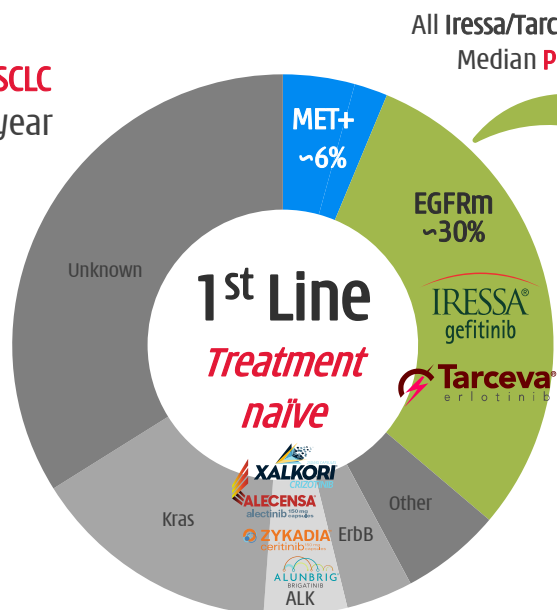


# Savolitinib

Biggest opportunity is MET+ NSCLC

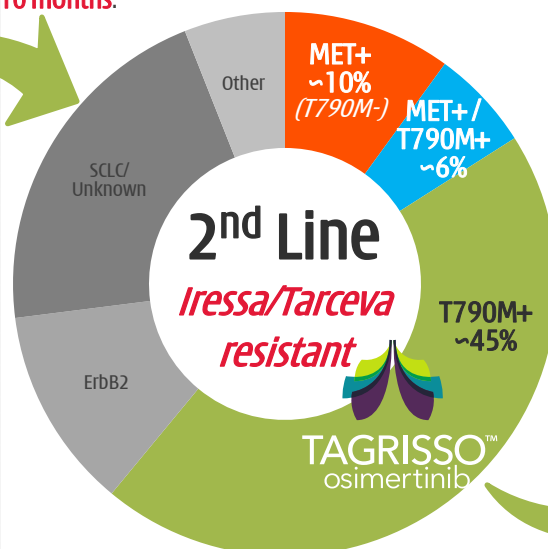
## Primary NSCLC

1.8 million NSCLC patients per year

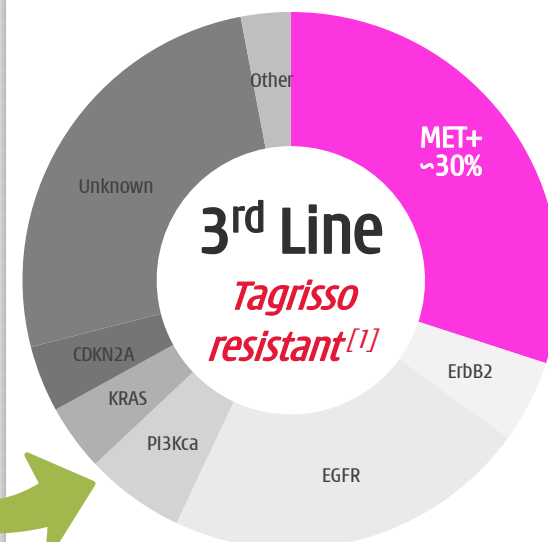


All Iressa/Tarceva patients relapse  
Median PFS 9-10 months.

## Resistance-driven EGFRm+ NSCLC



All Tagrisso patients relapse  
Median PFS 9-10 months.



	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	H1 2019
Dec-15	423	955	1,860	1,414 (+86%)

Est. global sales of ~\$4-5 bn by 2022<sup>[2]</sup>.

TAGRISSO<sup>™</sup> osimertinib

# Savolitinib - MET Exon 14 deletion NSCLC

## China's lead MET inhibitor



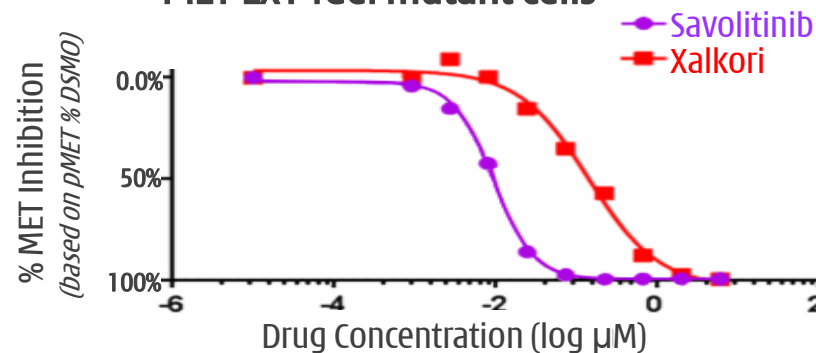
### 1. Competitive landscape outside China:

			Treatment Line	N	BICR <sup>[1]</sup> ORR	95% CI
Capmatinib (Novartis/ Incyte)	selective MET	ASCO 2019 #9004	2/3L	69	40.6% (28/69)	28.9%, 53.1%
		ASCO 2019 #9004	1L	28	67.9% (19/28)	47.6%, 84.1%
Tepotinib (Merck Serono)	selective MET	ASCO 2019 #9005	39% 1L, 61% ≥2L	51	45.1% (23/51)	31.1%, 59.7%
Xalkori® (Pfizer)	multi-kinase	WCLC 2018 #13453	38% 1L	65	32.3% (21/65) <sup>[2]</sup>	21%, 45% <sup>[2]</sup>
		WCLC 2018 #12937	Median 1L (1L-4L)	25	40.0% (10/25)	21%, 61%

### 2. Xalkori® a multi-kinase TKI - selective MET inhibitors reporting better response - superior selectivity.

	Savolitinib IC <sub>50</sub>	Xalkori® IC <sub>50</sub>	Savolitinib vs. Xalkori®
EBC1 Viability	2nM	19nM	10x
EBC1 pMET	1	39	40x
293T MET (wild type)	7	79	11x
293T MET (Ex14del)	9	140	16x

### 3. Savolitinib better target coverage in MET Ex14del mutant cells<sup>[3]</sup>



[1] BICR = blinded independent central review; [2] Investigator reviewed data (not BICR); [3] Paik, P.K., et al., Response to MET inhibitors in patients with stage IV lung adenocarcinomas harboring MET mutations causing exon 14 skipping. Cancer Discov. 2015. 5(8): p. 842-9.

# Savolitinib - MET Exon 14 deletion NSCLC <sup>[1]</sup>

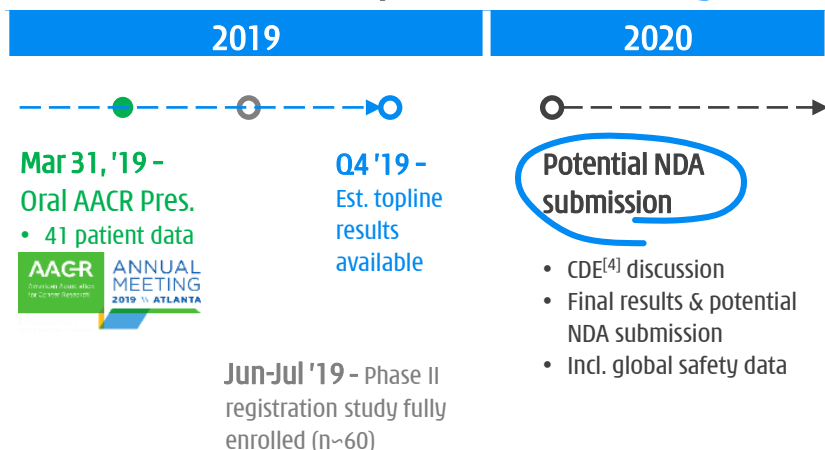
## Potential China NDA submission in 2020 <sup>[2]</sup>

### 4. Encouraging MET Exon14d NSCLC study China data at AACR 2019 <sup>[3]</sup>

- 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 <sup>[2]</sup>



### 6. Savolitinib monotherapy China market opportunity

		Annual Incidence	Estimated mPFS	Pricing Reference
Non-small Cell Lung Cancer <sup>[4]</sup>	100%	737,400		
MET Exon 14d NSCLC	2%	14,700	TBD	Tagrisso® -- China NRDL
MET gene ampl. NSCLC	2-4%	14,700 - 29,000		
Gastric Cancer	100%	442,300		
MET gene ampl. Gastric Cancer	4-10%	18,000 - 44,000		

Potential first savo monotherapy indication MET Exon 14d NSCLC

Two further MET-driven patient populations - savo monotherapy

[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.

# Savolitinib - 2L NSCLC<sup>[1]</sup> combo w/ TAGRISSO<sup>™</sup> osimertinib

## TATTON B Study at AACR 2019



...TATTON B<sup>[2]</sup> - ...**promising efficacy in MET+ T790M- Iressa/Tarceva failure patients**

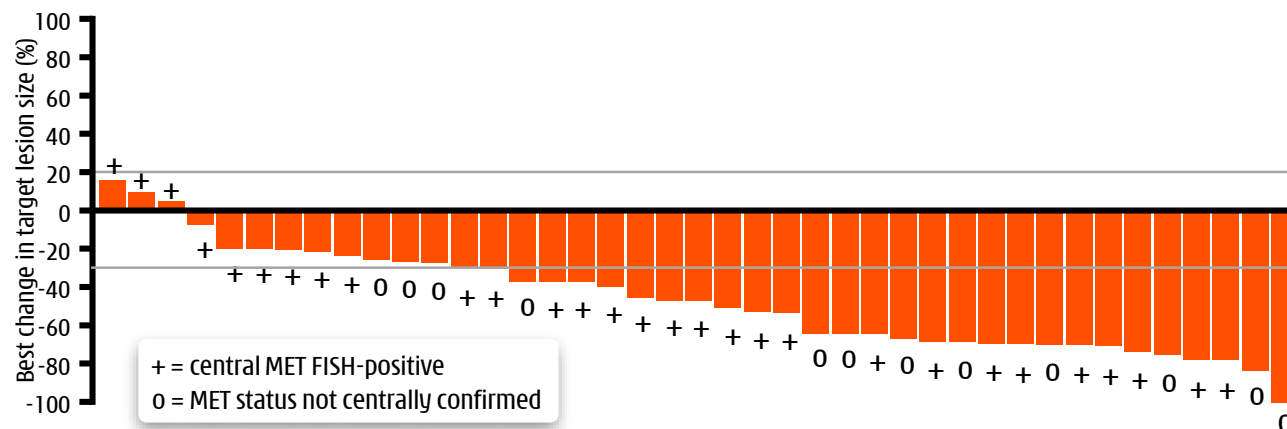
2L post Iressa<sup>®</sup>/ Tarceva<sup>®</sup>



... after 4 weeks on  
savolitinib combination.



Best response after treatment with savolitinib and Tagrisso	# pts	% Enrolled (n=46)	% Efficacy Evaluable (n=43)
Complete or partial response	24	52%	56%
Stable disease (≥6 weeks)*	16	35%	37%
Progressive disease	3	7%	7%
Not evaluable	3	7%	-
Time to response, median (IQ range)	43 days (40-43)		
Duration of response, median (IQ range)	7.1 months (4.1 - 10.7)		



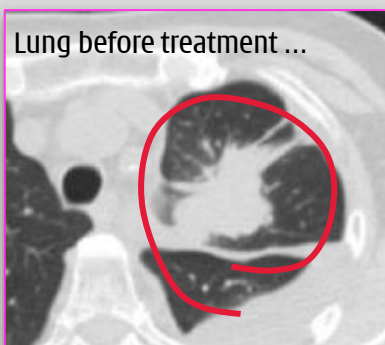
# Savolitinib - 2L/3L NSCLC<sup>[1]</sup> combo w/ TAGRISSO<sup>™</sup> osimertinib

## TATTON B Study at AACR 2019

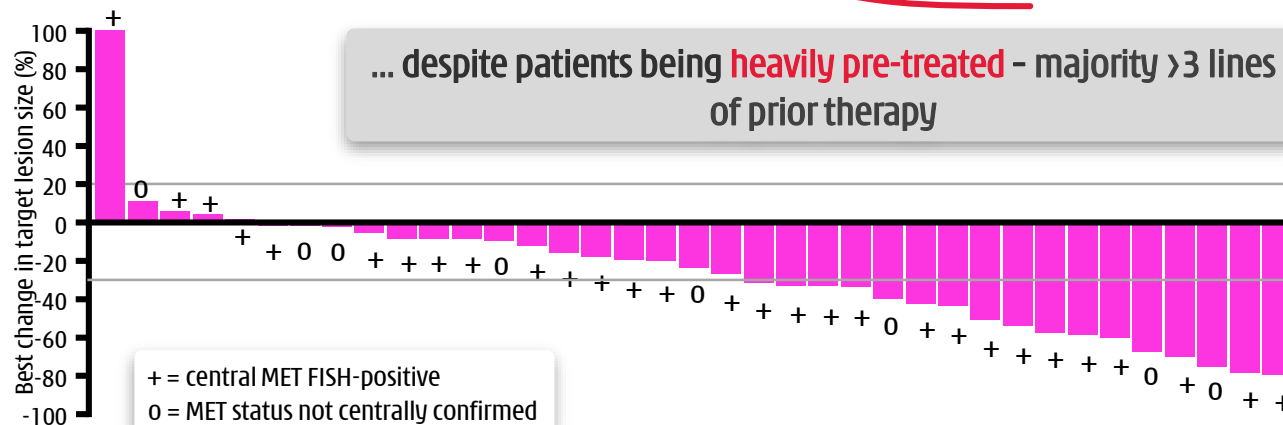


...TATTON B<sup>[2]</sup> - ...**promising efficacy in MET+ Tagrisso failure patients...**

### 2L/3L post Tagrisso<sup>®</sup>



Best response after treatment with savolitinib and Tagrisso	# pts	% Enrolled (n=48)	% Efficacy Evaluable (n=39)
Complete or partial response	12	25%	31%
Stable disease (≥6 weeks)*	21	44%	54%
Progressive disease	6	13%	15%
Not evaluable	9	19%	-
Time to response, median (IQ range)	46 days (43-51)		
Duration of response, median (IQ range)	9.7 months (5.5 - NC)		





# SAVANNAH Study

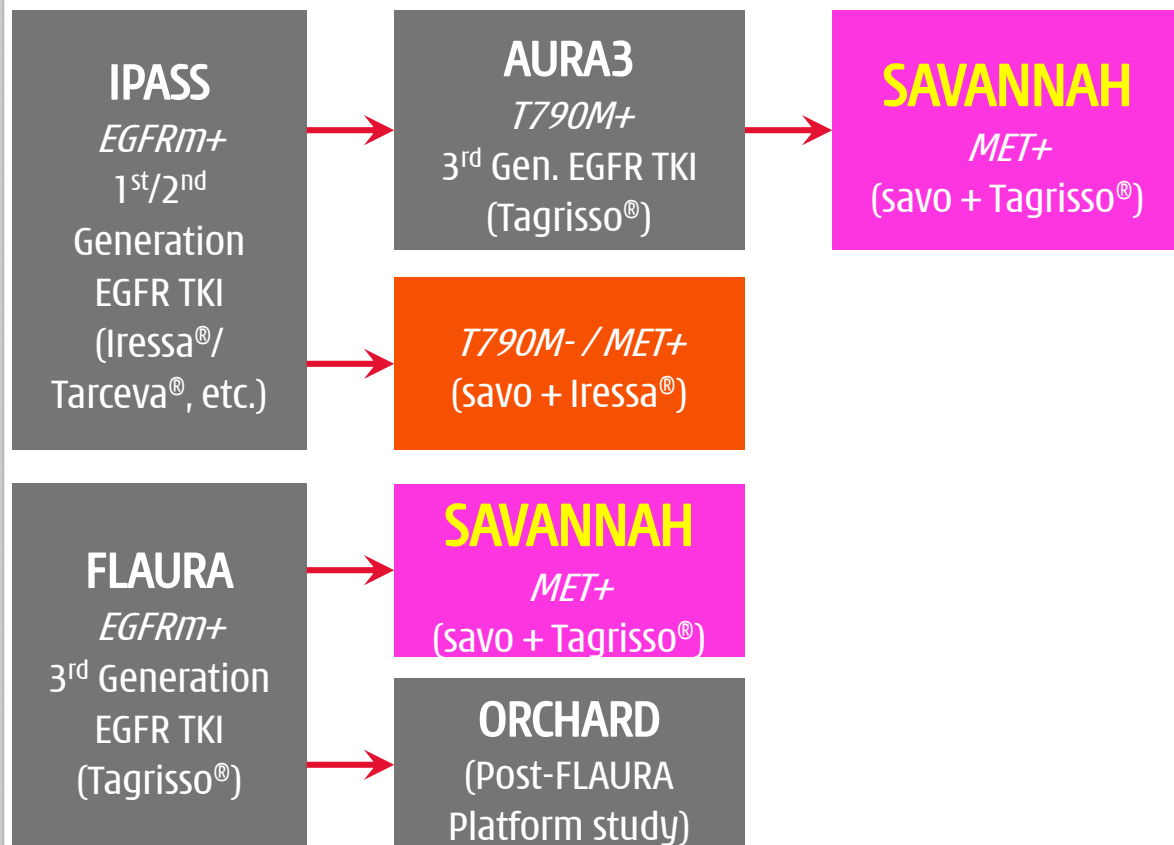
Encouraging TATTON data - led to the initiation of SAVANNAH



Addressing resistance with combinations

1<sup>st</sup> Line Metastatic

2<sup>nd</sup> Line+ Metastatic



## SAVANNAH (NCT03778229)

### 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.

### Weight-based dosing regimen:

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

### ORCHARD study:

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

# Savolitinib + Imfinzi® combination

## 1. Could **MET + PD-L1** inhibition be **synergistic**?

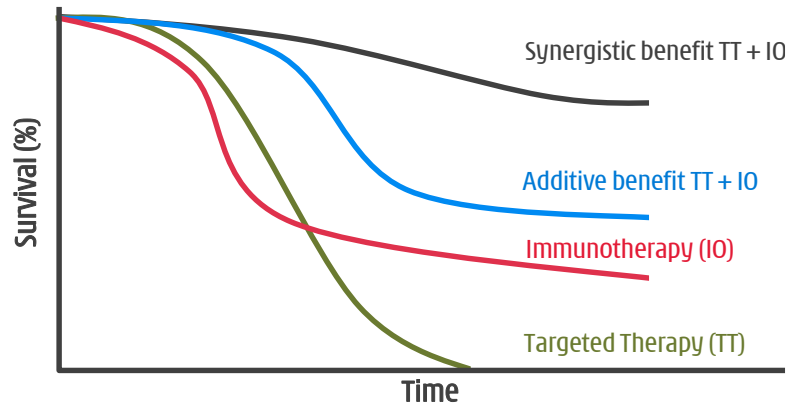
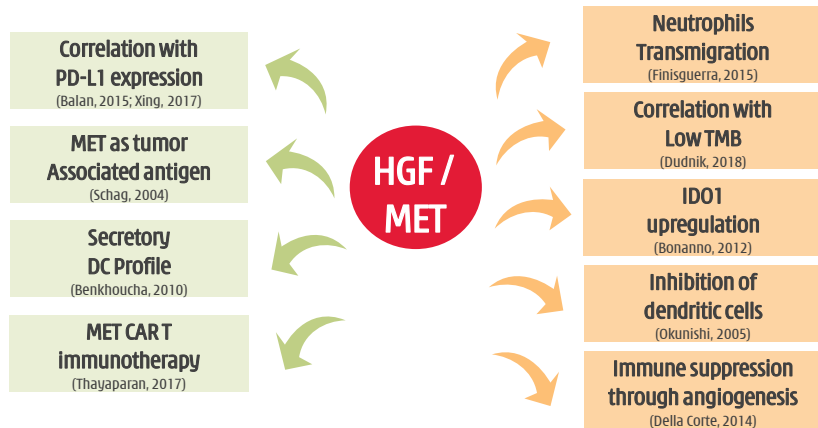


Illustration by Tracy L Rose MD MPH at ASCO GU 2019 presentation, showing what synergistic vs additive benefit could hypothetically look like; not based on clinical data.

## 2. **MET/HGF** complex interplay with immune system.



Papaccio et al Int J Molec Sciences, 2018; 19(3595)

## 3. PD-1/PD-L1s important in non-ccRCC but **need to see mature mPFS/mOS & further biomarker analysis** [1]

**MET+ Papillary RCC**  
(~\$1.0b)  
~8% of RCC  
~ 28k new patients/yr.

**MET- Papillary RCC**  
(~\$1.0b)  
~8% of RCC  
~ 28k new patients/yr.

**Other non-ccRCC**  
(~\$0.6b)  
~5% of RCC  
~ 16k new patients/yr.

**Savo mono.**  
All lines: (n=44)  
ORR 18.2%  
DCR 73.2%  
mPFS 6.2 mo.

**Keytruda® mono.**  
First line: (n=118)  
ORR 25.4%  
DCR 43.2%  
mPFS na

**Savo + Imfinzi®**  
All lines: (n=41)  
ORR 26.8%  
DCR na  
mPFS 5.3 mo.  
First line: (n=28)  
ORR 32.1%  
DCR na  
mPFS na  
*Interim Data*

**Tecentriq® + Avastin®**  
All lines: (n=39)  
ORR 25.6%  
DCR na  
mPFS na  
*Not confirmed ORR*




**Keytruda® mono. (all nRCC)**  
First line: (n=165)  
ORR 24.8%  
DCR 40.6%  
mPFS 4.1 mo.



**Other Operating Highlights – H1 2019**

# Other H1 2019 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 (PI3Kδ) - **Phase II dose selected** in China & expansion underway;
-  **US/EU Phase I sites open & screening** for both HMPL-523 & HMPL-689.

## Organization

-  **Accelerating expansion of New Jersey-based international C&R operations;**
-  **Establishing China oncology commercial team** - ~60 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?

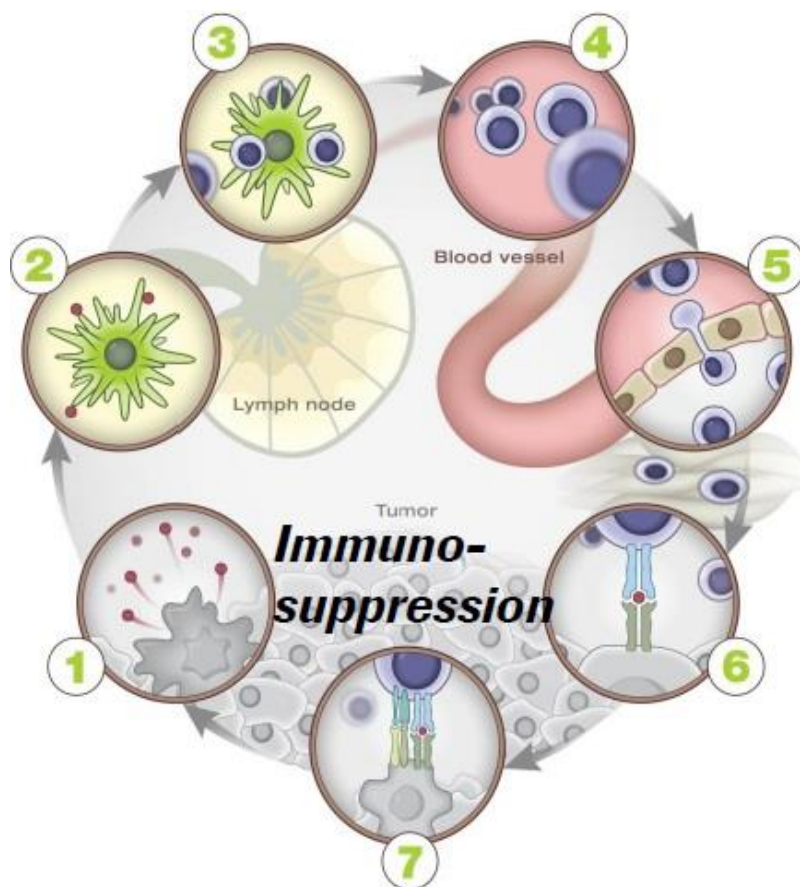
## Differentiated assets against multiple targets

### Priming & activations

- aOX40
- 4-1BB

### Antigen release

- MET (savolitinib)
- EGFR (epitinib/theliatinib)
- Syk (HMPL-523)
- PI3K $\delta$  (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)

- IDO1
- AhR1
- TIM3
- TCBs

- Pre-clinical - small molecule
- Pre-clinical - antibody

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



CHI-

MED



3

**Pipeline & Potential Upcoming Events**

# Portfolio summary

Multiple waves of innovation – progressing rapidly



Dose Finding / Safety Run-In	Proof-of-Concept	Registration Intent	Marketed
Fruquintinib + Tyvyt (PD-1) Solid Tumors <sup>[1]</sup>	Savolitinib MET Exon 14 deletion NSCLC →	Savo + Tagrisso (SAVANNAH) 2L/3L Tagrisso-refractory MET+ NSCLC	Elunate (Fruquintinib capsules) ≥3L Colorectal cancer
Surufatinib + Tuoyi (PD-1) Solid Tumors <sup>[1]</sup>	Savo / Savo + Imfinzi (CALYPSO) X2: PRCC & ccRCC	Savolitinib MET Exon 14 deletion NSCLC →	SXBX <sup>[3]</sup> Pills Coronary artery disease
HMPL-523 (Syk) Indolent NHL <sup>[1][2]</sup>	Savolitinib (VIKTORY) MET+ Gastric cancer	Fruquintinib + Taxol (FRUTIGA) 2L Gastric cancer	>10 other Rx / OTC drugs
HMPL-689 (PI3Kδ) Indolent NHL <sup>[1]</sup>	Savolitinib (CCGT 1234B) MET+ Prostate cancer	Surufatinib (SANET-p) Pancreatic NET	
Fruquintinib + Tyvyt (PD-1) Solid tumors <sup>[1]</sup>	Fruquintinib 3L/4L Colorectal cancer <sup>[1]</sup> →	Surufatinib (SANET-ep) → Non-Pancreatic NET	
Fruquintinib + genolimzumab (PD-1) Solid tumors	Surufatinib → 2L Pancreatic NET	Surufatinib 2L Biliary Tract cancer	
Surufatinib + Tuoyi (PD-1) Solid tumors	Savolitinib + Iressa → 2L 1 <sup>st</sup> Gen EGFR TKI ref. NSCLC		
HMPL-453 (FGFR1/2/3) Solid tumors	Fruquintinib + Iressa 1L EGFRm+ NSCLC		
	HMPL-523 → Indolent NHL		
	HMPL-523 + azacitidine AML		
	HMPL-523 Immune thrombocytopenia purpura		
	HMPL-689 Indolent NHL		
	Epitinib Glioblastoma		

**Global Innovation**

**China Oncology**

**Existing China Business**

**IN TRANSITION**

[1] In planning / imminent; [2] Proof-of-concept in Australia; [3] SXBX = She Xiang Bao Xin (cardiovascular); [4] Drugs licensed from third parties. Targets: Savolitinib = MET; Fruquintinib = VEGFR1/2/3; Surufatinib = VEGFR1/2/3 / FGFR1 / CSF-1R; HMPL-523 = Syk; HMPL-689 = PI3Kδ; Epitinib = EGFRm in the brain; Theliatinib = EGFR wild-type; HMPL-453 = FGFR1/2/3. Indications: NHL = Non-Hodgkin's Lymphoma; NET = Neuroendocrine tumors; RCC = Renal cell carcinoma; AML = Acute myeloid leukemia; ITP = Immune thrombocytopenia; NSCLC = Non-small cell lung cancer.

# Potential upcoming events

H1-19

H2-19

H1-20



Global  
Innovation

Savo + Imfinzi®  
Papillary RCC (CALYPSO)  
Ph. II Interim Data

Savo + Tagrisso®  
NSCLC (TATTON)  
Ph. Ib Data (AACR)

HMPL-523 (Syk)  
Indolent NHL  
Ph. I Start (US/EU)

HMPL-689 (PI3Kδ)  
Indolent NHL  
Ph. I Start (US/EU)

Savo Lung Cancer  
Anticipate further  
Ph.II/III studies

Savo  
2L gastric (VIKTORY)  
Ph. II Data

Savo + Imfinzi®  
Papillary RCC (CALYPSO)  
Ph. II Interim Data

Suru  
P NET (US/EU)  
Ph. II/III Start\*\*

Savo + Tagrisso®  
NSCLC (SAVANNAH)  
Ph.II Interim

Fruq  
3L/4L colorectal (US/EU)  
Ph. II/III Start\*\*

Fruq / Suru + PD-1  
Initiation of U.S  
development



China  
Oncology

Savo  
NSCLC Exon14del  
Ph. II Data (AACR)

Suru  
2L Biliary tract  
Ph.II/III Start

Fruq / Suru  
PD-1 combos  
Phase I Start

Fruq + Taxol®  
2L gastric (FRUTIGA)  
1<sup>st</sup> Ph. III Interim

Savo  
NSCLC Exon14del  
Reg. Study Enrolled

Suru  
Non-P NET (SANET-ep)  
Ph.III Interim

Suru  
Non-P NET (SANET-ep)  
Ph.III Data\*

Suru  
Non-P NET (SANET-ep)  
NDA Submission

Fruq  
3L NSCLC (FALUCA)  
Ph. III Data\*

Reimbursement  
Possible Elunate®  
NRDL inclusion

HMPL-306  
IDH 1/2 inhibitor  
Ph.I Start

Fruq + Taxol®  
2L gastric (FRUTIGA)  
2<sup>nd</sup> Ph. III Interim

Savo  
NSCLC Exon14del  
NDA Submission\*\*

Suru  
P NET (SANET-p)  
Ph.III Interim

Suru  
2L Biliary tract  
Ph. Ib/II Data\*

HMPL-523 (Syk)  
Indolent NHL  
Reg. Study Start\*\*

\* 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.



4

## H1 2019 Financial Results, Cash & Guidance



# H1 2019 Financial results

R&D expense accelerated to **\$74.5m** in first 6 months



Global  
Innovation



China  
Oncology



Existing China  
Business

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

[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.

(US\$ millions, except per share data) 40



# Cash position & 2019 Guidance

**\$384 million** in available cash resources <sup>[1]</sup>

## Cash Position

(at end June 2019)

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



Global  
Innovation



China  
Oncology

(US\$ millions)	2019 Previous Guidance	2019 Current Guidance
Research & Development Expenses	(160) - (200)	(130) - (170)
Adj. (non-GAAP) Group Net Cash Flows <sup>[4]</sup>	(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. <sup>[5]</sup>

[1] Including cash, cash equivalents, short-term investments & unutilized banking facilities; [2] Short-term investments: deposits over 3 months; [3] From Bank of America Merrill Lynch, Deutsche Bank, Hong Kong Shanghai Banking Corporation; [4] Adjusted (non-GAAP) Group net cash flows excluding financing activities. Please refer to the slides titled "Use of Non-GAAP Measures and Reconciliation" for more information and a reconciliation of these measures to the most comparable GAAP measure; [5] Potential for non-dilutive finance derived from the disposal of certain non-core Commercial Platform assets.



## 5 Summary

# Objectives for existing assets 2019-2021



## 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



## China Oncology

- **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 & PI3Kδ
- **Expanded life cycle development** on all assets, incl. PD-1 combos



## Existing China Business

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

# 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





## Appendix

A1

Strategies

Global Innovation

P47

China Oncology

P55

Existing China Business

P61

A2

Product Candidate Details

P67

A3

Further Corporate Information

P105

CHI-

MED



A1a

## Strategies – Global Innovation

*Pushing the envelope on our most valuable assets*

# One of China's largest & most established discovery platforms in oncology



## Global step-change innovation

- *Aiming for multiple potential first-in-class assets*



## Kinase selectivity - enable combos

- *Limit off-target toxicity & address TKI resistance*



## Discovery of broad range of assets against novel targets





# Attack cancer from multiple angles at same time

## Immune Desert

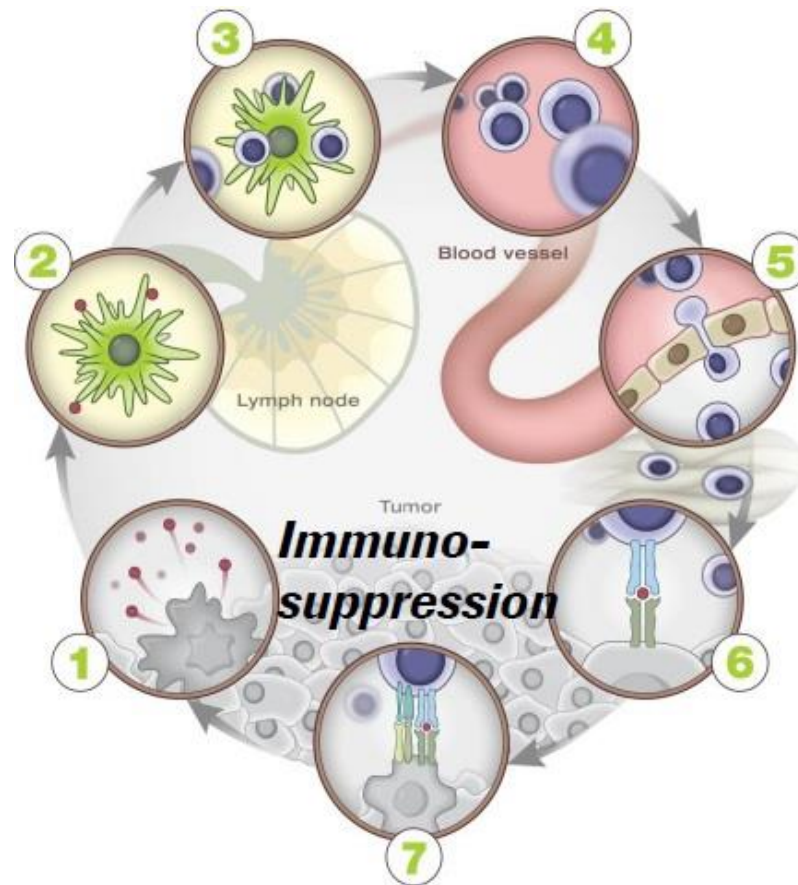
Insufficient T cell response

- Chemotherapies
- Vaccines
- CAR-T (pro-inflammatory strategies)
- TCB's

## Antigen Release

Aberrant genetic drivers

- Targeted therapies (small molecule & antibody)



## Excluded Infiltrate

Inadequate T cell homing

- Anti-angiogenics
- Stromal targets
- Chemokines
- Vaccines

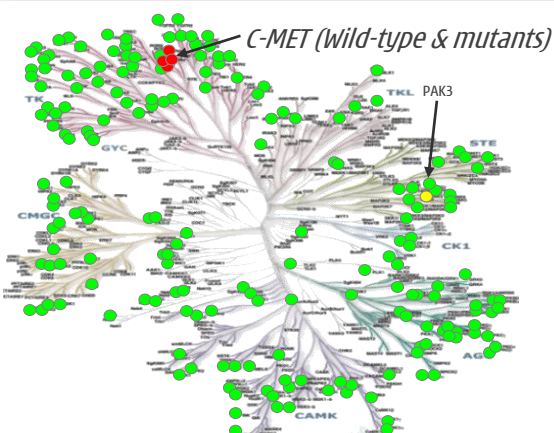
## Inflamed

Inactivated T cell response

- Immunotherapies (address negative regulators)
- Vaccines

**Need combinations of potent, yet tolerable drugs against specific targets**

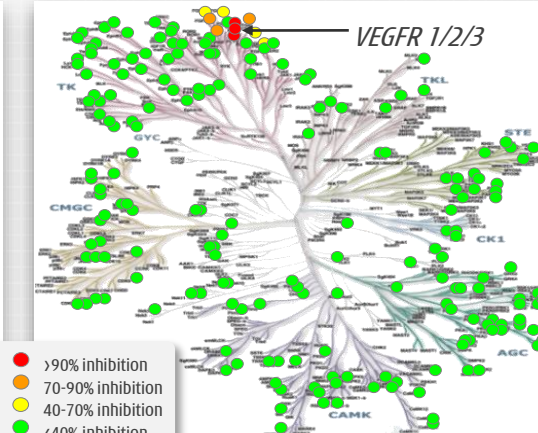
# Our advanced medicinal chemistry provides superior selectivity & safety profiles...



## Savolitinib

~1,000 times  
more selective to c-MET  
than next kinase (PAK3) [5]

Screening at  
1  $\mu$ M against  
253 Kinases



**ELUNATE®**  
Fruquintinib Capsules

~250 times  
more selective to  
VEGFR3 than next non-  
VEGFR kinase (Ret) [6]

• >90% inhibition  
• 70-90% inhibition  
• 40-70% inhibition  
• <40% inhibition

Non-small cell lung cancer (NSCLC)	Discontinuations as % Enrolled		
	Due to AE	Withdrawn / Other	Total [1]
<b>Monotherapy - Tagrisso® / savolitinib</b>			
Tagrisso® (osimertinib)	6%	6%	13%
savolitinib 600mg QD PRCC (for reference only - not NSCLC) [2]	9%	5%	14%
<b>Combination - Tagrisso® + savolitinib</b>			
savolitinib 600mg QD + Tagrisso® [3]	29%	6%	35%
<b>Approved treatments in NSCLC</b>			
Zykadia® (ceritinib)	10%	10%	20%
Cyramza® (ramucirumab) + Taxotere®	15%	21%	37%
Keytruda® (pembrolizumab) 2mg/kg	10%	26%	37%
Opdivo® (nivolumab)	15%	4%	20%
Chemo doublet (platinum + pemetrexed)	11%	17%	27%
Taxotere® (docetaxel)	13%	22%	36%

3rd-Line Metastatic CRC	FRESCO Study Mainland China		CONCUR Study (China, HK, Taiwan) [4]	
	Elunate®	Placebo	Stivarga®	Placebo
<b>VEGFR on-target related AEs:</b>				
Hypertension $\geq$ G3	21.2%	2.2%	12.5%	8.3%
Hand-Foot Syndrome (Palmar-plantar), $\geq$ G3	10.8%	0.0%	17.0%	0.0%
<b>Off-target (i.e. non-VEGFR) related AEs:</b>				
Hypophosphatemia, $\geq$ G3	0.0%	0.0%	8.0%	0.0%
Hypokalemia, $\geq$ G3	0.7%	0.7%	6.3%	0.0%
Rash/desquamation, $\geq$ G3	0.0%	0.0%	4.4%	0.0%
Lipase increase, $\geq$ G3	0.0%	0.0%	6.3%	1.7%
<b>Hepatic function (Liver function) AEs:</b>				
ALT increased, $\geq$ G3	0.7%	1.5%	7.1%	3.3%
AST increased, $\geq$ G3	0.4%	0.7%	8.9%	0.0%
Blood bilirubin increased, $\geq$ G3	1.4%	1.5%	8.9%	8.3%
<b>Tolerability:</b>				
AE Leading to dose interruption	35.3%	10.2%	68.8%	25.0%

[1] Total discontinuations = Discontinuations NOT due to Disease Progression or Death; [2] September 2017 Journal of Clinical Oncology; [3] 2019 AACR # CT032, CT033; [4] Efficacy & safety of regorafenib monotherapy in Chinese patients with previously treated metastatic colorectal cancer: subgroup analysis of the CONCUR trial; R Xu; [5] W. Su, et al, 2014 American Association of Cancer Research; [6] Sun et al., Cancer Biology & Therapy 15:12, 1635--1645; December 2014.



# Global clinical drug portfolio (1/2)

## Savolitinib

Potential First-in-class small molecule selective MET inhibitor

**Indications:** MET-driven NSCLC; RCC; Gastric; Prostate cancer

**Dosed to-date:** [2] ~1,000 patients

**Summary Data:** NSCLC - Tagrisso® EGFR TKI refractory combinations:  
Post 1<sup>st</sup>-gen TKI (n=43): ORR 52-56%  
Post 3<sup>rd</sup>-gen TKI (n=39): ORR 25-31%  
PRCC (n=44): ORR 18%; mPFS 6.2mo.

**SAVANNAH global  
Ph.II/reg. underway[3]  
Tagrisso® + savo**

## Fruquintinib

Potential Best-in-class small molecule selective VEGFR 1/2/3 inhibitor

**Indications:** Colorectal; NSCLC; Gastric cancer

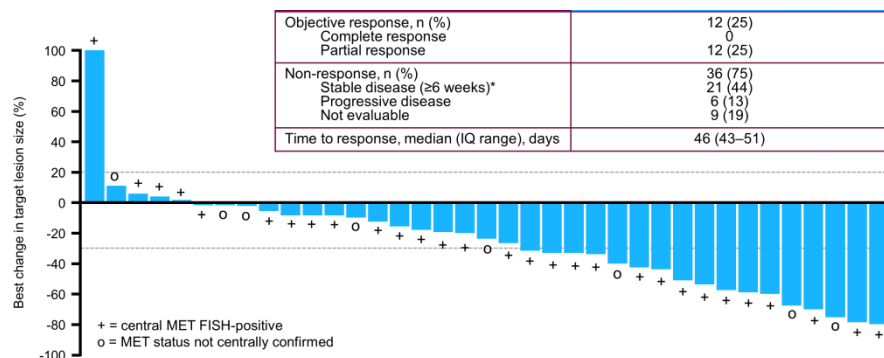
**Dosed to-date:** ~1,650 patients in trials

**Launched in CRC  
Nov 2018 in China**

**Summary Data:** 3L CRC (n=416): mOS 9.3mo. vs. 6.6mo. (SoC)  
3L NSCLC (n=91): ORR 13%; mPFS 3.8mo. vs 1.1 mo. (SoC)  
1L NSCLC (Iressa® combo) (n=50): ORR 76% [1]  
2L Gastric (Taxol® combo) (n=28): ORR 36%



### Osimertinib plus savolitinib for patients with disease progression on prior third-generation EGFR-TKI: Preliminary anti-tumor activity

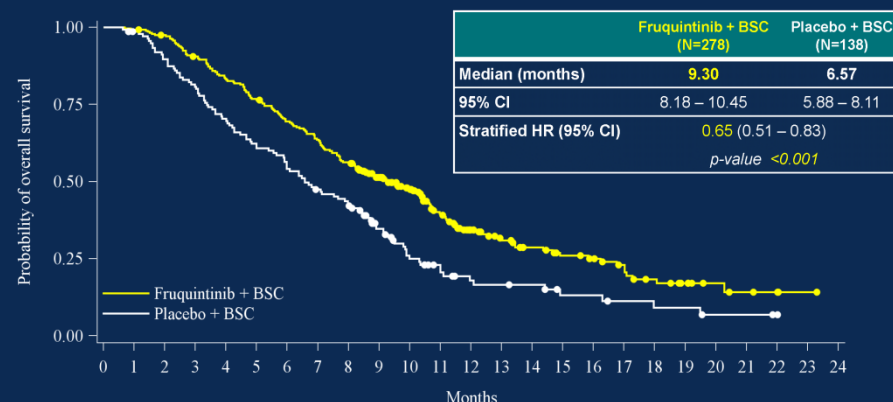


\*Includes 5 patients with unconfirmed partial response.  
Waterfall plot of the best percentage change in target lesion size, assessed in the safety analysis set. Best change in target lesion size is the maximum reduction from baseline or the minimum increase from baseline in the absence of a reduction.  
Gen, generation; OSI, osimertinib; SAVO, savolitinib

### PRESENTED AT: ASCO ANNUAL MEETING '17

#### Overall Survival (Primary Endpoint)

FRESCO clearly succeeded in meeting the primary efficacy endpoint of OS



MET = mesenchymal epithelial transition receptor, VEGFR = vascular endothelial growth factor receptor, NSCLC = non-small cell lung cancer, RCC = renal cell carcinoma, PRCC = papillary RCC, CRC = colorectal cancer;

[1] Efficacy Evaluable Patients. Data cut-off: Oct. 10, 2017; [2] Dosed to-date = patients in all clinical trials (treatment & placebo); [3] Phase II registration intent study subject to regulatory discussions.

# Global clinical drug portfolio (2/2)

## Surufatinib

Unique small molecule VEGFR 1/2/3, FGFR1 & CSF-1R inhibitor

**Indications:** Neuroendocrine tumors (pNET/ep-NET); Thyroid; Biliary Tract

**Dosed to-date:**<sup>[1]</sup> ~800 patients

**Ep-NET Phase III  
Met Primary Endpoint**

**Summary Data:** PhII interim pNET (n=41): ORR 17%; mPFS 19.4mo.  
PhII interim ep-NET (n=40): ORR 15%; mPFS 13.4mo.

## HMPL-523

Potential First-in-class small molecule selective Syk inhibitor

**Indications:** Indolent non-Hodgkin's lymphoma; AML; Immunol.

**Dosed to-date:** >150 pts. & ~118 healthy vol.

**Summary Data:** Dose escalation (5 cohorts)<sup>[2]</sup>  
FL (n=10): ORR 30%  
CLL/SLL (n=3): ORR 33%

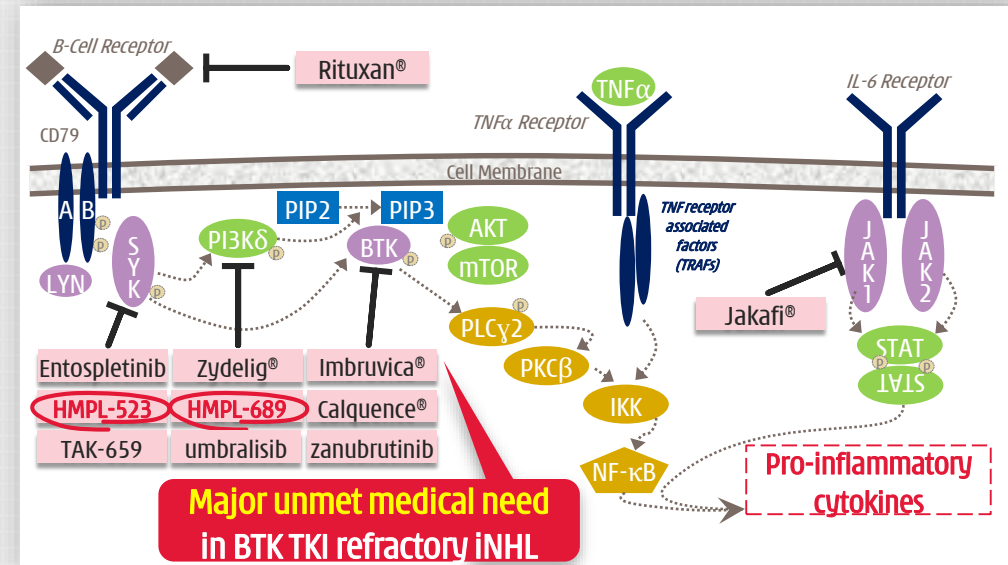
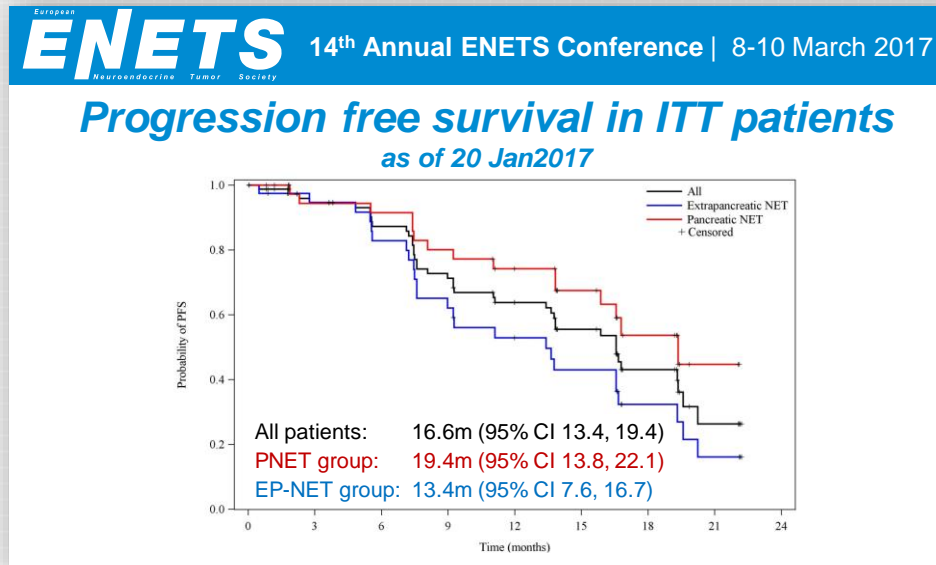
## HMPL-689

Potential Best-in-class small molecule selective PI3Kδ inhibitor

**Indications:** Indolent non-Hodgkin's lymphoma

**Dosed to-date:** ~40 pts. & ~48 healthy vols.

**Summary Data:** Phase I dose escalation data not yet published



[1] Dosed to-date = patients in all clinical trials (treatment & placebo); [2] American Society of Hematology. Blood, vol. 132 no. Suppl 1 5324 (Nov 2018); VEGFR = vascular endothelial growth factor receptor, FGFR1 = fibroblast growth factor receptor 1, CSF-1R = colony stimulating factor-1 receptor, Syk = spleen tyrosine kinase, PI3Kδ = Phosphatidylinositol-3-Kinase delta, pNET = pancreatic neuroendocrine tumors, ep-NET = non-pancreatic neuroendocrine tumors, AML = acute myeloid leukemia, FL = follicular lymphoma, CLL = chronic lymphocytic leukemia, SLL = small lymphocytic leukemia.

# 5 assets in global development

## ...US/EU clinical & regulatory team fully operational



Program	Treatment	Indication	Target patient	Study name	Sites	Dose finding / safety run-in	Proof-of-concept	Registration
<b>Savolitinib</b> MET	Savolitinib + Tagrisso®	NSCLC	2L/3L EGFRm; Tagrisso® ref.; MET+	SAVANNAH	Global	Oxnard/Ahn - DF/SMC		
	Savolitinib + Tagrisso®	NSCLC	2L EGFRm; EGFR TKI ref.; MET+	TATTON	Global	Oxnard - Dana Farber		
	Savolitinib + Imfinzi® (PD-L1)	Papillary RCC	All	CALYPSO	UK/Spain	Powles - Queen Mary's		
	Savolitinib + Imfinzi® (PD-L1)	Clear cell RCC	VEGFR TKI refractory	CALYPSO	UK/Spain	Powles - Queen Mary's		
	Savolitinib	Gastric cancer	MET+	VIKTORY	S Korea	Lee - Samsung Med. Ctr		
	Savolitinib + Taxotere®	Gastric cancer	MET+	VIKTORY	S Korea	Lee - Samsung Med. Ctr [1]		
	Savolitinib + Taxotere®	Gastric cancer	MET over expression	VIKTORY	S Korea	Lee - Samsung Med. Ctr [1]		
	Savolitinib	Prostate cancer	MET+	CCTG 1234B	Canada	Kolinsky/Muk'jee/Ong/Chi		
<b>Fruquintinib</b> VEGFR 1/2/3	Fruquintinib	Colorectal cancer	3L/4L; Stivarga®/Lonsurf® ref./intol.		US	Eng /Desari - MD And. [2]		
	Fruquintinib + Tyvyt® (PD-1)	Solid tumors	1L		US	In planning		
<b>Surufatinib</b> VEGFR 1/2/3; FGFR1; CSF-1R	Surufatinib	Pancreatic NET	2L; Sutent®/Afinitor® refractory		US	Dasari/Yao - MD Anderson		
	Surufatinib + Tuoyi® (PD-1)	Solid tumors				In planning		
<b>HMPL-523</b> Syk	HMPL-523	Indolent NHL			Australia	N/A		
	HMPL-523	Indolent NHL			US	Fowler - MD Anderson [3]		
<b>HMPL-689</b> PI3Kδ	HMPL-689	Healthy volunteers			Australia			
	HMPL-689	Indolent NHL			US	Ghosh/Cohen - Levine/Emory [3]		

Full Ph.II data at AACR Apr 2019

Prelim. PoC at ASCO GU Feb 2019

Prelim. PoC H2 2019

Planning US/EU registr. study based on FRESCO/US Ph.Ib

Planning US/EU registr. study based on China Ph.II/US Ph.Ib

Global Ph.I/PoC data-set now at n >140

Data-set now emerging in China Ph.I (n ~40)

[1] Further patient enrollment directed to savolitinib monotherapy arm due to the high efficacy observed; [2] in U.S., in E.U. Tabernero - Vall d'Hebron & Sobrero - Genova; [3] In planning.

Note: MET = mesenchymal epithelial transition receptor, VEGFR = vascular endothelial growth factor receptor, EGFRm = epidermal growth factor receptor mutation, FGFR1 = fibroblast growth factor receptor 1, CSF-1R = colony stimulating factor-1 receptor, Syk = spleen tyrosine kinase, PI3Kδ = Phosphatidylinositol-3-Kinase delta, NSCLC = non-small cell lung cancer, RCC = renal cell carcinoma, NHL = Non-Hodgkin's Lymphoma, AACR = American Association of Cancer Research annual meeting, ASCO GU = American Society of Clinical Oncology Genitourinary Cancer Symposium, PoC = Proof of Concept.

# Global Innovation

Main targets for 2019-2021



 **Aim for Savolitinib / Tagrisso® combo NDA submission**

 **Build out US/EU development operation**

- *US/EU C&R operation set up in Florham Park, NJ*



 **Accelerate development of 4 un-partnered global assets**

- *Fruq (ex-China) & suru registration studies & exploration of combos with PD-1s;*
- *Syk & PI3K $\delta$  registration studies & exploration of combos with other TKIs*

 **Aim to continue to move novel drug candidates into global development each year**





A1b

## Strategies – China Oncology

*Next-gen oncology drugs to meet major needs in China*



# China oncology - ~24% of world's cancer patients<sup>[1]</sup>



## Industry's attention turning to unmet medical need in China oncology

- *Regulatory reforms in China - addressing low SoC<sup>[2]</sup>*
- *Major investment inflow*



## Chi-Med is a first mover

- *Elunate<sup>®</sup> launch in 3L mCRC; First ever in China<sup>[3]</sup>*
- *Deep pipeline - 8 clinical drug candidates with 5 registration studies underway/set to start in China*



## Major commercial opportunity

- *National Drug Reimbursement; Medical coverage*



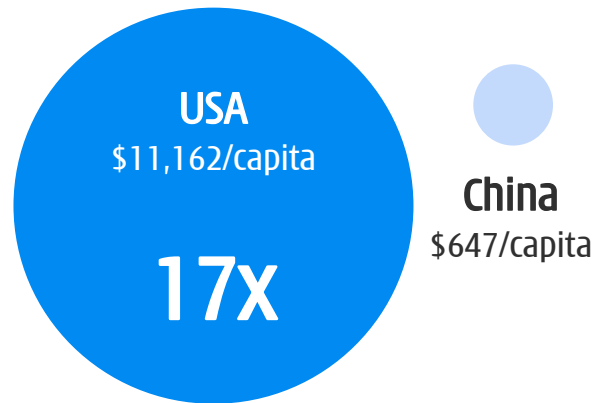
[1] Global Cancer Observatory, WHO, ACS, NCCR, Frost & Sullivan analysis;

[2] SoC = Standard of Care; [3] Believed to be the first ever China-discovered novel oncology drug to receive full NDA approval in China.

# China now world's 2<sup>nd</sup> largest pharma market

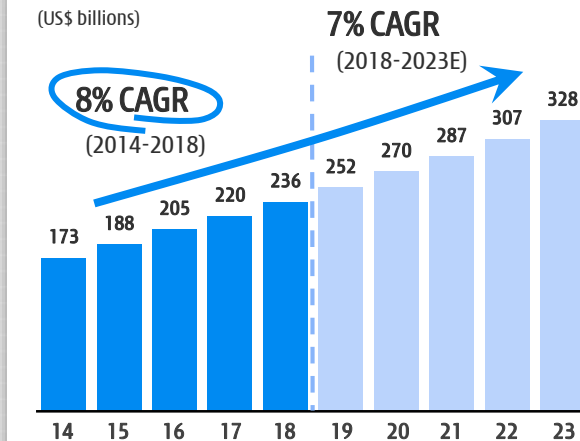
...investment, approvals & access all accelerating rapidly

## Per Capita Healthcare Spending



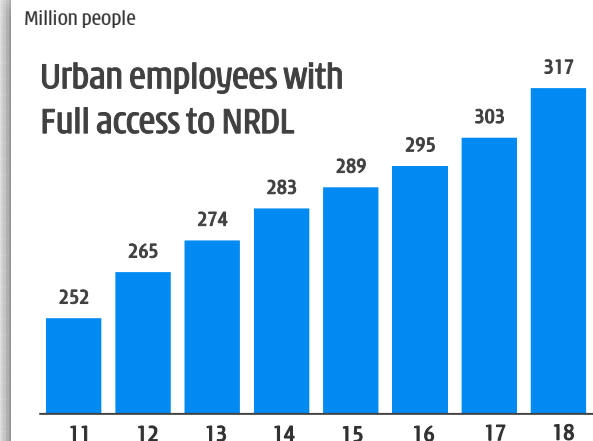
Source: Frost & Sullivan (2018)

## PRC Pharmaceutical Market Size

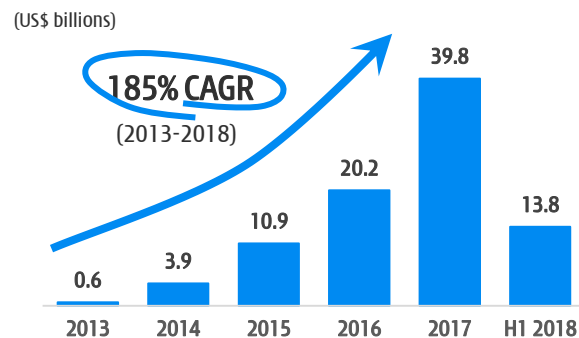


Source: Frost & Sullivan

## Medical Insurance Coverage <sup>[1]</sup>

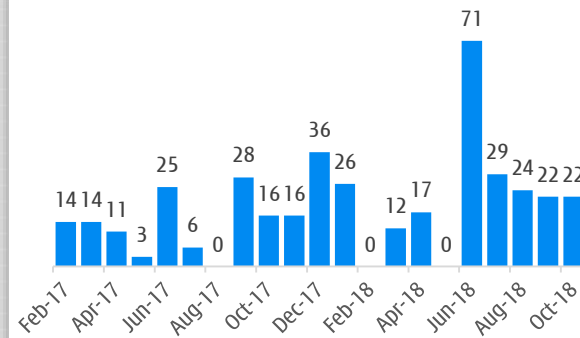


## PRC Healthcare VC/PE Funds <sup>[2]</sup>



Source: McKinsey; ChinaBio 2018 report

## Number of Priority Review NDAs <sup>[3]</sup>



Source: McKinsey; National Medical Products Administration

## Improved Access since 2017

- 128 western drugs added to NRDL;
- Further 17 oncology drugs added to NRDL in Oct 2018 (15 in Jul 2017);
- Essential drug list expanded from 520 to 685 molecules. Including oncology.

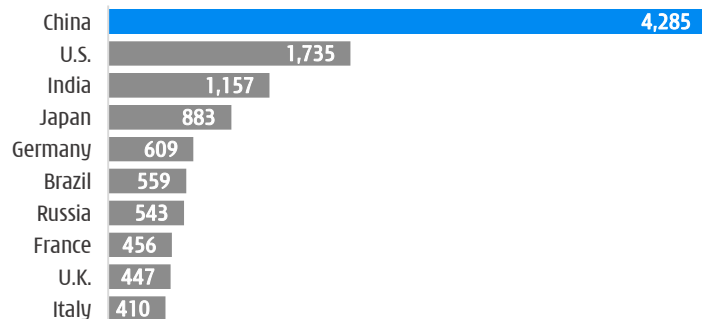
Source: McKinsey

[1] Urban Basic Medical Care Insurance (for both employees & residents) - total persons covered at year-end. National Bureau of Statistics (2017); includes rural residents from 2017 and beyond; [2] Funds raised; [3] NDA = New Drug Application. Note: CAGR = Compound annual growth rate.

# Cancer is a major unmet need in China

## ...investments in launches/access starting to have an impact

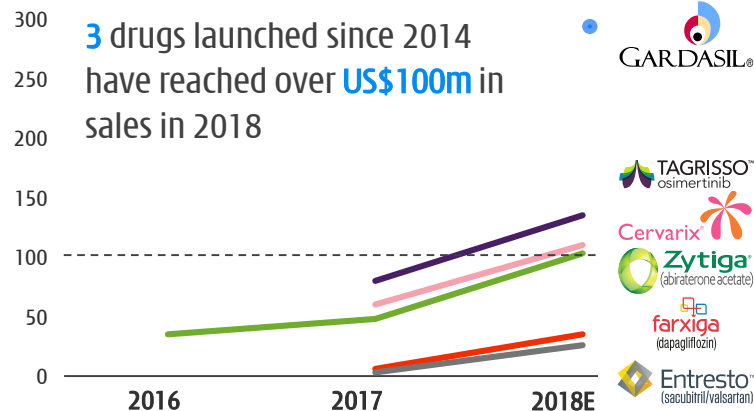
### Cancer Incidence in China (2018)



Source: Global Cancer Observatory, WHO

(Incidence '000s)

### Rapid uptake of new launches in China



Source: McKinsey; RDPAC 2018 estimated based on Q3 RDPAC data

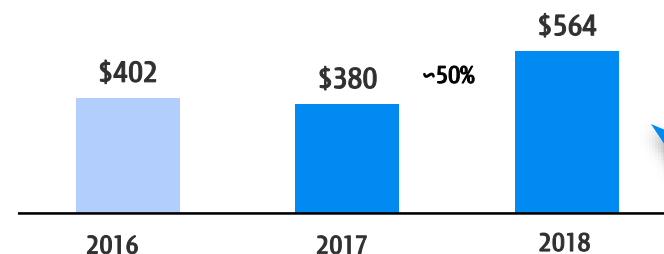
### Novel drugs post NRDL inclusion



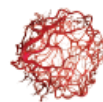
**Herceptin®**  
trastuzumab

(Bar Chart US\$ millions)

Price per cycle: US\$4,505 **-66%** US\$1,538 (RMB10,364)

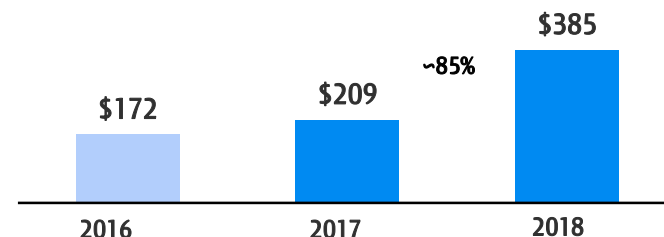


Major  
Increases in  
Access,  
Volume &  
Penetration



**AVASTIN®**  
bevacizumab

Price per cycle: US\$11,608 **-62%** US\$4,447 (RMB29,970)



Source: McKinsey; RDPAC ex-manufacturer sales 2016-2018. Frost & Sullivan. Price per cycle assumptions: Herceptin 440mg 20ml, ~RMB22,267 avg tender price, RMB7,600 NRDL price; Avastin 100mg/4ml, ~RMB5,216 avg tender price, RMB1,998 NRDL price. US\$ figures based on calculations assuming a constant exchange rate of US\$1 = RMB6.74.

# 8 assets in China development

...fruq launched - savo/suru NDAs & Syk/PI3K $\delta$  PoC ahead



Program	Treatment	Indication	Target patient	Study name	Sites	Dose find / safety run-in	Proof-of-concept	Registration	
Savolitinib MET	Savolitinib	NSCLC	MET Exon 14 deletion		China	Lu Shun - SH Chest Hosp.			Enrolled n >60
	Savolitinib + Iressa®	NSCLC	2L EGFRm; Iressa® ref.; MET+		China	Wu Yilong - GD General			
	Savolitinib	Gastric cancer	MET+		China	Shen Lin - BJ Univ. Tumor			
Fruquintinib VEGFR 1/2/3	Fruquintinib	Colorectal cancer	≥3L; chemotherapy refractory	FRESCO	China	Li Jin - Fudan Univ.			Launched Nov 2018
	Fruquintinib + Taxol®	Gastric cancer	2L	FRUTIGA	China	Xu Ruihua - Sun Yat Sen			Interim OK April 2019
	Fruquintinib	NSCLC	3L; chemotherapy refractory	FALUCA	China	Lu Shun - SH Chest Hosp.			Publish 2019
	Fruquintinib + Iressa®	NSCLC	1L EGFRm		China	Lu Shun - SH Chest Hosp.			
	Fruquintinib + genolimzumab (PD-1)	Solid tumors			China	Li Jin - Fudan Univ.			
	Fruquintinib + Tyvyt® (PD-1)	Solid tumors			China	Bai Yuxian - Harbin Med. U.			Interim H1 2020
Surufatinib VEGFR 1/2/3; FGFR1; CSF-1R	Surufatinib	Pancreatic NET	All	SANET-p	China	Xu Jianming - #5 Med. Ctr.			Met primary endpoint June 2019
	Surufatinib	Non-Pancreatic NET	All	SANET-ep	China	Xu Jianming - #5 Med. Ctr.			
	Surufatinib	Biliary Tract cancer	2L; chemotherapy refractory		China	Xu Jianming - #5 Med. Ctr.			
	Surufatinib + Tuoyi® (PD-1)	Solid tumors			China	Shen Lin - BJ Univ. Tmr.			
HMPL-523 Syk	HMPL-523 + azacitidine	Acute Myeloid Leuke.	1L		China	Wang/Qi - CN Hem. Hosp.			Planning China Ph.II/III in several iNHL types Ph.Ib data now n >140
	HMPL-523	B-cell malignancies	All		China	Multiple leads by sub-types			
	HMPL-523	ITP	All		China	Yang - CN Hem. Hosp. [1]			
HMPL-689 PI3K $\delta$	HMPL-689	Indolent NHL			China	Cao/Zhou - Fudan/Tongji			Data-set emerging in China Ph.I (n ~40)
Epitinib EGFR	Epitinib	NSCLC	EGFRm with brain metastasis		China	Wu Yilong - GD General			
	Epitinib	Glioblastoma	EGFR gene amplified		China	Ying Mao - SH Huashan			
Theliatinib EGFR wt	Theliatinib	Esophageal cancer	EGFR over expression		China	Shen Lin - BJ Univ. Tumor [2]			
HMPL-453 FGFR 1/2/3	HMPL-453	Solid tumors			China	Xu Ruihua - SYS			

[1] In planning; [2] Discontinued. ITP = immune thrombocytopenic purpura; PoC= proof of concept.

# China Oncology

Main targets for 2019-2021



## Establish Elunate® as the best-in-class VEGFR TKI in China market

- *Work with Lilly to maximize penetration & sales performance;*
- *Aggressively expand PD-1 combination collaborations & broader LCI program*



## Launch our un-partnered oncology drugs

- *Target surufatinib NDA in neuroendocrine tumors;*
- *Expand Oncology Commercial Organization in China*



## Savolitinib NDA in MET Exon 14 NSCLC



## Progress development pipeline

- *Syk & PI3Kδ into registration studies & aim to establish PoC for epitinib, theliatinib & FGFR;*
- *Aim for further novel drug candidates into early development each year*



CHI-

MED



A1C

## Strategies – Existing China Business

*Cash generation & China commercial know-how / infrastructure*

# Existing China business



## Chi-Med spent 17 years building China commercial presence

- *Valuable know-how in operating within the complex medical system in China*
- *Clear operating synergies with our novel oncology assets*
- *China operations/JVs have generated >\$210 million dividends since inception*



## China pharma industry grew at circa. 10% CAGR over last 15 years<sup>[1]</sup>

- *Aging population; rapid urbanization; economic development*

[1] Frost & Sullivan;

People crowd the outpatient service registration center at Zhengzhou First, China's largest hospital, in Zhengzhou, Henan province, June 28, 2015. Photographer: Xu Xiaolin/Sixth Tone.



# Chi-Med's Commercial Platform in China

## Integrated platform built from ground up



### 2 National House-Hold Name Brands



### Major Commercial & Production Scale

>2,400 RX & ~900 OTC sales people in over 330<sup>[1]</sup> cities & towns in China.

Drugs in ~24,400 hospitals detailing ~88,400 doctors.

Sold ~4.8 billion doses of medicine in 2018.

### Leadership Market Shares

Market leader in the sub-categories/markets in which we compete<sup>[2]</sup>:

<b>SXBX pill:</b> <sup>[3][4]</sup>	~17%
Rx Cardiovascular TCM	
<b>Banlangen:</b> <sup>[5]</sup>	~54%
OTC Anti-viral /flu TCM	
<b>FFDS tablet:</b> <sup>[6]</sup>	~38%
OTC Angina TCM	

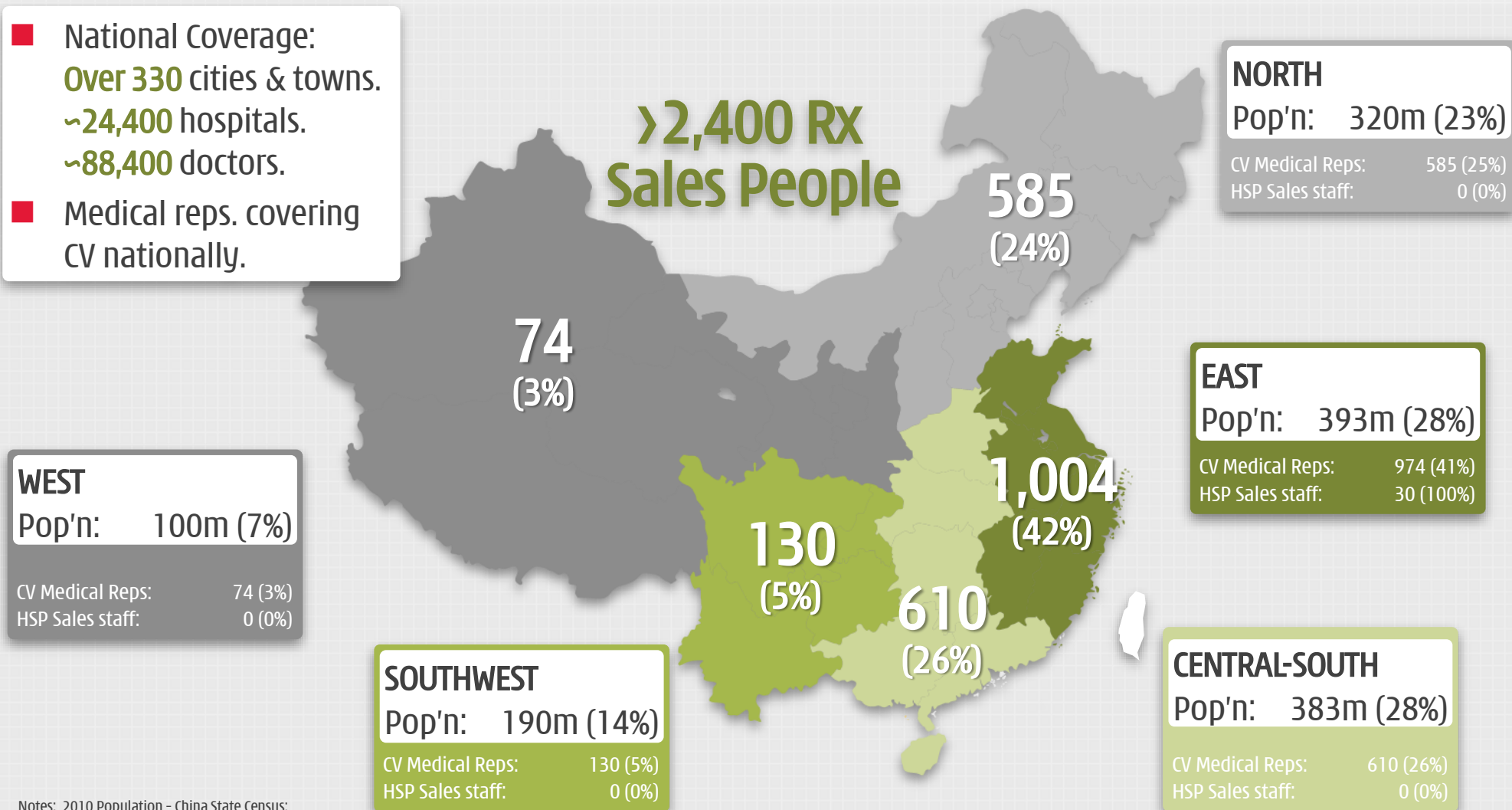
### JVs with 3 Major China Pharmas



[1] 330 cities & towns covered by Prescription Drug Business and 600 cities & towns including OTC business; [2] Frost & Sullivan 2018 market share data; [3] China coronary heart disease oral Chinese patented drugs market share; [4] She Xiang Bao Xin Pill ("SXBX pill") - Rx Coronary artery disease; [5] Banlangen Granules ("Banlangen") - OTC Antiviral; [6] Fu Fang Dan Shen tablets ("FFDS") - OTC Angina.

# Established Rx Commercial Platform in Mainland China...

## Chi-Med management run all day-to-day operations



Notes: 2010 Population - China State Census;  
CV = Cardiovascular  
Chi-Med Rx sales team data = June 30, 2019

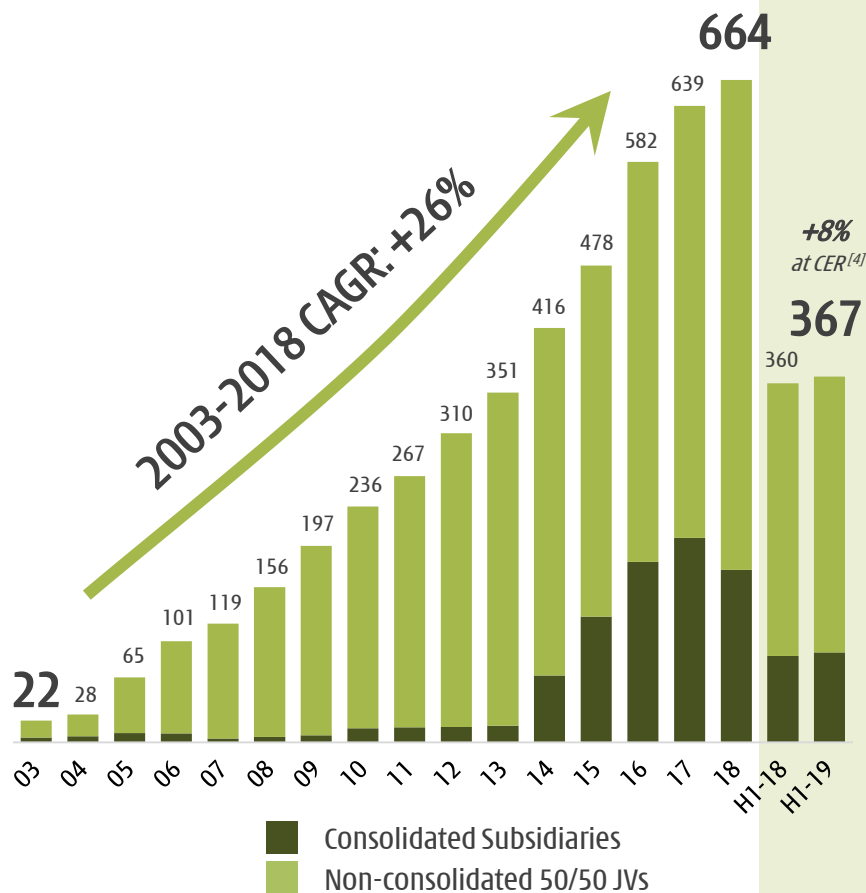
# Chi-Med's Commercial Platform in China

Proven track record, ~\$300 million in net income since inception



## Revenues (Non-GAAP) <sup>[1][2]</sup>

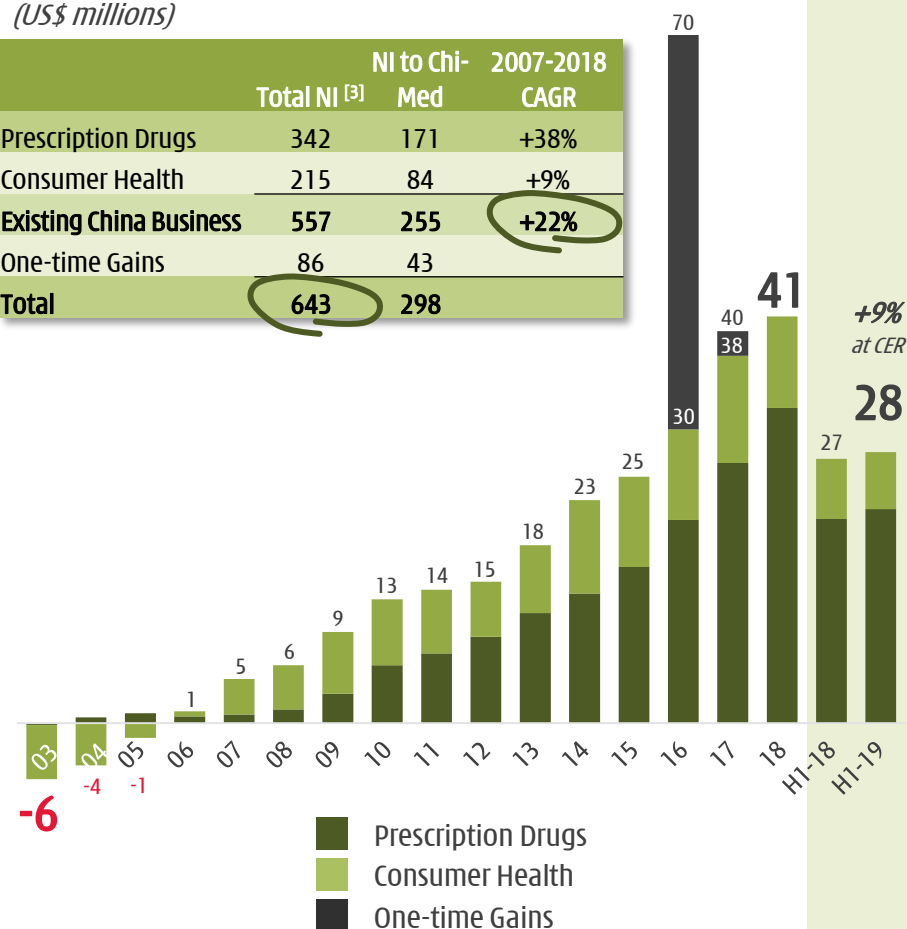
(US\$ millions)



## Net Income/(Loss) attrib. to Chi-Med

(US\$ millions)

	Total NI <sup>[3]</sup>	NI to Chi-Med	2007-2018 CAGR
Prescription Drugs	342	171	+38%
Consumer Health	215	84	+9%
Existing China Business	557	255	+22%
One-time Gains	86	43	
Total	643	298	






[1] 2003-2006 incl. disco. operation; [2] Excluding Guanbao (from 2011 until divested in Sep 2017); [3] Based on aggregate Non-GAAP net income / (loss) of consolidated subsidiaries and non-consolidated joint ventures of Commercial Platform, please see appendix "Non-GAAP Financial Measures and Reconciliation"; [4] at Constant Exchange Rate (at CER), 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 slide titled "Non-GAAP Financial Measures and Reconciliation" for more information and a reconciliation of these measures to the most comparable GAAP measure.



# Existing China Business

Plans for 2019-2021



-  **Continue organic growth**
  - *Focus on proprietary prescription drug products*
-  **Build out synergies with China Oncology Organization**
-  **Strategically evaluate potential for M&A**
-  **Focus on cash generation**



A2

## Product Candidate Details

*Further details on each drug candidate*

# Superior safety allows for combinations

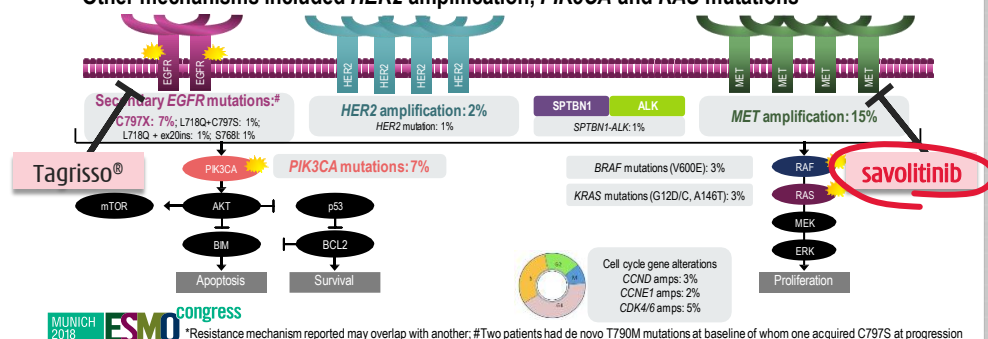
## TKI + TKI combos to address acquired resistance



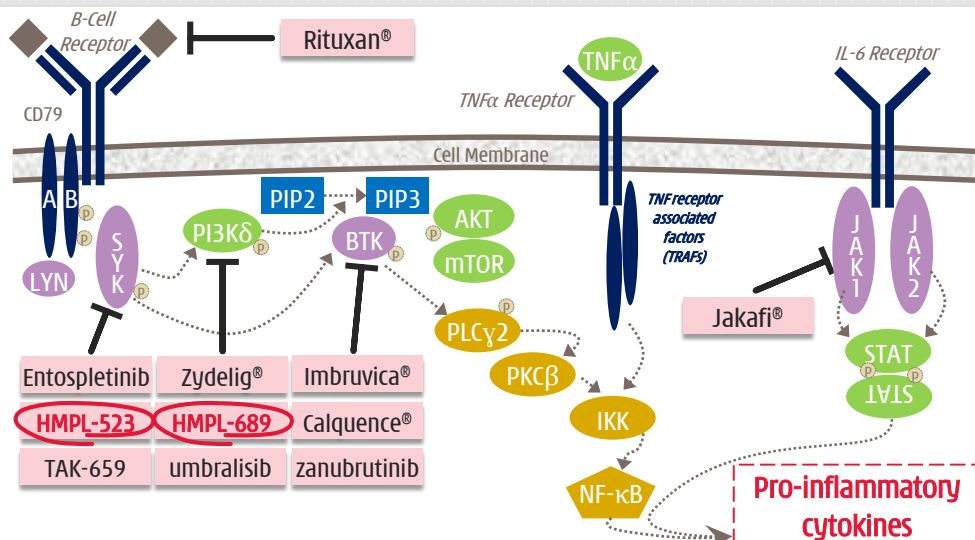
- **MET amplification** is the most common resistance mechanism for Tagrisso®.
- Requires addition of **MET inhibitor - savolitinib** - in combo with Tagrisso®.

### RESULTS: CANDIDATE ACQUIRED RESISTANCE MECHANISMS WITH OSIMERTINIB (n=91)\*

- No evidence of acquired EGFR T790M
- The most common resistance mechanisms were **MET amplification** and **EGFR C797S** mutation
- Other mechanisms included **HER2 amplification**, **PIK3CA** and **RAS** mutations



- **C481S** or **PLCγ** are the most common resistance mechanisms for Imbruvica®.
- Invalidating BTK inhibitor requires a **possible Syk, PI3Kδ &/or BTK TKIs**.





A2a

**Savolitinib (AZD6094)**

*Potential first-in-class selective MET inhibitor*



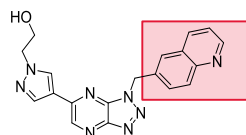
# Savolitinib (AZD6094)

## Potential first-in-class selective MET inhibitor

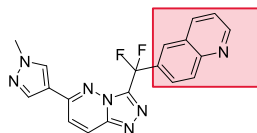
### 1. Strong potential to become first selective MET inhibitor approved in certain indications.

- ✓ Clear clinical efficacy observed in **non-small cell lung ("NSCLC"), kidney, gastric and colorectal** cancers.
- ✓ Partnered with AstraZeneca - **key comp. advantages in NSCLC (Tagrisso® combo) & biomarker testing.**

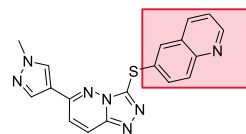
### 3. Savolitinib design eliminates renal toxicity first generation of selective MET inhibitors encountered - ~900 patients involved in clinical studies to date.



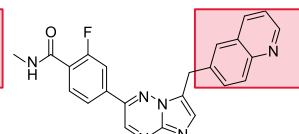
Pfizer PF-04217903



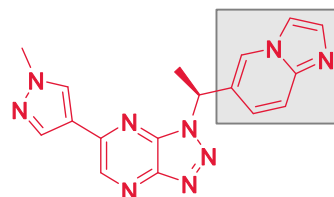
Janssen JNJ-38877605



Lilly SGX-523



Novartis/Incyte INC-280



savolitinib

*2-quinolinone metabolite in humans in 1<sup>st</sup>-gen MET compounds has dramatically reduced solubility and appeared to crystallize in the kidney resulting in obstructive toxicity.*

### 2. MET is aberrant in many tumor settings. [7]

Indication	MET			New Cases (2018)	
	Amplification	Mutation	Over-Expression	Global	China
Gastric	10%	1%	41%	1,033,700	442,300
Non-small Cell Lung Cancer	4%/16%/30% [1]	2% [2]	39%	1,779,800	737,400
Head & Neck	17-39%	11% [3]	46% [4]	887,700	137,000
Colorectal	10%	3%	65%	1,801,000	426,700
Papillary Renal Cell Carcinoma	64%	70-100% [5]	55%	45,400	3,700
Clear Cell Renal Cell Carcinoma	54%	NA	35%	281,300	57,500
Esophagus	8%	NA	92%	572,000	271,600
Prostate	NA	NA	54/83% [6]	1,276,100	99,300

### 4. AstraZeneca collaboration & 2016 amendment.

- \$20m received upfront (Dec 2011);
- \$120m in development/approvals milestones (\$25m received as of June 2019);
- Several hundred million in commercial milestones;
- Development costs: AZ pay 100% ex-China (excl. \$50m by Chi-Med) & 75% development cost in China (Chi-Med 25%);
- **From 9% up to 18% tiered royalty ex-China [8]** & 30% flat rate China royalty on all product revenues.

[1] MET amplification in non-small cell lung cancer patients occurs in approximately 4% of patients not previously exposed to systemic therapies and in approximately 16% to 30% of patients with acquired resistance to EGFR inhibitors; [2] MET Exon 14 skipping mutation only; [3] Oropharynx squamous cell cancer only; [4] Head and neck squamous cell cancer only; [5] Type 1 papillary renal cell carcinoma only; [6] MET expression is increased with progression of prostate cancer, which is 54% of lymph node metastases and 83% of bone metastases; [7] Company estimates considering Frost & Sullivan data, National Central Cancer Registry of China and publicly available epidemiology data; [8] Base royalty of 9%-13%. Additional 5% royalty subject to approval in the papillary renal cell carcinoma (PRCC) indication, for a total of 14%-18% tiered royalty. After total aggregate sales of savolitinib have reached \$5bn, the royalty will step down over a two-year period, to an ongoing royalty rate of 10.5% to 14.5%.



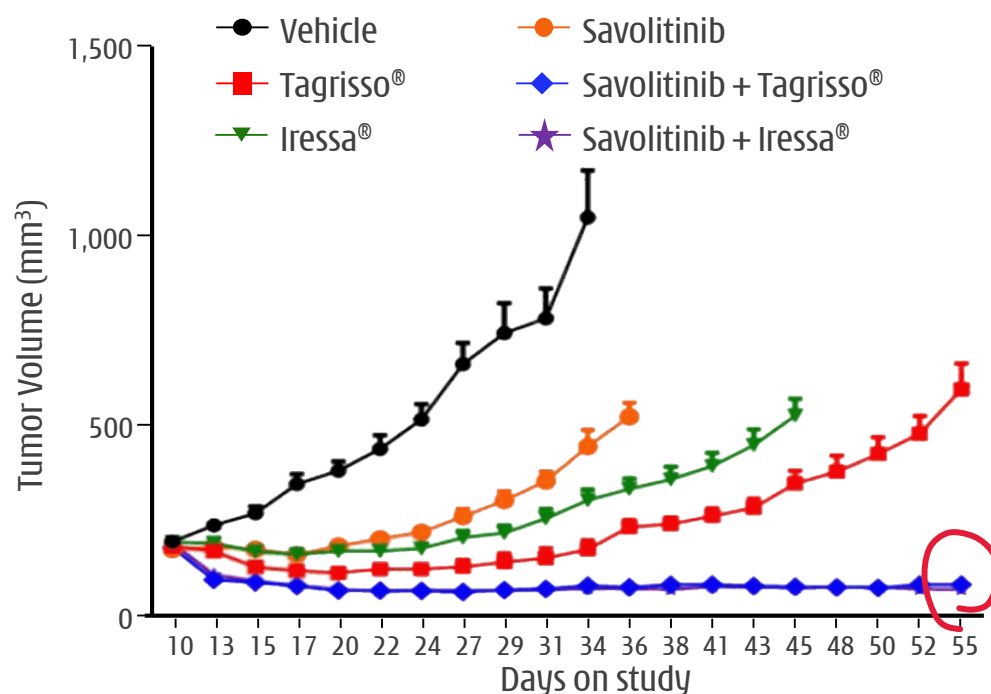
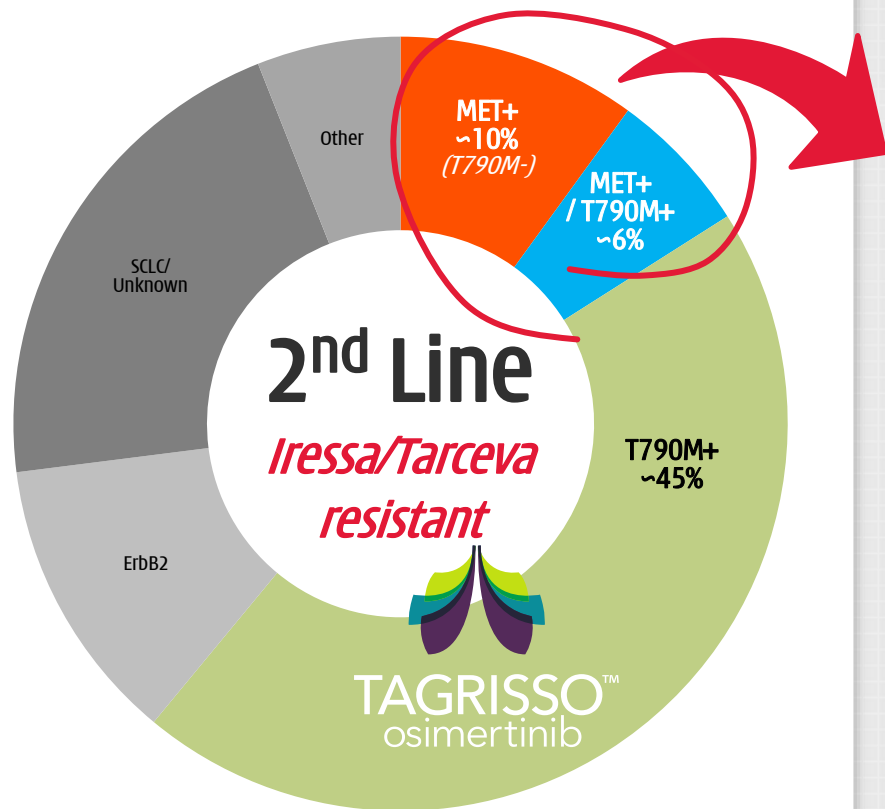
# Savolitinib - 2L EGFRm NSCLC

Very strong preclinical rationale for combination w/ EGFR-TKIs

1. 2<sup>nd</sup> Line NSCLC is a **fast and attractive indication for savolitinib** to go after. Also important unmet medical need and potential **Breakthrough Therapy** area.

2. Potential in **EGFR-TKI resistant NSCLC**:

- ✓ Must **shut down both EGFRm & MET** signaling pathways;
- ✓ **Prolonged tumor growth suppression** by combining savolitinib with Tagrisso® (osimertinib - EGFR/T790M) or Iressa® (gefitinib/EGFR) in **MET+ / T790M-** patients.



# Savolitinib - 2L NSCLC<sup>[1]</sup> combo w/ IRESSA<sup>®</sup> gefitinib

## Encouraging in MET+ / T790M-, next step under discussion

IRESSA<sup>®</sup>  
gefitinib

CHI-  
MED

### Savo / Iressa<sup>®</sup> combo in 1<sup>st</sup> gen. EGFRm-TKI refractory patients<sup>[2]</sup>...outstanding response in MET+ / T790M-

WCLC 2017	MET+ / T790M+ (n = 23)	MET+ (T790M-) (n = 23)	MET+ / T790M unk. (n = 5)
Confirmed response	2 (9%)	12 (52%)	2 (40%)
Stable disease ≥ 6 weeks	9 (39%)	7 (30%)	2 (40%)
Progressive disease / death	7 (30%)	3 (13%)	0
Not Evaluable	5 (22%)	1 (4%)	1 (20%)

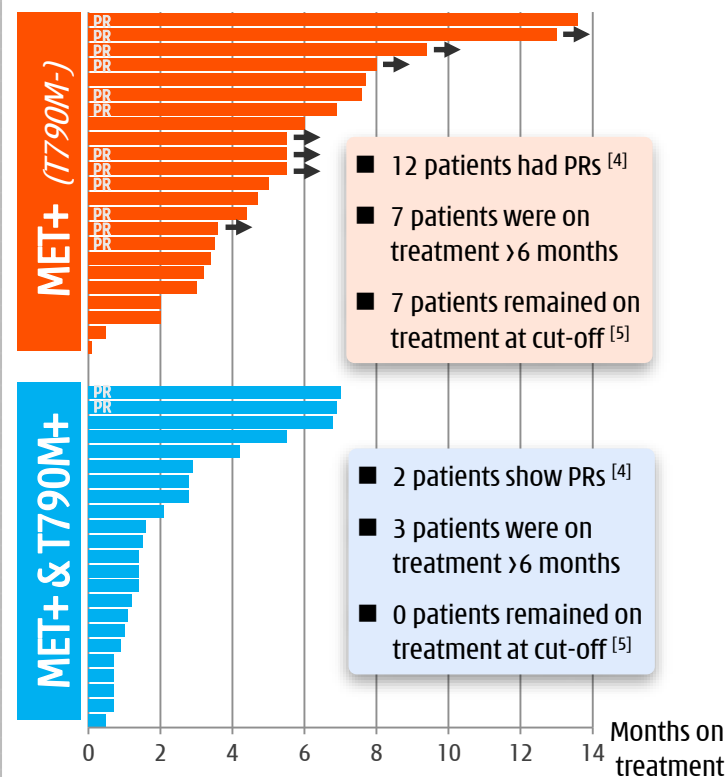
MET status all centrally confirmed.

### ...vs. TATTON B data (savo / Tagrisso<sup>®</sup> combo)<sup>[3]</sup>

	MET+ / T790M+ (n = 11) WCLC 2017 <sup>[2]</sup>	MET+ (T790M-) (n = 46) AACR 2019 <sup>[3]</sup>
Confirmed response	6 (55%)	24 (52%)
Stable disease ≥ 6 weeks	NA (43% central confirm.)	16 (35%)
Progressive disease / death	NA (0 central confirm.)	3 (7%)
Not Evaluable	NA (0 central confirm.)	3 (7%)

MET status locally or centrally confirmed.

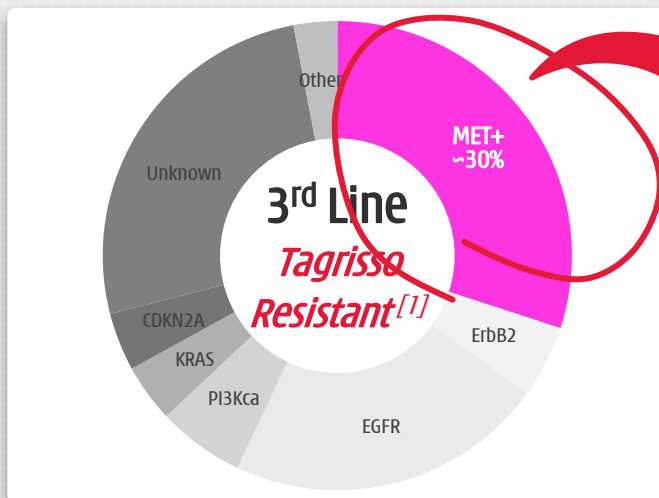
### ...Iressa<sup>®</sup> combo - ~6mo. Duration of Response in MET+ / T790M- patients



[1] EGFRm NSCLC; [2] WCLC 2017 - Yang J-J, et al. A Ph.Ib Trial of savolitinib plus gefitinib for patients with EGFR-mutant MET-amplified advanced NSCLC; [3] AACR 2019 - Sequist, *et al.* TATTON Phase Ib expansion cohort: Osimertinib plus savolitinib for patients (pts) with EGFR-mutant, MET-amplified NSCLC after progression on prior epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI); [4] PR = Partial Response; [5] Aug 21, 2017.

# Savolitinib - 2L/3L NSCLC<sup>[1]</sup> - TAGRISSO<sup>™</sup> osimertinib resistant

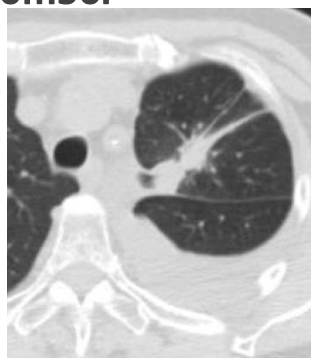
## MET+ driven resistance in ~30% of patients



**3 out of 3 MET+ patients responded to savo/Tagrisso<sup>®</sup> combo.**



LUL Mass Pre-Treatment



6 wks. on savo/Tag. Treatment

### Tagrisso<sup>®</sup> resistant tissue & ctDNA analysis<sup>[2]</sup>



Pt	EGFR mutation	# Prior Therapies	Prior 3 <sup>rd</sup> gen TKI	TISSUE (NGS, FISH)	PLASMA ctDNA (NGS)
1	L858R	1		METamp, T790 WT	METamp, T790M ND
2	Del19	1		-	T790M ND
3	Del19	2	Y	-	T790M ND
4	L858R (de novo T790M)	2	Y	METamp, EGFRamp T790M (germline)	-
5	L858R	3	Y	T790wt, EGFRamp	T790M ND
6	L858R	4	Y	T790 WT	T790M ND
7	Del19	3	Y	-	T790M ND
8*	Del19	3		T790M/C797S	T790M/C797S
9	L858R	4	Y	T790 WT	-
10	Del19	3	Y	-	PIK3CA E545K, PIK3CA amp, T790M ND
11	Del19	2	Y	METamp, EGFRamp, T790 WT	T790M ND
12	Del19	2	Y	-	T790M/C797S
13	Del19	9		T790 WT	-
14	Del19	2	Y	T790 WT	T790M ND
15	Del19	1		T790 WT	FGFR1 D60N, FGFR1 amp, T790M ND
16	L858R	2		METamp, T790 WT	MET, EGFRamp, T790M ND
17	L858R	3	Y	T790 WT	T790M ND
18	Del19 (de novo T790M)	3		SCLC, T790 WT	T790M ND, EGFRamp
19	Del19	3	Y	T790 WT	T790M/C797S, METamp, EGFRamp
20	L858R	2		METamp, EGFRamp, T790 WT	-
21	L858R	3		-	T790M/C797S, EGFRamp
22*	L858R	1		MET amp, T790 WT	-
23	Del19	4	Y	-	T790M/C797S

(-) Testing not performed; EGFR - Epidermal Growth Factor Receptor; TKI- Tyrosine Kinase Inhibitor; amp - amplification; WT - wild type; ND - not detected

# Safety & tolerability

Tagrisso® & savo both highly selective/tolerable monotherapies



US FDA Approval	Treatment	Disease setting	n	Efficacy		Discontinuations as % Enrolled		
				ORR	Median PFS (mo.)	Due to AE	Withdrawn / Other	Total <sup>[5]</sup>
Monotherapy - Tagrisso® / savolitinib								
30-Mar-17	Tagrisso® (osimertinib)	2L EGFRi-refractory T790M+ NSCLC (AURA3)	279	71%	10.1	6%	6%	13%
	savolitinib 600mg QD monotherapy <sup>[3]</sup>	All-lines Papillary RCC -- <i>FOR REFERENCE ONLY NOT NSCLC</i>	109 <sup>[1]</sup>	18%	6.2	9%	5%	14%
Combination - Tagrisso® + savolitinib								
	savolitinib 600mg QD + Iressa® (gefitinib) <sup>[2]</sup>	≥2L EGFRm+ MET+ T790M- NSCLC after 1 <sup>st</sup> -gen EGFR TKI (expansion)	51	52%	ND	20%	14%	33%
	savolitinib 600mg QD + Tagrisso® <sup>[3]</sup>	≥2L EGFRm+ MET+ T790M-/± NSCLC after 1 <sup>st</sup> -gen EGFR TKI (TATTON B)	46	56%	ND	37%	9%	46%
	savolitinib 600mg QD + Tagrisso® <sup>[4]</sup>	≥3L EGFRm+ MET+ NSCLC after 3 <sup>rd</sup> -gen EGFR TKI (TATTON B)	48	31%	ND	21%	4%	25%
Approved treatments in NSCLC								
29-Apr-14	Zykadia® (ceritinib)	2L ALK+ NSCLC after Xalkori (single arm)	163	56%	6.9	10%	10%	20%
12-Dec-14	Cyramza® (ramucirumab) + Taxotere®	2L NSCLC after plat-chemo	624	23%	4.5	15%	21%	37%
24-Oct-16	Keytruda® (pembrolizumab) 2mg/kg	2L PD-L1+ (TPS≥1%) NSCLC after plat-chemo (KEYNOTE-010)	345	18%	3.9	10%	26%	37%
2-Oct-15	Keytruda® (pembrolizumab) 10mg/kg	2L PD-L1+ (TPS≥1%) NSCLC after plat-chemo (KEYNOTE-010)	346	18%	4.0	9%	27%	36%
9-Oct-15	Opdivo® (nivolumab)	2L NSCLC after plat-chemo	292	19%	2.3	15%	4%	20%
4-Mar-15	Opdivo® (nivolumab)	2L squ. NSCLC after plat-chemo	135	20%	3.5	12%	8%	20%
2008	Chemo doublet (platinum + pemetrexed)	2L NSCLC (AURA3)	136	31%	4.4	11%	17%	27%
1999	Taxotere® (docetaxel)	2L NSCLC (REVEL; KEYNOTE-010; Opdivo x2 aggregate total)	1,391	12%	3.5	13%	22%	36%

**Tagrisso® + savo combo tolerable even in late-stage ≥3L patients**

[1] PRCC Phase II - Efficacy data from MET+ patients (n=44), discontinuation data from late 2017 data cut-off; Tolerability data from all patients (n=109); [2] WCLC 2017 #8995; [3] AACR 2019 CT032; 43 efficacy evaluable patients, 46 safety evaluable patients; ECOG = 0 in 30% of patients; [4] 2019 AACR CT033; 39 efficacy evaluable patients, 48 safety evaluable patients; ECOG = 0 in 50% of patients; [5] Total discontinuations = Discontinuations NOT due to Disease Progression or Death; ND = Not Disclosed.

# PRCC – unmet medical need

## Lower response rates to treatments

### 1. Limited treatment options for non-ccRCC

#### Several approved therapies in ccRCC [3]

*Immunotherapy setting new treatment paradigm*

FIRST LINE - clear-cell RCC [4]	ORR	mPFS	mOS
Placebo (avg. multiple studies)	~2%	~3.5	~15.0
Torisel® (mTOR)	8.6%	5.5	10.9
VEGFR, multi-kinase small molecule (multiple compounds)	12-31%	6-11	21-28
Opdivo® + Yervoy® (PD-1/CTLA-4 immunotherapy) [5]	42%	~11.6	NR
Keytruda® + Inlyta® (PD-1/VEGFR combo)	59.3%	15.1	NR
Bavencio® + Inlyta® (PD-L1/VEGFR combo)	51.4%	13.8	NR

#### SECOND LINE - clear-cell RCC

Placebo (avg. multiple studies)	~0%	~2.0	~14.0
Cabometyx® (VEGFR/MET, multi-kinase SM) (METEOR)	17%	7.4	21.4
Inlyta® (VEGFR, multi-kinase SM)	23%	8.3	20.1
Lenvima® + Afinitor® (VEGFR, multi-kinase SM + mTOR)	35%	14.6	25.5
Opdivo® (PD-1 mAb) (CheckMate025)	25%	4.6	25.0

**non-ccRCC: NCCN preferred strategy: clinical trials**  
*No category 1 recommendation*

FIRST LINE - non clear-cell RCC [4]	ORR	mPFS	mOS
Sutent® (VEGFR, multi-kinase SM) [4]	9%	6.1	16.2
Afinitor® (mTOR) [4]	3%	4.1	14.9
SECOND LINE - non-clear-cell RCC [4]			
Sutent® (VEGFR, multi-kinase SM) [4]	10%	1.8	na
Afinitor® (mTOR) [4]	9%	2.8	na

### 2. RCC est. ~\$13.0 bn. market by 2030 [1]

#### Clear-cell RCC (~\$10.4b)

~80% of RCC

~ 290k new patients/yr. [2]

#### Non-Clear-cell RCC (~\$2.6b)

~20% of RCC

~ 73k new patients/yr. [2]

### 3. Unmet medical need:

#### MET+ Papillary RCC (~\$1.0b)

~8% of RCC

~ 28k new patients/yr. [2]

#### MET- Papillary RCC (~\$1.0b)

~8% of RCC

~ 28k new patients/yr. [2]

#### Other non-ccRCC (~\$0.6b)

~5% of RCC

~ 16k new patients/yr. [2]

[1] Frost & Sullivan; [2] Frost & Sullivan, based on US incidence mix and global incidence rate in 2018; [3] NCCN Guideline for kidney cancer (Version 1.2020, June 7, 2019) preferred or category 1 options, RCC = renal cell carcinoma; [4] ORR = Objective Response Rate, mPFS = median Progression-Free Survival, mOS = median Overall Survival, NR = not reached; For approved subgroup of patients; [5] only approved for patients with intermediate or poor risk RCC.

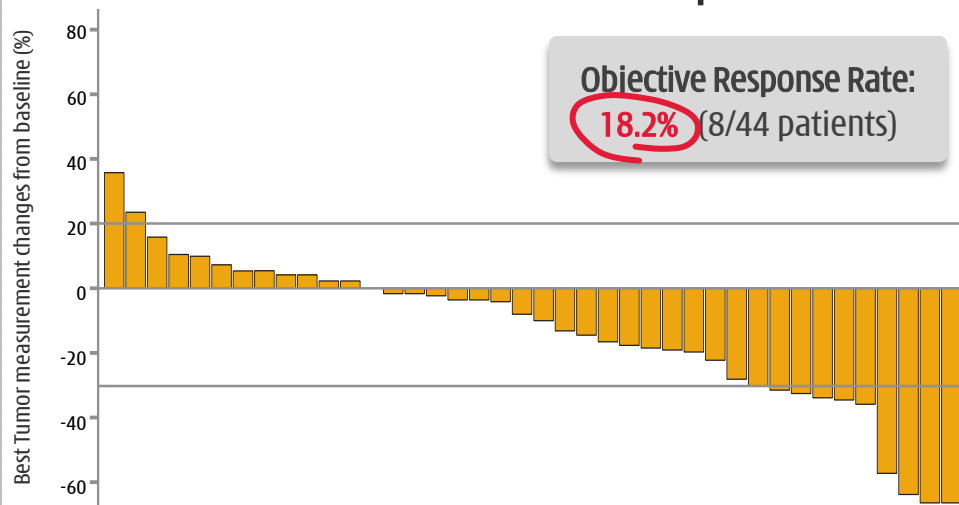


# Savolitinib - PRCC Phase II

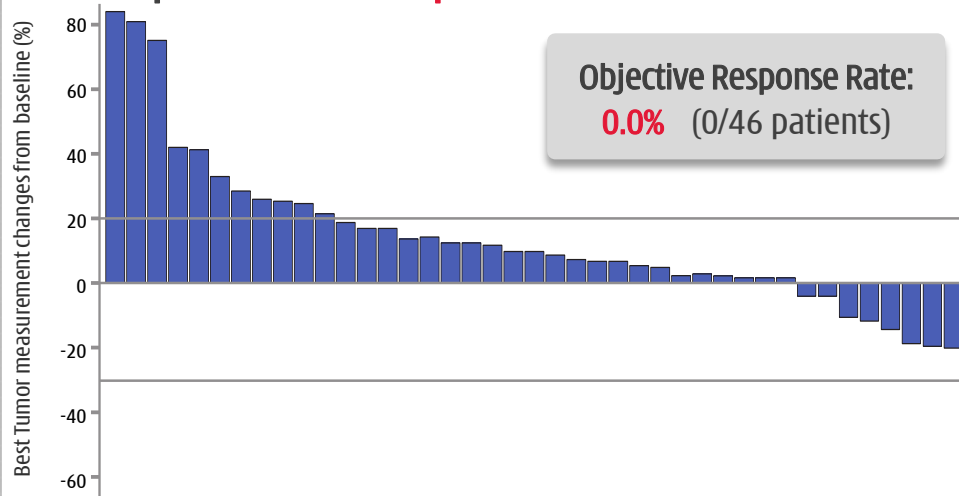
## Clear efficacy & durable response in MET+ PRCC patients



### 1. Savolitinib **clear ORR benefit** in MET+ patients.



### 2. MET- patients - **no response to savo.**



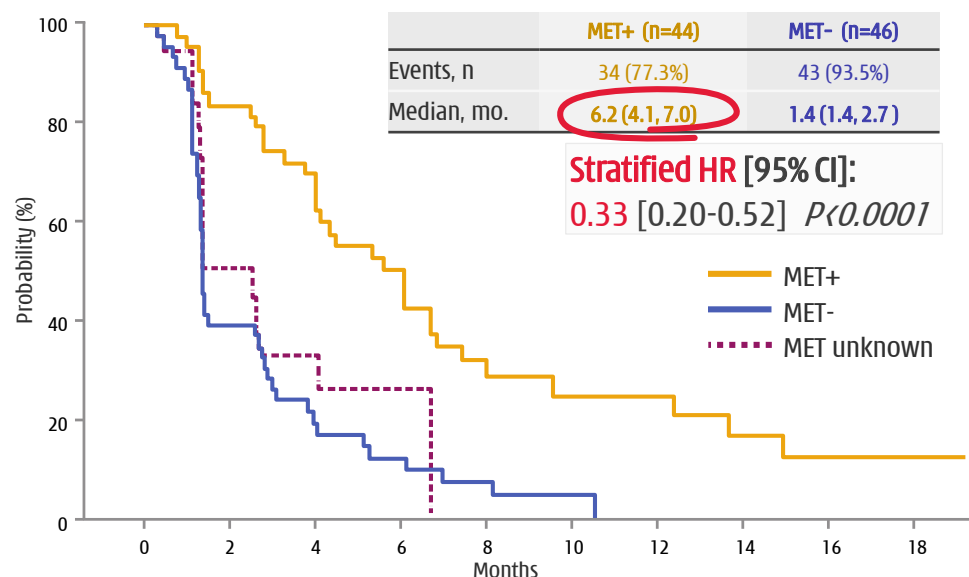
### 3. Disease Control Rate ("DCR") - **big advantage** in MET+ with **DCR 73.2%** vs. MET- **28.2%**.<sup>^</sup>

Tumor responses in the overall treatment population and by MET status

RECIST response, n (%)	MET+ (n=44)	MET- (n=46)	MET unknown (n=19)	Total (n=109)
Partial Response <sup>†</sup>	8 (18.2%)*	0 (0.0%)	0 (0.0%)	8 (7.3%)
Stable Disease	22 (50.0%)	11 (23.9%)	5 (26.3%)	38 (34.9%)
Progressive Disease	11 (25.0%)	28 (60.9%)	9 (47.3%)	48 (44.0%)
Not Evaluable	3 (6.8%)	7 (15.2%)	5 (26.3%)	15 (13.8%)

\* P=0.002 versus MET-independent subgroup (Fisher exact test). Responses assessed according to RECIST version 1.1. <sup>†</sup> Unconfirmed responses excluded. <sup>^</sup> Evaluable patients.

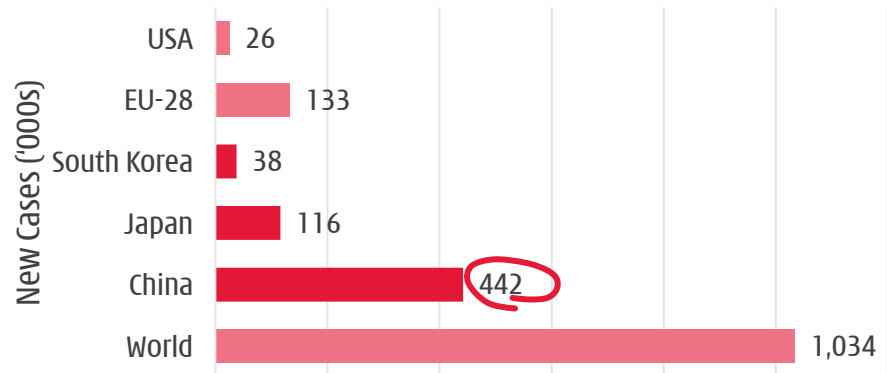
### 4. Median PFS - **big advantage** in MET+ patients.



# Savolitinib - gastric cancer

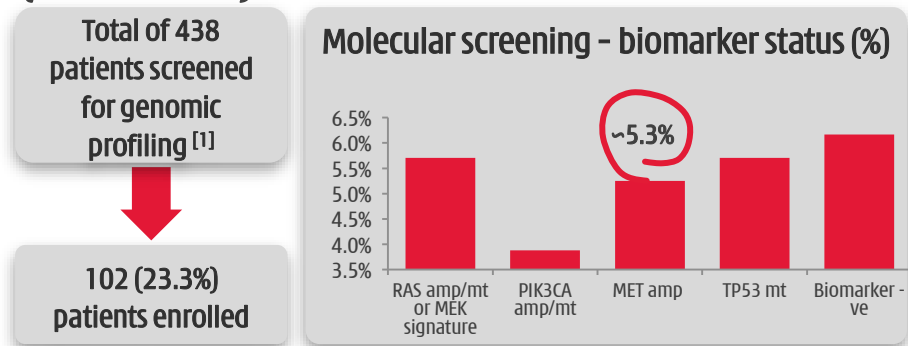
A major problem in east Asia - Japan, South Korea & China

1. Gastric (stomach) cancer is the 5<sup>th</sup> most common cancer globally - **782,700 deaths/year**



World Cancer Research Fund International, WHO, ACS, NCCR, Lancet, Frost & Sullivan Analysis.

2. **VIKTORY - umbrella trial** in gastric cancer (South Korea).

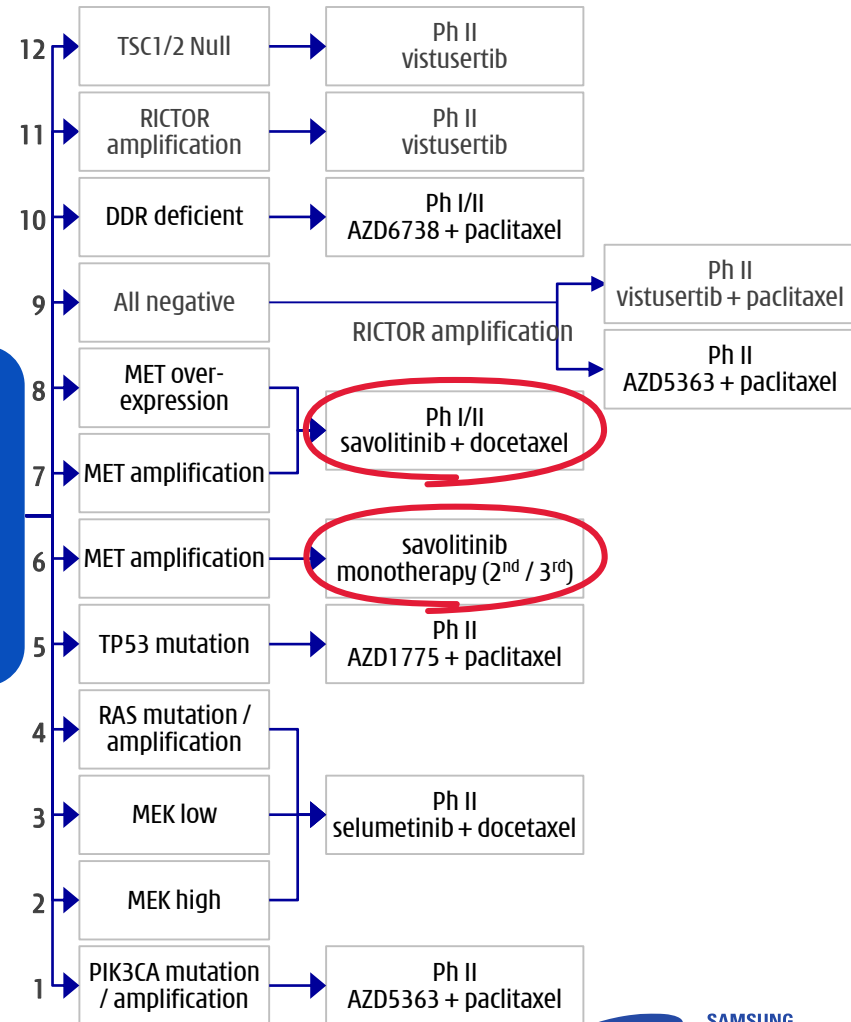


Jeeyun Lee, ASCO 2017

SMC Genomic Screening Program

mGC failing to 1<sup>st</sup> line cytotoxic regimen

Targeted Seq  
MEK  
signature by  
nanosttring  
IHC panel

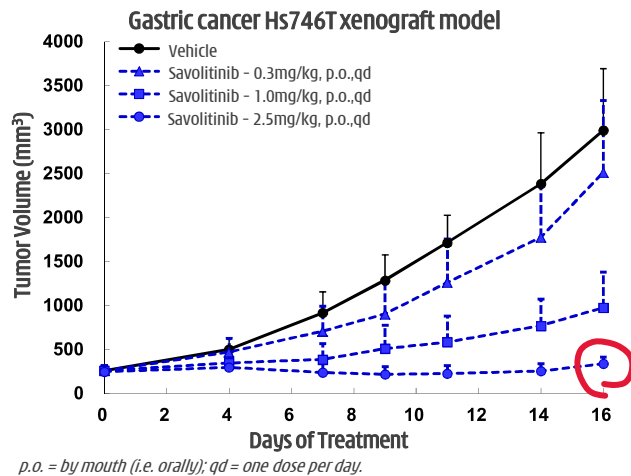


Jeeyun Lee, ASCO 2017.

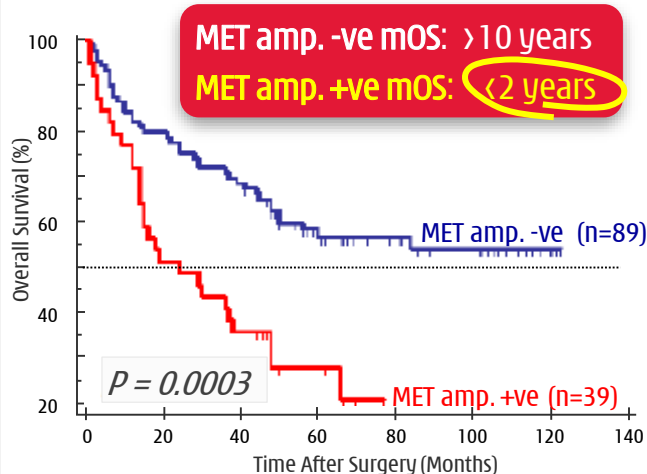
# Savo potential not only in NSCLC...

## ...highly promising efficacy in MET+ gastric cancer (...& kidney)

### Strong preclinical efficacy.



### MET+ gastric - very poor survival.<sup>[1]</sup>

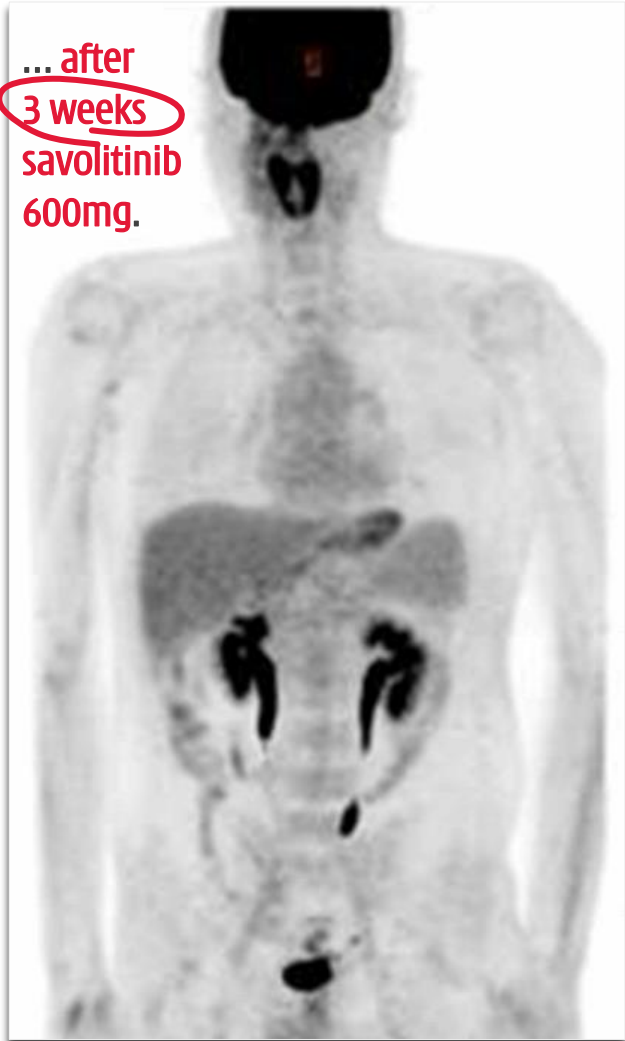


### 3. VIKTORY trial - 34-year old male; surgery ruled-out; failed 4-cycles XELOX.

Baseline  
PET CT...



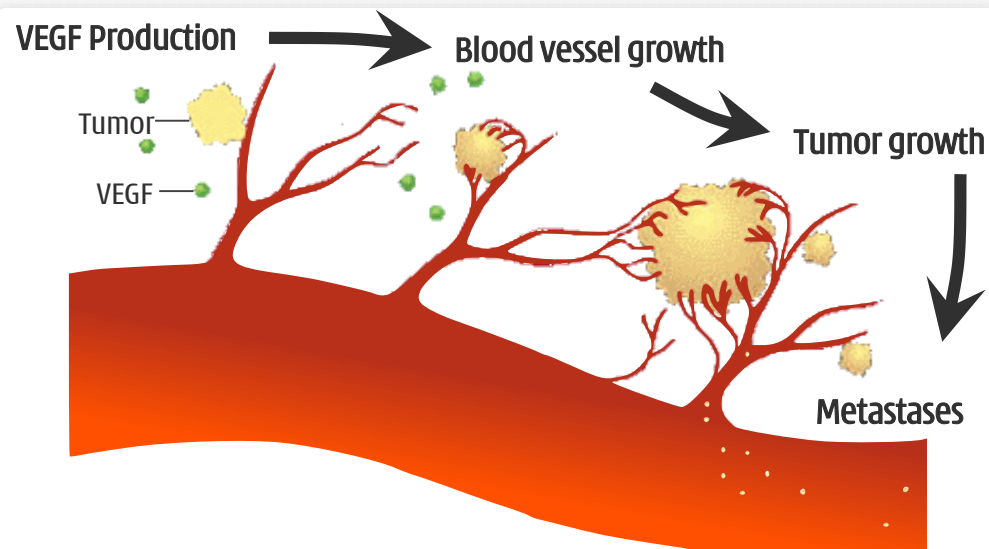
... after  
3 weeks  
savolitinib  
600mg.



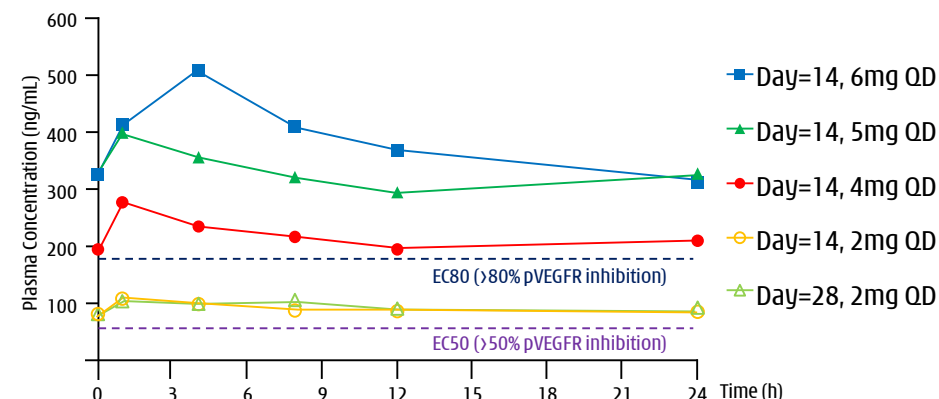
Jeeyun Lee, AACR 2016.

# Fruquintinib - 24hr full target coverage

The most selective VEGFR inhibitor in clinical trials globally <sup>[1]</sup>



**1. Only inhibits VEGFR - limits off-target toxicity & allows for full & sustained target inhibition.**



## 2. Selectivity and potency superior to competitors' drugs.

	Sutent® (sunitinib)	Nexavar® (sorafenib)	Stivarga® (regorafenib)	Tivozanib	Fruquintinib
Kinase profile	VEGFR1,2,3, PDGFRβ, FLT3, CSF-1R, c-Kit, Ret	RAF, VEGFR2, PDGFRβ, Flt3, c-Kit, FGFR1	VEGFR1,2,3, Raf, Ret, PDGFR, c-Kit	VEGFR1,2,3, BRK, PDGFRα, PDGFRβ, c-Kit, Tie2, EphB2	VEGFR1,2,3
AUC at ED50/ED60 in mouse (ng/mL*hr)	2,058	25,473	na	1,640	898
MTD in human (mg/day)	50, qd	400, bid	160, qd	1.5, qd	4, qd; 6, 3wk/1wk
AUC, 0~24h at Steady state MTD (ng/mL*hr)	592	47,780 x2 (D28)	58,270 (D21)	1,180 (D28)	5,000~6,000 (D28)
Efficacy in Phase I	22 patients PR: 4 (18%), DCR: 27%	45 patients <sup>[2]</sup> PR: 1 (2%), DCR: 58%	53 patients PR: 3 (6%), DCR: 66%	37 evaluable patients PR: 1 (3%), DCR: 51%	34 evaluable patients PR: 13 (38%), DCR: 82%

[1] Among small molecule tyrosine kinase inhibitors and to the best of Chi-Med's knowledge; [2] (≥100 mg bid); PR = Partial Response; DCR = Disease Control Rate.



**Elunate<sup>®</sup> (fruquintinib capsules)**

*Highly selective anti-angiogenesis inhibitor*

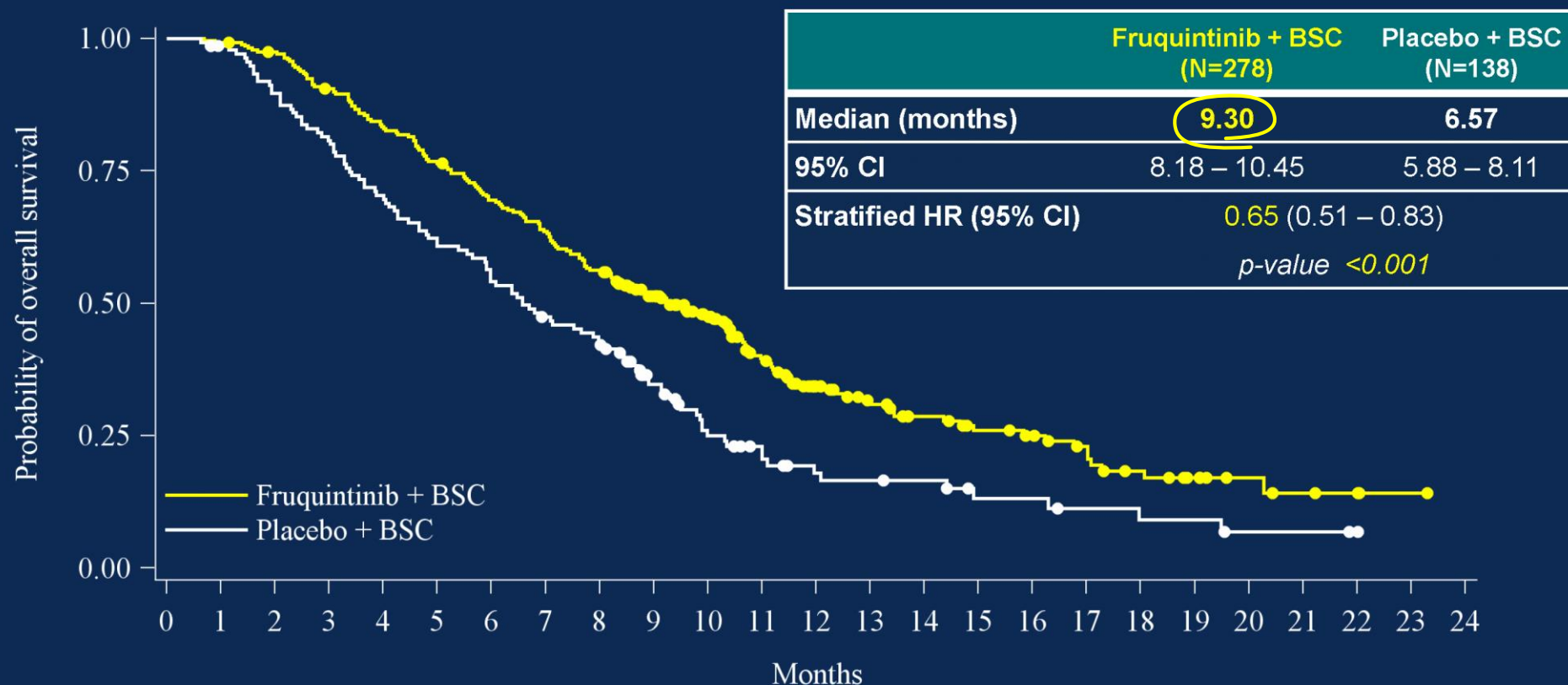


# Fruquintinib - 3L/4L colorectal cancer

Develop in US/EU for rego/TAS-102 ref./intol. patients<sup>[1]</sup>

## Overall Survival (Primary Endpoint)

FRESCO clearly succeeded in meeting the primary efficacy endpoint of OS



PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17

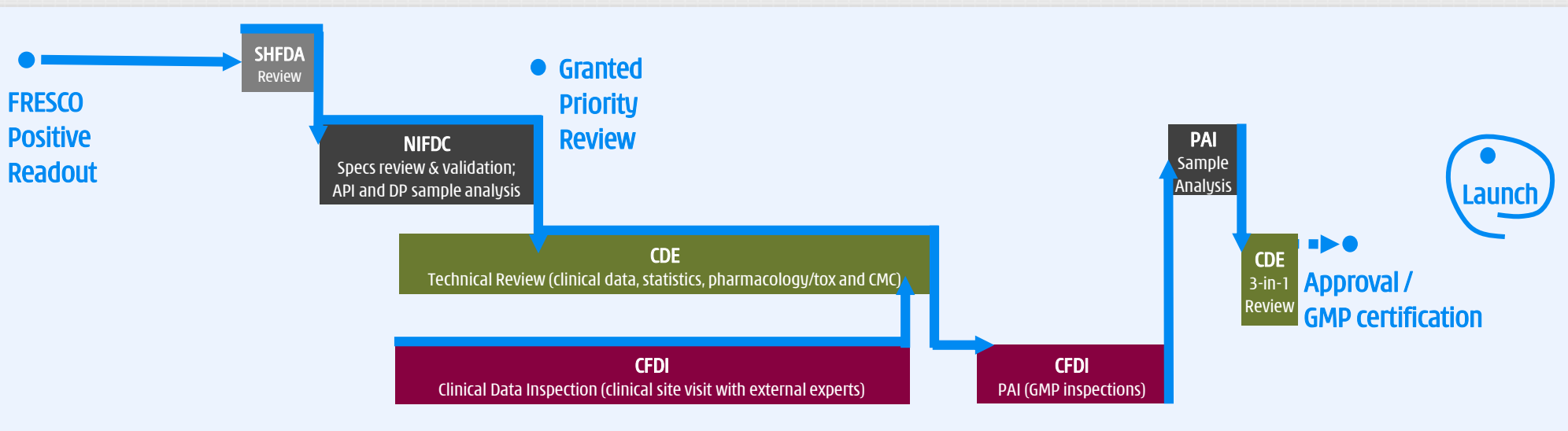
Slides are the property of the author. Permission required for reuse.

Presented by: Jin Li, MD PhD

June 5, 2017

10

# Many "Firsts" for China biotech



Shanghai Food and Drug  
Administration (SHFDA)



National Institutes for Food  
and Drug Control (NIFDC)



Center for Drug  
Evaluation (CDE)

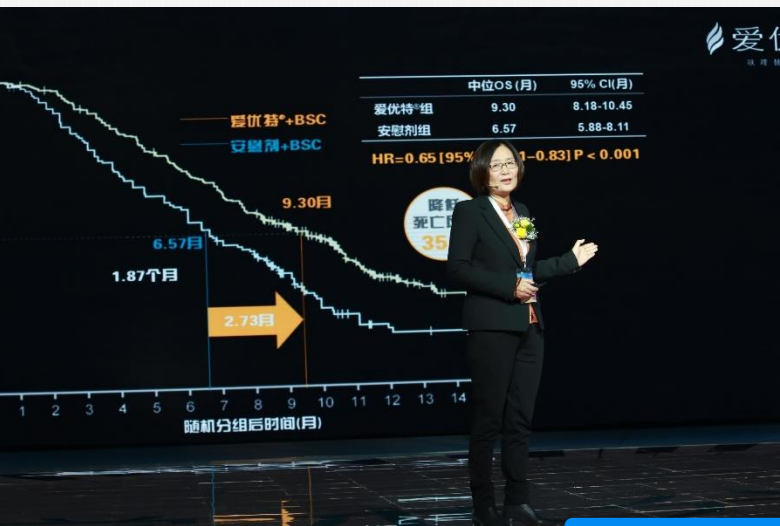


Center for Food and Drug  
Inspection (CFDI)



Critical Path

Launched - Nov. 25, 2018



**First ever oncology drug  
discovered & launched in China <sup>[1]</sup>**





# FALUCA – Third-line NSCLC Monotherapy

## Presented at WCLC 2019



**FALUCA Phase III (enrolled Dec. 2015 to Feb. 2018)**

- **Met all secondary endpoints:** mPFS; ORR; DCR; & DoR [1];
- Did not achieve primary endpoint of median OS, however:
  - **Anti-tumor therapies after disease progression** reduced OS diff.
  - **Higher percentage of placebo pts** received subsequent treatments.

**Significant difference in subsequent anti-tumor treatments (ATT)**

- **Chemotherapy:** Fruq. **29.7%** vs. Placebo **53.8%**
- **Targeted therapies (VEGFi and/or EGFRi):**  
Fruq. **20.9%** vs. Placebo **31.2%**
- **Tagrisso® & anlotinib just approved in 2017**

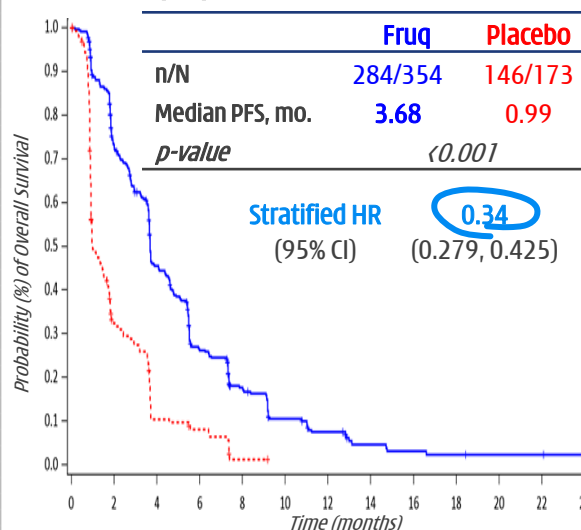
**Efficacy Endpoints (Intent-to-Treat) [2]**

	Fruq. (N=354)	Placebo (N=173)	<i>p-value</i>
mOS (mths)	<b>8.94</b>	10.38	<i>0.841</i>
mPFS (mths)	<b>3.68</b>	0.99	<i>&lt;0.001</i>
ORR	<b>13.8% (49)</b>	0.6% (1)	<i>&lt;0.001</i>
DCR	<b>66.7% (236)</b>	24.9% (43)	<i>&lt;0.001</i>

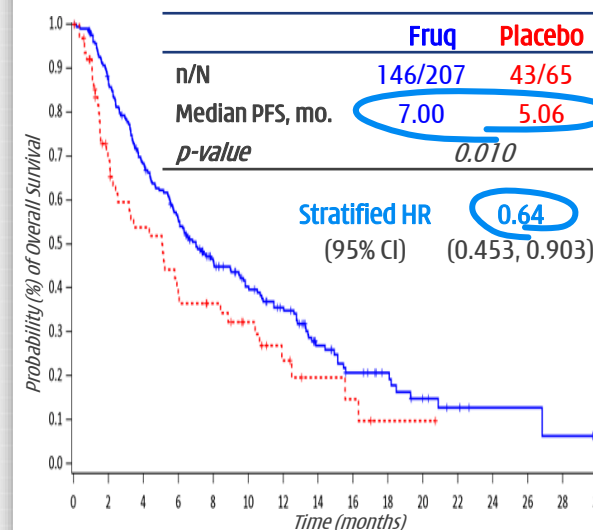
**Good safety; most Grade ≥3 TEAEs target-related & clinically manageable.**

Patient (%)	Fruq (N=354)	Pbo (N=173)
TEAE ≥ Grade 3	216 (61.2%)	47 (27.6%)
Leading to discontinuation	37 (10.5%)	9 (5.3%)
Leading to interruption	61 (17.3%)	7 (4.1%)
Leading to dose reduction	85 (24.1%)	2 (1.2%)
Hypertension	74 (21.0%)	5 (2.9%)
Hand-foot syndrome	39 (11.0%)	0

**PFS in ITT population**



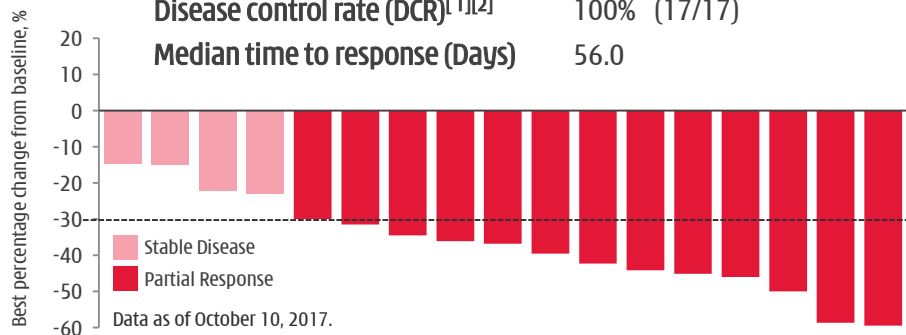
**OS in pts w/o subsequent ATT**



[1] mOS = median Overall Survival; mPFS = median Progression Free Survival; ORR = Objective Response Rate; DCR = Disease Control Rate; DoR = Duration of Response; HR = hazard ratio; 95% CI = 95% Confidence Interval; [2] Lu, et al. "A Randomized Phase III trial of Fruquintinib versus Placebo in Patients with Advanced Non-Small Cell Lung Cancer (FALUCA)." WCLC 2019 Abstract #MA14.05; [3] Lu, et al. Randomized, Double-Blind, Placebo-Controlled, Multicenter Phase II Study of Fruquintinib After Two Prior Chemotherapy Regimens in Chinese Patients with Advanced Non-squamous Non-Small-Cell Lung Cancer. Journal of Clinical Oncology 36, no. 12 (April 20 2018): 1207-1217. DOI: 10.1200/JCO.2017.76.7145; [4] Li, et al. Effect of Fruquintinib vs Placebo on Overall Survival in Patients with Previously Treated Metastatic Colorectal Cancer: The FRESKO Randomized Clinical Trial. JAMA. 2018 Jun 26;319(24):2486-2496. doi: 10.1001/jama.2018.7855. \*Post-hoc analysis

**IRESSA®**  
gefitinib

**- 76% ORR**



Adverse Events ("AEs")	Iressa® or Tarceva® FLAURA <sup>[5]</sup> N = 277, n (%)	Avastin® + Tarceva® <sup>[6]</sup> N = 75, n (%)	Fruquintinib + Iressa® N = 26, n (%) <sup>[3]</sup>
All AEs, any grade	273 (98%)	≥74 (≥99%)	23 (89%)
All AEs, Grade ≥3	124 (45%)	68 (91%)	8 (31%)
AEs leading to death	6 (2%)	0 (0%)	0 (0%)
AEs leading to VEGFRi discontin.	NA	31 (41%)	1 (4%)
<b>Grade ≥3 AEs:</b>			
Liver function (e.g. ALT, AST incr.)	33 (12%)	6 (8%)	6 (23%)
Hypertension	NA	45 (60%)	1 (4%)
Proteinuria	NA	6 (8%)	1 (4%)
Rash	13 (5%)	19 (25%)	0 (0%)
Decreased appetite	22 (8%)	1 (1%)	NA

[illegible]

Duration of Treatment (days)

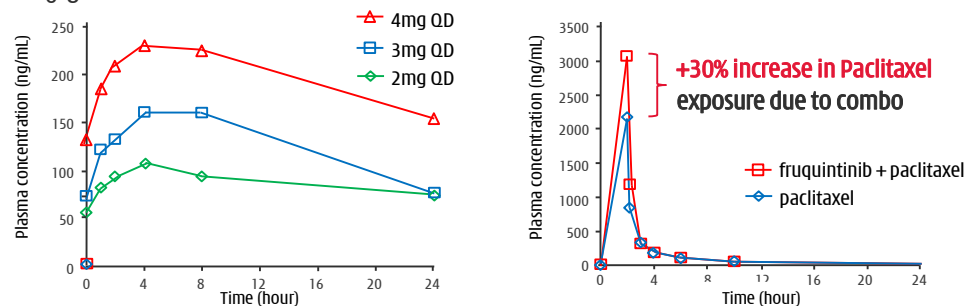
[4] Drug discontinuation due to Grade 3 or proteinuria and Grade 3 QTC prolonged; [5] Ramalingam S, et al, "LBA2 PR 050: Sunitinib vs standard of care (SOC) EGFR TKI as first-line therapy in patients (pts) with EGFRm advanced NSCLC: FLAURA", ESMO 2017 Congress, Madrid, Spain, September 9, 2017; [6] Seto T, et al, "erlotinib alone or with bevacizumab as first-line therapy in patients with advanced non-squamous non-small-cell lung cancer harboring EGFR mutations (J025567): an open-label, randomised, multicentre, phase 2 study", The Lancet 2014, 15 (11) 1236-1244.



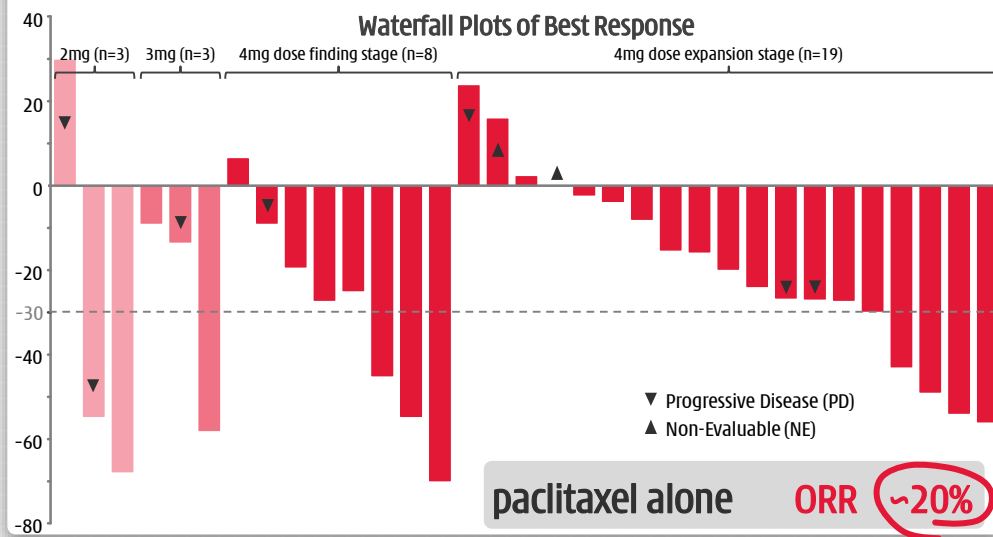
# Fruquintinib - Gastric combo with paclitaxel

Phase III initiated Oct 2017 - Interim analysis early 2019

1. **Dose proportional increase of fruquintinib AUC at steady state.** Over **30%** increase in paclitaxel drug exposure (mean  $AUC_{0-8}$ ) following multiple dose fruquintinib.



2. **ORR of 36%** (10/28) & **DCR of 68%** in efficacy evaluable pts. Fruquintinib 4mg,  $\geq 16$  wk. PFS of 50% &  $\geq 7$  mo. OS of 50%.



3. Encouragingly low level of dose reduction/interruption. Actual mean administered dose in the first cycle was **3.32mg/day for fruquintinib** (83.0% planned dose) & **78.6 mg/m<sup>2</sup>/week for paclitaxel** (98.3% planned dose).

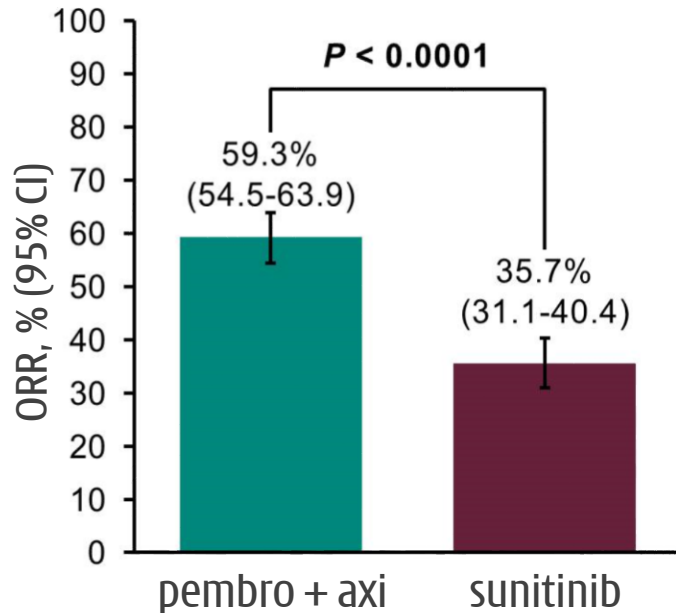
Characteristics (Unit)	Drug Expansion Stage (N=19) Fruquintinib 4 mg + paclitaxel 80 mg/m <sup>2</sup>	
	Drug interruption	Drug reduction
Dose modification with Fruquintinib N (%)	2 (10.5%)	2 (10.5%)
Dose modification with Paclitaxel N (%)	5 (26.3%)	1 (5.3%)

4. **AE profile in-line with expectations.** Neutropenia - a paclitaxel driven AE - with 57.9% Grade  $>3$  AEs. **Similar to 60% level seen in RAINBOW study of ramcirumab (VEGF mAb) combo with paclitaxel in second-line gastric cancer.**

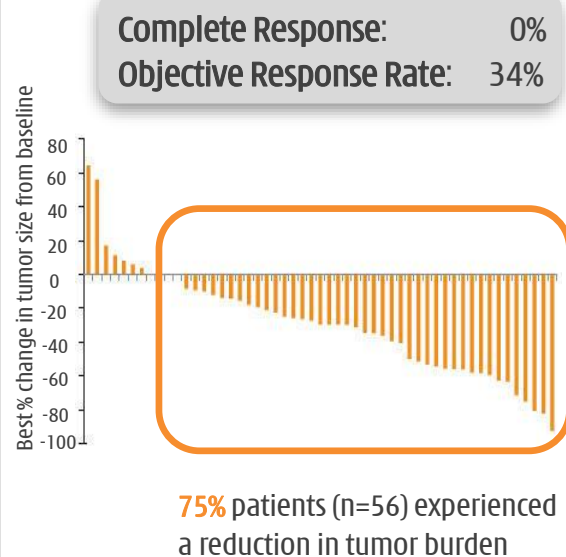
Drug related grade 3 or 4 AEs (NCI-CTCAE v 4.0) term	Dose Expansion Stage (N=19) Fruquintinib 4 mg + paclitaxel 80 mg/m <sup>2</sup>
Neutropenia	11 (57.9%)
Leukopenia	4 (21.0%)
Hypertension	2 (10.6%)
PLT decreased	1 (5.3%)
Anemia	1 (5.3%)
HFSR	1 (5.3%)
Mucositis oral	1 (5.3%)
Hepatic disorder	1 (5.3%)
Upper gastrointestinal hemorrhage	1 (5.3%)

# VEGFR / immunotherapy (PD-1s) combinations

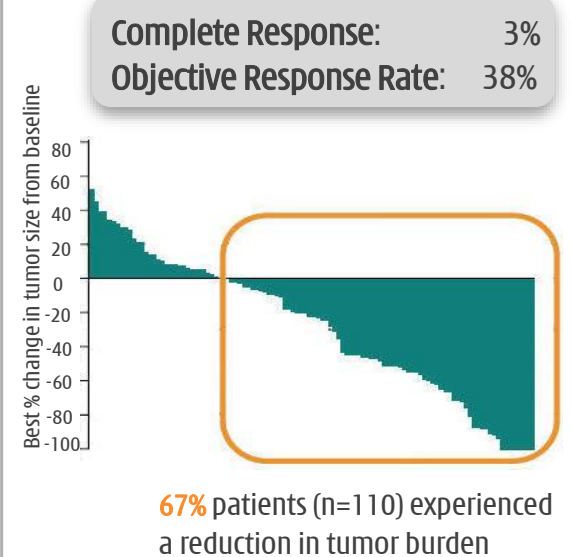
## Pembrolizumab (PD-1) + axitinib (VEGFR) versus sunitinib (VEGFR) monotherapy in 1L ccRCC



## Axitinib (VEGFR) monotherapy in 1L ccRCC



## Pembrolizumab (PD-1) monotherapy in 1L ccRCC



**Potent two prong attack – Anti-angiogenesis + activated T-cell response**

# Fruquintinib & surufatinib both unique VEGFR TKIs

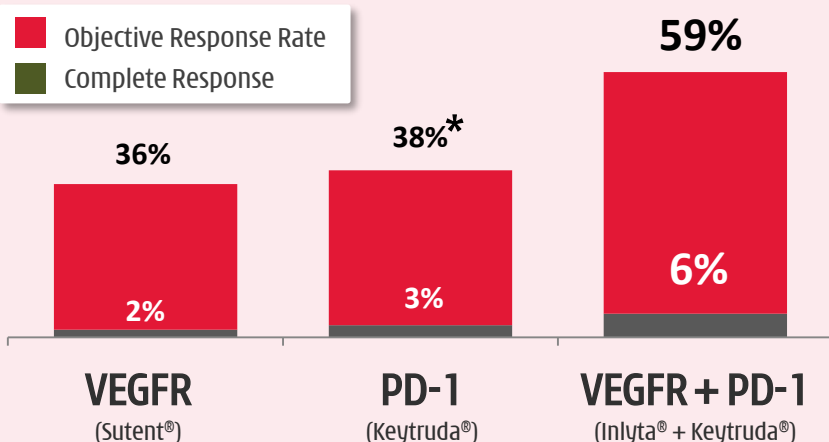
## ...potentially ideal VEGFR combo partners for immunotherapy

TKI	1 <sup>st</sup> Generation			2 <sup>nd</sup> Generation			Next Generation	
Selectivity	Multiple targets			Relatively selective			Highly selective	Selective angio-immuno kinase inhibitor
Inhibitors	Sutent®	Nexavar®	Focus V®	Fotivda®	Lenvima®	Inlyta®	Fruquintinib	Surufatinib <sup>[1]</sup>
Status	Launched	Launched	Launched	Launched	Launched	Launched	Launched	Ph. IIIs ongoing
VEGFR1 (nM)	2	26	27	30	22	3	33	2
VEGFR2 (nM)	9	90	0.2	6.5	4	7	25	24
VEGFR3 (nM)	19	20	0.7	15	5	1	0.5	1
Phos-KDR (nM)	10	30	0.1-1	0.16	0.8	0.2	0.6	2
Other kinases (IC <sub>50</sub> < 100nM)	PDGFR $\alpha$ PDGFR $\beta$ c-Kit Flt3 Ret CSF-1R	Raf-1 b-raf Flt3 P38 c-Kit Ret	PDGFR $\alpha$ PDGFR $\beta$ FGFR1-4 c-Kit	PDGFR $\alpha$ PDGFR $\beta$ EphB2 c-Kit Tie2	PDGFR $\alpha$ PDGFR $\beta$ FGFR1-4 Ret c-Kit	PDGFR $\alpha$ PDGFR $\beta$ c-Kit	none	CSF-1R FGFR1 FLT3 TrkB
Patent Expiration					2021/10/19 (US7253286B2)	2025/04/29 (US6534524B1)	2029 (without extension)	2030 (without extension)

- **Fruquintinib is uniquely selective** - unlike other TKIs with off-target toxicity
- **Surufatinib inhibits TAM<sup>[2]</sup> production** - amplifying PD-1 induced immune response

# Immunotherapy combinations... assets potentially ideal TKI combo partners for immunotherapy

## 1L Clear Cell Renal Cell Carcinoma [1]



### Potent two-prong attack - BTD [2]:

Anti-angiogenesis + activated T-cell response

	Inlyta®	Fruquintinib	Surufatinib
<b>Selectivity</b>	Relatively selective	Highly selective	Selective angio-immuno kinase inhibitor
<b>Status</b>	Launched	Launched	Ph. IIIs ongoing
<b>VEGFR1 (nM)</b>	3	33	2
<b>VEGFR2 (nM)</b>	7	25	24
<b>VEGFR3 (nM)</b>	1	0.5	1
<b>Phos-KDR (nM)</b>	0.2	0.6	2
<b>Other kinases (IC<sub>50</sub> &lt; 100nM)</b>	PDGFR $\alpha$ PDGFR $\beta$ c-Kit	none	CSF-1R FGFR1 FLT3 TrkB
<b>Patent Expiration</b>	2025/04/29 (US6534524B1)	2029 (without extension)	2030 (without extension)

**Fruq. uniquely selective** - unlike other TKIs with off-target toxicity

**Suru. inhibits TAM production** - amplifying PD-1 induced immune response

Multiple global immunotherapy combo deals...

Managed by AstraZeneca

AstraZeneca

savolitinib + Imfinzi® (PD-L1)

ccRCC/PRCC

Jointly managed by Chi-Med & partners

Innovent

Innovent Biologics

fruquintinib + Tyvyt® (PD-1)

Solid tumors



君实生物  
Junshi Biosciences

surufatinib + Tuoyi® (PD-1)

Solid tumors

**3 PD-1 / PD-L1 combos** - Development now underway / in planning on savo, fruq & suru

[1] Sources: (i) B. Rini et al, for the KEYNOTE-426 Investigators, NEJM 2019 Feb 16. doi: 10.1056/NEJMoa1816714, Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma; (ii). D.F. McDermott et al, ASCO 2018 #4500, Pembrolizumab monotherapy as first-line therapy in advanced clear cell renal cell carcinoma (ccRCC): Results from cohort A of KEYNOTE-427; \* ORR =38.2% for all PD-L1 expression combined positive scores (CPS) - ORR=50.0% for CPS≥1 pts, ORR=26.4% for CPS<1 pts.; [2] BTD = Breakthrough Therapy Designation.

# Chi-Med immunotherapy collaborations

## Global Development

*Managed by AstraZeneca*

AstraZeneca 

savolitinib + Imfinzi® (PD-L1)

ccRCC/PRCC

*Jointly managed by Chi-Med & partners*

Innovent  
Innovent Biologics

fruquintinib + Tyvyt® (PD-1)

Solid tumors

 君实生物  
Junshi Biosciences

surufatinib + Tuoyi® (PD-1)

Solid tumors

## China only

*Managed by partners*

 嘉和生物药业  
Genor Biopharma

fruquintinib + GB226 (PD-1)

Solid tumors

Taizhou Hanzhong  
泰州翰中生物医药

surufatinib + HX008 (PD-1)

Solid tumors

**5 PD-1/PD-L1 combos** underway/in planning on savo, fruq & suru



# Lilly amendment - Dec 2018

## Secures long-term commercial potential

- Chi-Med will pay full cost of any future development in China. In return, Chi-Med gains:
- Freedom to operate in selecting & pursuing any future indications in China;
- Materially higher milestones & royalties upon launch in new LCI<sup>[1]</sup>;
- Freedom to collaborate with any third-party in clinical development; and
- Possible promotion rights in 30-40% of China for Elunate®.<sup>[2]</sup> Not expected before 2021, until then, Lilly responsible for all launch & commercialization costs in China. If we assume promotion rights, we will receive service fees, which we expect to be net income accretive.

	Original 2013 Agreement		Amendment (Dec 2018)
LCI <sup>[1]</sup> Development Costs - Paid by Lilly	70%		0%
LCI Development Costs - Paid by Chi-Med	30%	↗	100%
LCI Regulatory Approval Milestones - Paid to Chi-Med <sup>[3]</sup>	12.5	↗	20.0
Royalty Payments - Paid to Chi-Med <sup>[4]</sup>	15 - 20%	↗	15 - 29%
Co-Promotion Rights in China (% of provinces)	0%	↗	30 - 40%
Co-Promotion Service Fees - paid to Chi-Med (% Net Sales)	0%	↗	Not disclosed

**More control & higher long-term economics on best-in-class asset**



**Surufatinib**

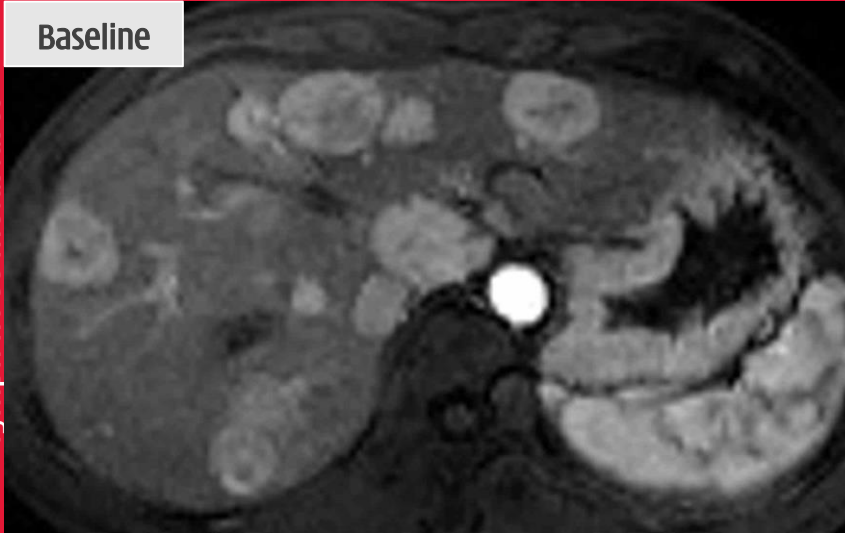
*Highly active TKI with unique angio-immuno activity*

# Surufatinib - China NET - Phase II (*ENETS 2017*<sup>[1]</sup>)

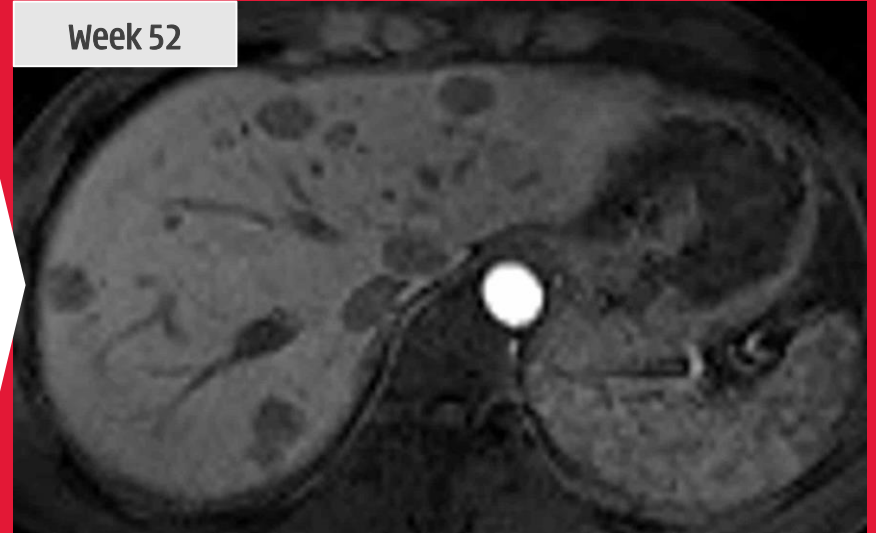
## Tumor devascularization & central necrosis

**Patient 1**  
**Duodenum NET G2**  
w/ multiple liver & retroperitoneal  
lymph node metastases

Baseline



Week 52

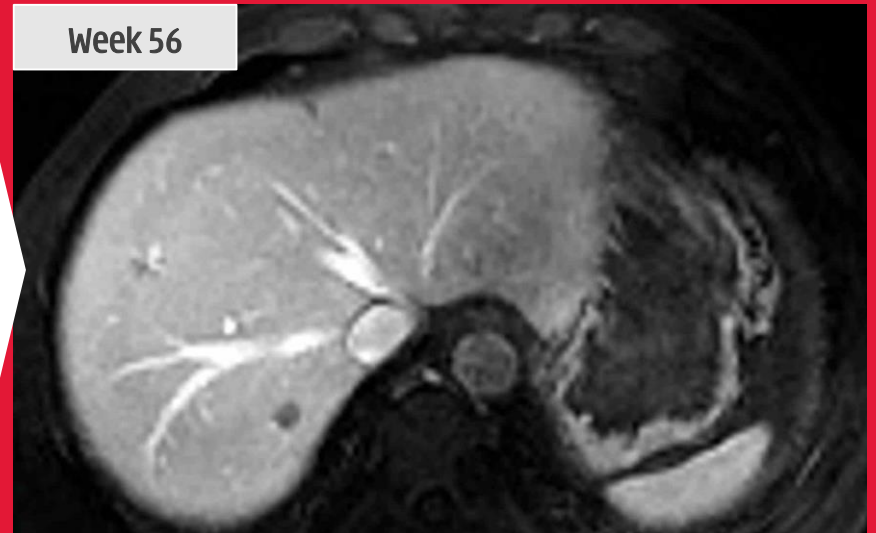


**Patient 2**  
**Rectum NET G2**  
w/ multiple liver metastases

Baseline



Week 56







**HMPL-523 (Syk) & HMPL-689 (PI3K $\delta$ )**

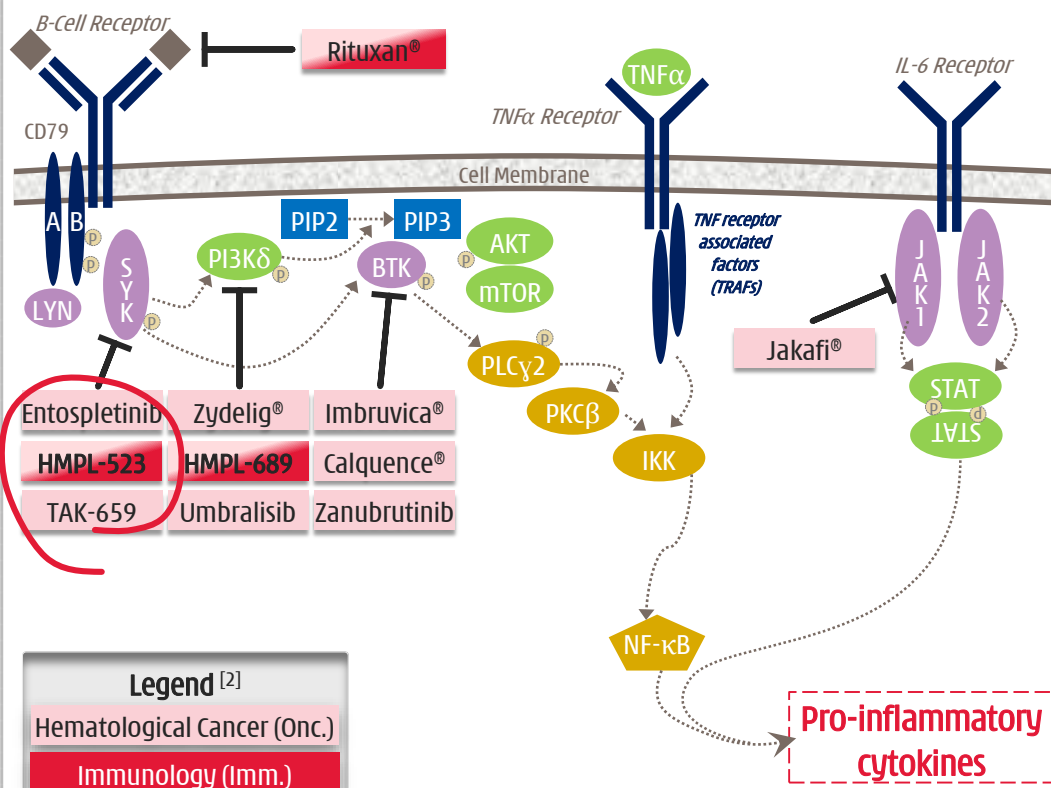
*Potential first-in-class (Syk) & best-in-class (PI3K $\delta$ ) assets*

# HMPL-523 - hematological malignancies

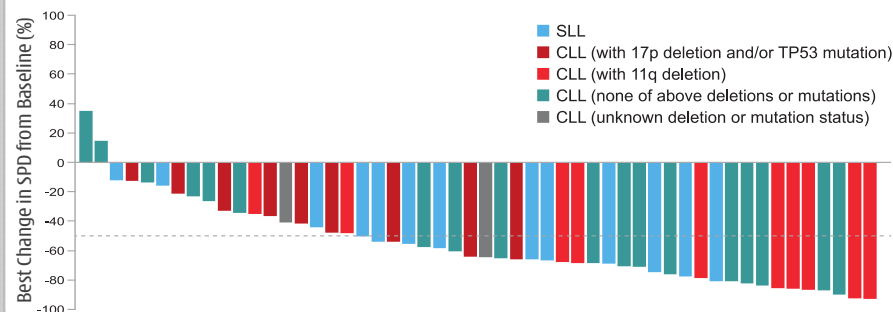
## Syk exciting target emerging - Lymphoma PoC ongoing

1. The B-cell signaling is **critical in hematological cancer** with three **breakthrough therapies** recently approved.

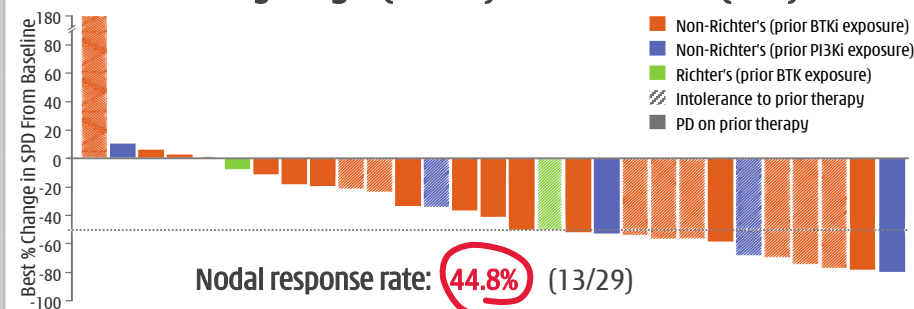
- 2018 sales: Imbruvica® \$6.2bn; Zydelig® \$0.1bn; Jakafi® \$2.4bn; & Rituxan® \$5.3bn [1].



2. Entospletinib - **65%** Nodal Response Rate CLL & SLL [4] [5].



3. Entospletinib potential for **overcoming resistance/intolerance** to Zydelig® (PI3Kδ) & Imbruvica® (BTK) [5].



4. Entospletinib **not a perfect compound** [6].

- Poor solubility/oral absorption & high variation in drug exposure.
- Some CYP [6] inhibition & increased risk of drug-drug interaction.
- 66% Grade ≥3 AEs, **49% SAEs**, **46% drug interruption** & 20% disco.



# HMPL-523 (Syk) in hematological cancer

Australia & China - large Ph.Ib expansion. US/EU Ph.I imminent



- Extensive **Ph.I dose escalation study now complete** in Australia & China (total n=60);
- RP2D<sup>[1]</sup> determined & **large Ph. Ib dose expansion study, total n=192**, underway in 13 active sites in Australia & China;
- Phase I/Ib **data set currently >150 patients**;
- **US IND application cleared by FDA** & U.S./E.U. Phase I imminent;
- **Plan to initiate China registration studies in 2019.**

## Australia & China Phase I/Ib studies

### Stage I: dose escalation

- Australia: Relapsed/refractory hematologic malignancy
- China: Relapsed/refractory mature B lymphoma

"3 + 3" each dose cohort

N = 33

N = 27

**Complete** ✓

Studied HMPL-523  
100-1,000mg QD &  
200-400mg BID in  
13 dose cohorts

until disease progression, death, intolerable toxicity, etc.

### Stage II: dose expansion

Relapsed or refractory, measurable disease - multiple arms:

- Chronic lymphocytic leukemia
- Small lymphocytic lymphoma
- Mantle cell lymphoma
- Follicular lymphoma
- Diffuse large B-cell lymphoma (PRC)

Aus  
N = 40

China  
N = 152

**...Now enrolling**

**600mg QD**

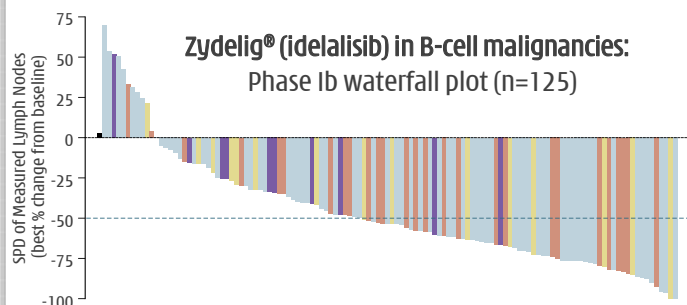
until disease progression, death, intolerable toxicity, etc.

# HMPL-689 - Phase I Australia & China ongoing

## Designed to be a best-in-class inhibitor of PI3Kδ

### 1. PI3Kδ now a proven target.

- PI3Kδ activation associated with allergy, inflammation & oncology.
- Evidence that PI3Kδ inhibitors effective in ibrutinib-resistant mutant population.



### 2. PI3Kδ inhibitors being developed in a very broad range of indications.

Compound		Indication	Status	Issue
<b>Zydelig®</b> (idelalisib) PI3Kδ	Gilead	Chronic lymphocytic leukaemia, non-Hodgkin's lymphoma	Marketed	High incidence of liver toxicity seen with idelalisib (150mg bid)
<b>AMG-319</b> PI3Kδ	Amgen	B-cell lymphoma, non-Hodgkin's lymphoma, T-cell lymphoma, chronic lymphocytic leukaemia	Phase I Trial	
<b>Copiktra®</b> (duvelisib) PI3Kγ/δ	Verastem/ Infinity <sup>[1]</sup>	Relapsed or refractory chronic lymphocytic leukaemia / small lymphocytic lymphoma	Approved	Need to spare PI3Kγ -- serious infection seen & associated with a boxed warning for 4 fatal and/or serious toxicities
		Relapsed or refractory follicular lymphoma	Approved <sup>[2]</sup>	
		Peripheral T-cell lymphoma	Phase II enrolling	
<b>Aliqopa®</b> (copanlisib) PI3Kα/δ	Bayer	Relapsed follicular B-cell non-Hodgkin lymphoma	Approved <sup>[2]</sup>	Serious and fatal infections and AEs

### 3. HMPL-689 -- Important asset.

Designed to improve on existing PI3Kδ inhibitors:

- **Improved isoform selectivity** (sparing PI3Kγ).
- **Improved potency at whole blood level** (>5X more potent than idelalisib) to cut compound related toxicity.
- **Improved PK properties** particularly efflux and drug/drug interaction due to CYP inhibition / induction, critical for combo therapy.

### 4. More potent / more selective than Zydelig®, Copiktra® & Aliqopa®.

Enzyme IC <sub>50</sub> (nM)	HMPL-689	Zydelig®	Copiktra®	Aliqopa®
PI3Kδ	0.8 (n = 3)	2	1	0.7
PI3Kγ (fold vs. PI3Kδ)	114 (142x)	104 (52x)	2 (2x)	6.4 (9x)
PI3Kα (fold vs. PI3Kδ)	>1,000 (>1,250x)	866 (433x)	143 (143x)	0.5 (1x)
PI3Kδ human <u>whole blood</u> CD63+	3	14	15	n/a
PI3Kβ (fold vs. PI3Kδ)	87 (109x)	293 (147x)	8 (8x)	3.7 (5x)

[1] AbbVie ended collaboration with Infinity in June 2016 following Phase II results in indolent non-Hodgkin's lymphoma. Duvelisib now licensed to Verastem; [2] Accelerated approval was granted based on ORR, and continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trials.



**Epitinib**

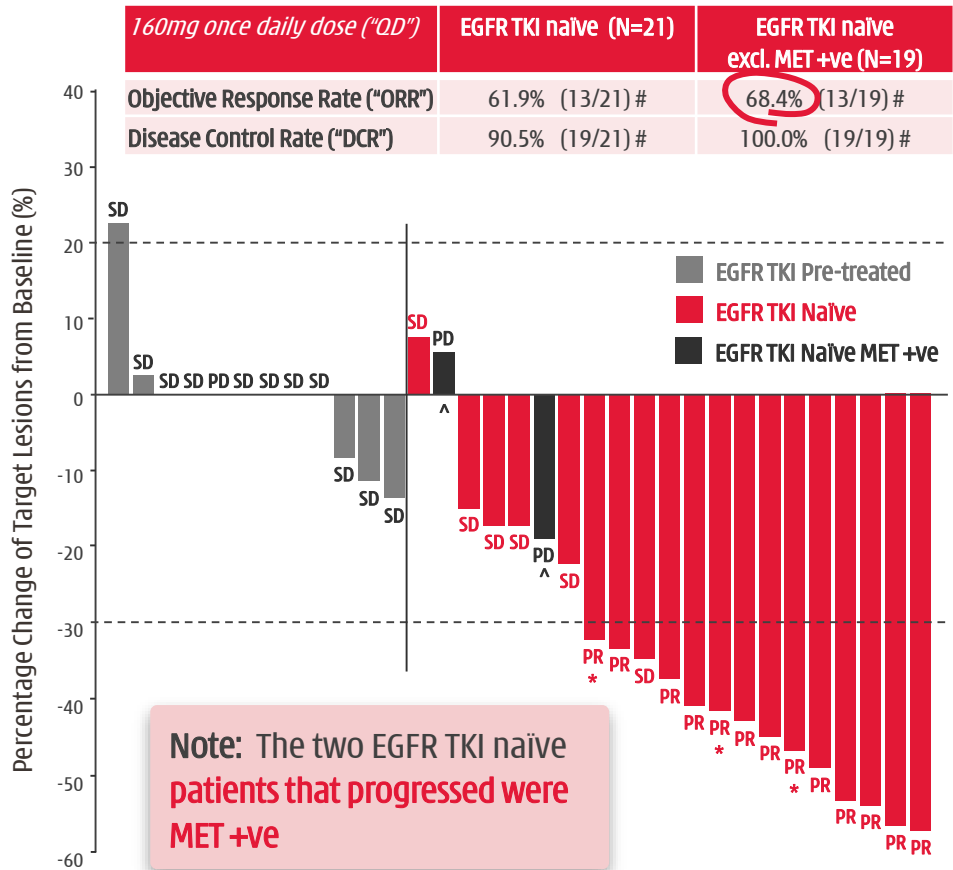
*EGFR inhibitor with blood-brain-barrier penetration*

# Epitinib - 70% response in NSCLC w/ brain mets<sup>[1]</sup>

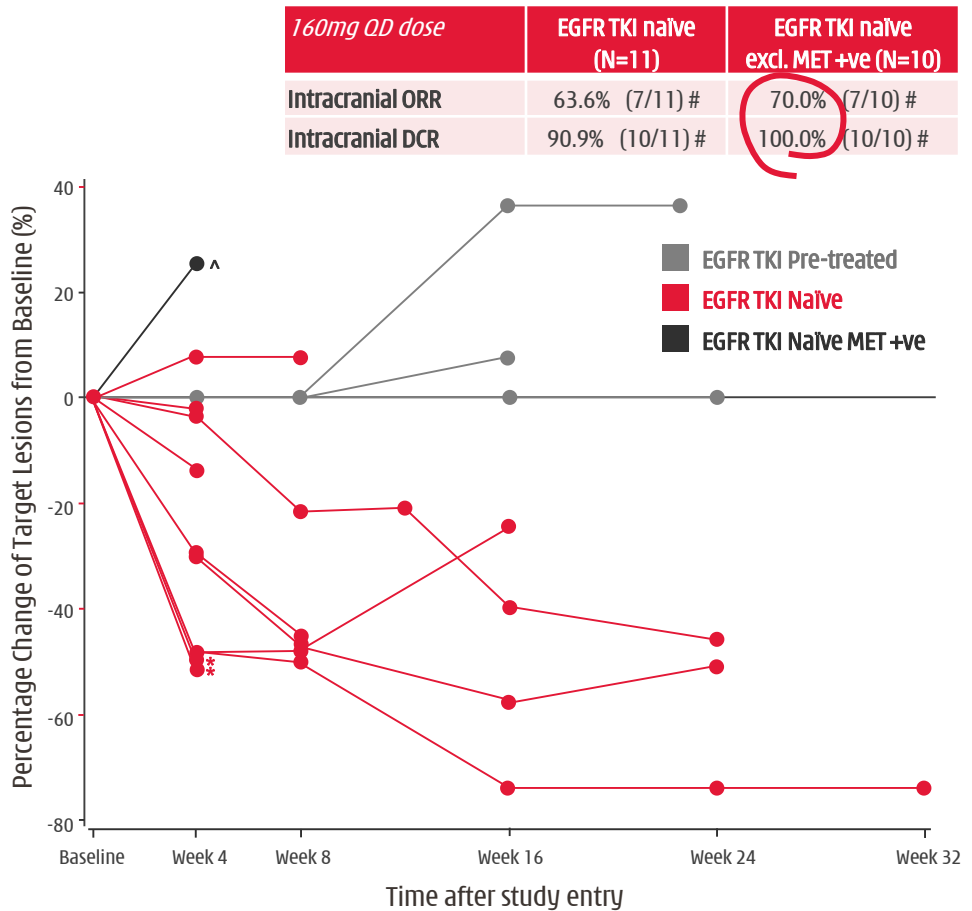
Unmet medical need. Investment case under review.



## 1. Phase Ib<sup>[1]</sup> - epitinib monotherapy in EGFRm+ NSCLC patients - efficacy in lung in-line with Iressa®/Tarceva®.



## 2. Phase Ib<sup>[1]</sup> - solid/durable efficacy in brain in EGFRm+ NSCLC patients with measurable brain mets (>10mm).

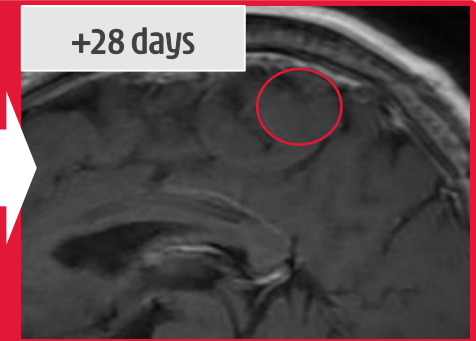
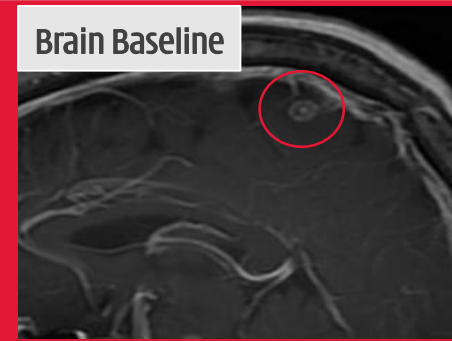
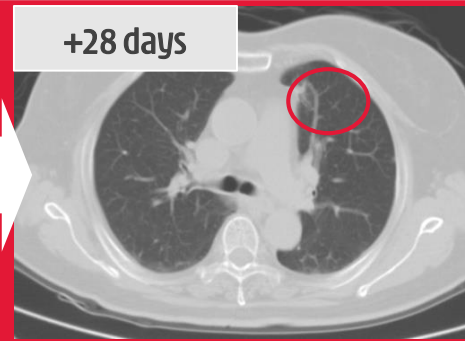
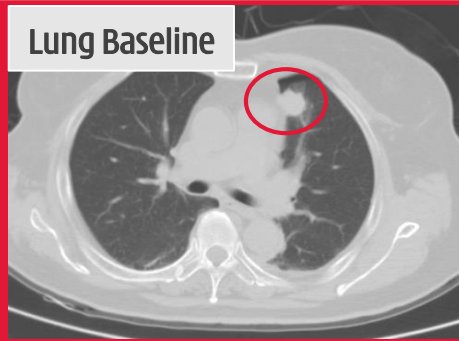


[1] EGFR tyrosine kinase inhibitor treatment naïve patients, Dose expansion stage - data cut-off September 20, 2016; [2] Li B, Bao YC, Chen B, *et al.* Therapy for non-small cell lung cancer patients with brain metastasis. Chinese-German J Clin Oncol, 2014, 13: 483-488; \* Unconfirmed PR, due to no further assessment at cut-off date; # Includes both confirmed and unconfirmed PRs; ^ MET amplification/high expression identified.

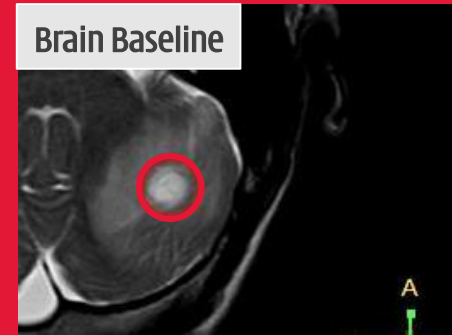
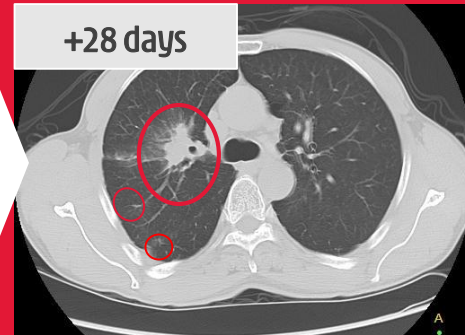


# Epitinib - Strong PoC efficacy - 160mg QD dose

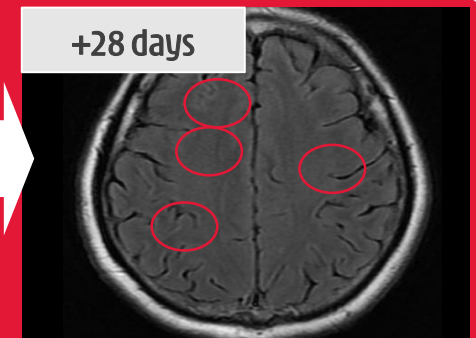
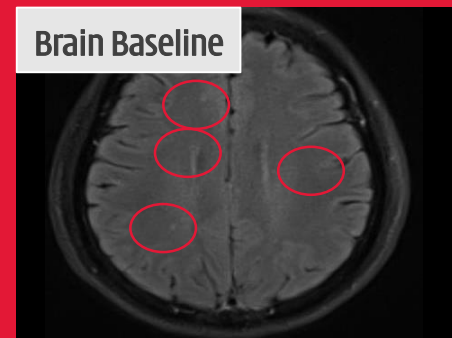
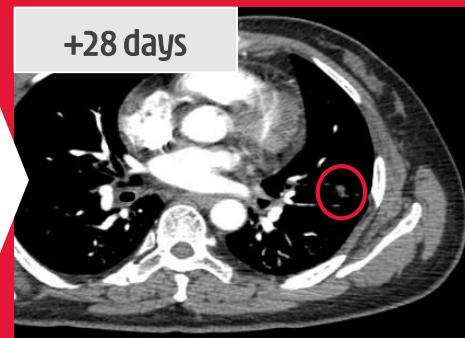
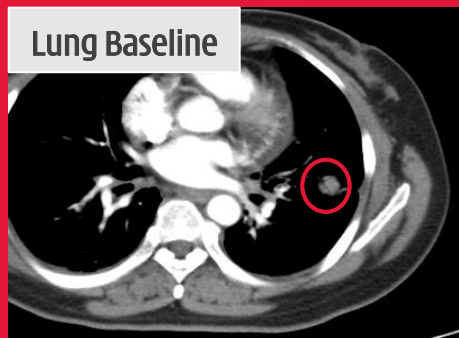
62-year-old female



57-year-old male



52-year-old male





# Epitinib - Safe & well tolerated

3. **Epitinib** well tolerated by patients<sup>[1]</sup> w/advanced solid tumors. Safety profile is consistent with that of approved EGFR-TKIs (e.g. Iressa®/ Tarceva®).

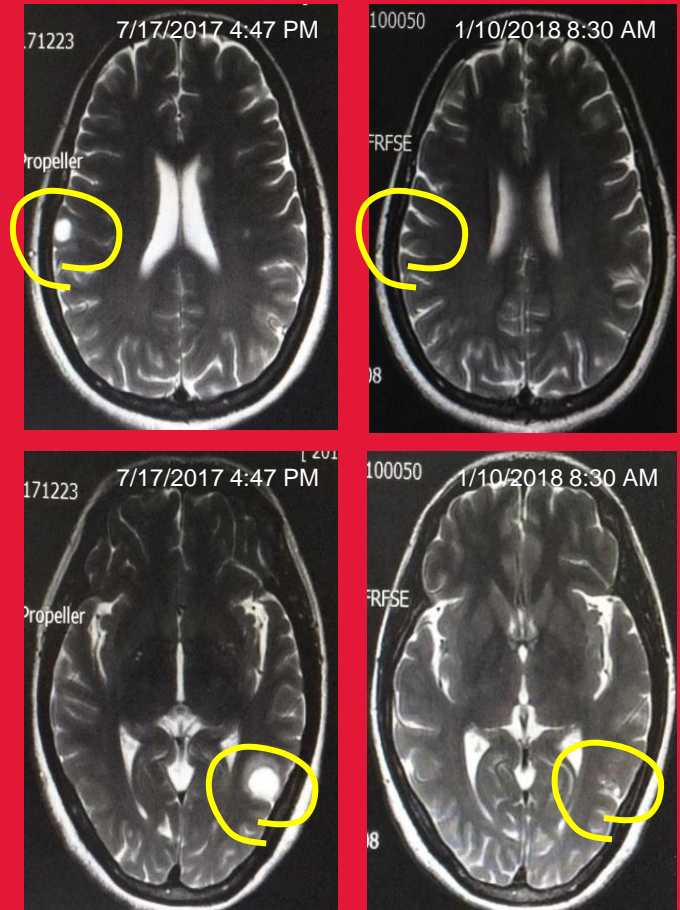
Dose Escalation Stage (n=35*) (Drug related AEs reported > 10%)			Dose Expansion Stage (n=37) (Drug related AEs reported > 10%)		
160mg QD dose	All Grades n (%)	Grade 3/4 n (%)	160mg QD dose	All Grades n (%)	Grade 3/4 n (%)
Skin rash	21 (60.0%)	1 (2.9%)	Skin rash	31 (83.8%)	2 (5.4%)
Diarrhea	12 (34.3%)	-	Hyper-pigmentation	18 (48.6%)	1 (2.7%)
AST increase	12 (34.3%)	1 (2.9%)	ALT increase	15 (40.5%)	7 (18.9%)
ALT increase	11 (31.4%)	1 (2.9%)	AST increase	15 (40.5%)	4 (10.8%)
Total bilirubin increase	10 (28.6%)	2 (5.7%)	ASP increase	11 (29.7%)	1 (2.7%)
Stomatitis	5 (14.3%)	-	Diarrhea	10 (27.0%)	-
Exfoliative dermatitis	5 (14.3%)	-	Proteinuria	10 (27.0%)	-
Pruritus	5 (14.3%)	-	Total bilirubin increase	9 (24.3%)	1 (2.7%)
Hyper-pigmentation	4 (11.4%)	-	Hyperuricemia	9 (24.3%)	2 (5.4%)
Gamma-GGT increase	4 (11.4%)	2 (5.7%)	Gamma-GGT increase	7 (18.9%)	4 (10.8%)
Conjugated bilirubin	4 (11.4%)	1 (2.9%)	Stomatitis	6 (16.2%)	-

4. EGFR gene amplified **Glioblastoma** (primary brain tumors):

■ Phase Ib/II proof-of-concept underway.

## CASE STUDY - EGFR-TKI naïve patient

- Male, 46, diagnosed with Stage IV **NSCLC adenocarcinoma** (Exon21)
- Metastases in the brain, meninges, & bone
- 1<sup>st</sup>-line chemo naïve
- **120mg QD dosage**
- 25 weeks (177 days) on treatment with clear response in multiple measurable (>10mm diameter) brain lesions



[1] No Dose Limiting Toxicity ("DLT") was observed in any cohort; \* One patient did not join multiple dosing.



**Theliatinib (EGFRwt) & HMPL-453 (FGFR)**

*Potential best-in-class assets*

# Theletinib

Potent & highly selective TKI - strong affinity to EGFRwt kinase



## 1. Major unmet medical need for wild-type EGFR activation tumors.

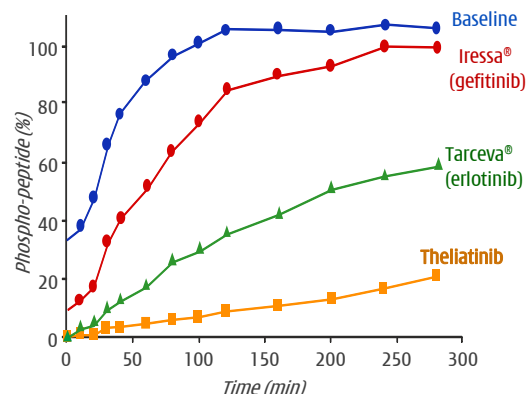
- EGFR TKIs are less effective in solid tumors with wild-type EGFR activation (gene amplification & protein over expression).
- Ph.Ib study in esophageal cancer - short-term response & stable disease observed. Does not warrant continued development as monotherapy. Consider potential immunotherapy combo.

Tumor Types	Wild-type: Gene Amplification	Wild-type: Over Expression	Mutations	TKIs approved: Iressa®, Tarceva®
NSCLC	29%	62%	10-30%	
Esophagus	8-30%	30-90%	12% (esophageal adenocarcinoma)	
Stomach	29%	44-52%	<5%	
Glioblastoma	36-51%	54-66%	27-54% (EGFR variant III)	
Colorectal	4.5%	53%	8%	
Head and neck	10-30%	66-84%	42% (EGFR variant III)	

MABs approved: Erbitux®, Vectibix®

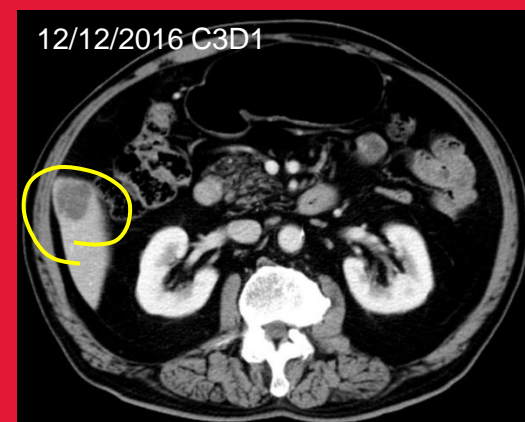
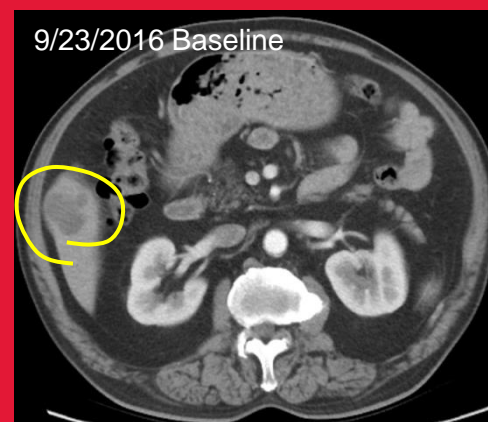
## 2. Superior anti-tumor activity of theletinib in pre-clinical studies with wild-type EGFR.

- 5-10-fold more potent than Tarceva®.
- Sustained target occupancy.



## CASE STUDY - EGFR protein over expression

- May 4, 2016: Man, 62, stage IV **esophageal squamous cell cancer** cT3N0M1 with **liver metastasis**. **High protein overexpression** - EGFR IHC local test: >75% of tumor cells 3+.
- May 4 to Sep 23, 2016: nimotuzumab/placebo + paclitaxel + cisplatin - **6 cycles with best tumor response: PD**.
- Oct 11, 2016: began theletinib 400mg daily.
- Dec 12, 2016: Cycle 3 Day 1 (C3D1) tumor assessment: **Target lesion (liver metastasis) shrank -33%** (36mm to 23mm diameter) - unconfirmed PR.
- Jan 23, 2017: Withdrew from study due to AEs - Gr 1 (diarrhea/pruritus/dental ulcer), Gr 2 (epifolliculitis/dermatitis).





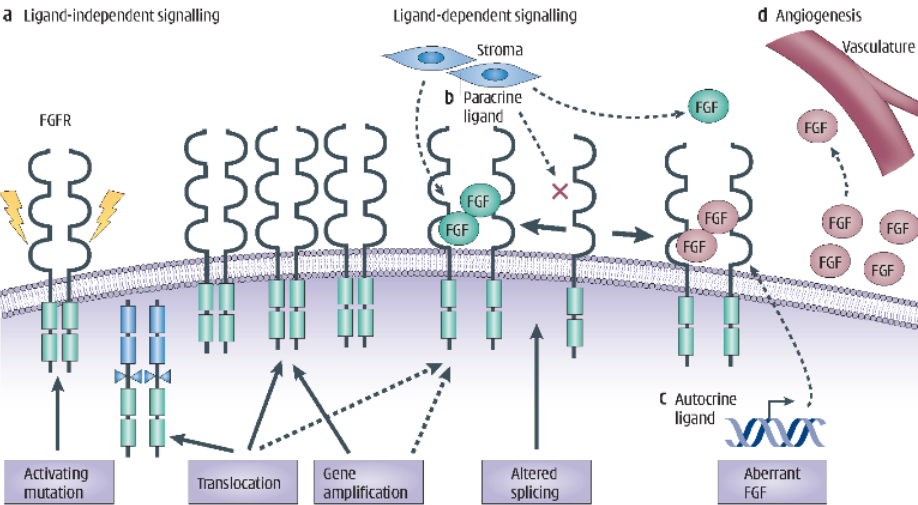
# HMPL-453 - Phase I in China ongoing

## Designed as best-in-class FGFR1/2/3 inhibitor



### 1. FGFR genetic alterations are oncogenic drivers.

- FGF/FGFR signaling normally involved in embryonic development, tissue repair, angiogenesis, neuroendocrine and metabolism homeostasis.
- Multiple oncogenic driver genetic alterations in FGFR pathway: gene amplification, mutation, translocation, fusion, splicing, etc.



### 2. FGFR - diverse & complicated genetic changes with multiple tumor types harboring low incidence.

	Gene amplification	Gene translocation	Gene mutation
FGFR1	Lung squamous (7~15%) H&N squamous (10~17%) Esophageal squamous (9%) Breast (10~15%)	Lung squamous (n/a) Glioblastoma (n/a) Myeloproliferative syndrome (n/a) Breast (n/a)	Gastric (4%) Pilocytic astrocytoma (5~8%)
FGFR2	Gastric (5~10%) Breast (4%)	Intra-hepatic biliary tract cancer (cholangiocarcinoma) (14%) Breast (n/a)	Endometrial (12~14%) Lung squamous (5%)
FGFR3	Bladder (n/a) Salivary adenoid cystic (n/a)	Bladder (3~6%); Lung squamous (3%); Glioblastoma (3%) Myeloma (15~20%)	Bladder (60~80% NMIBC; 15~20 MIBC) Cervical (5%)

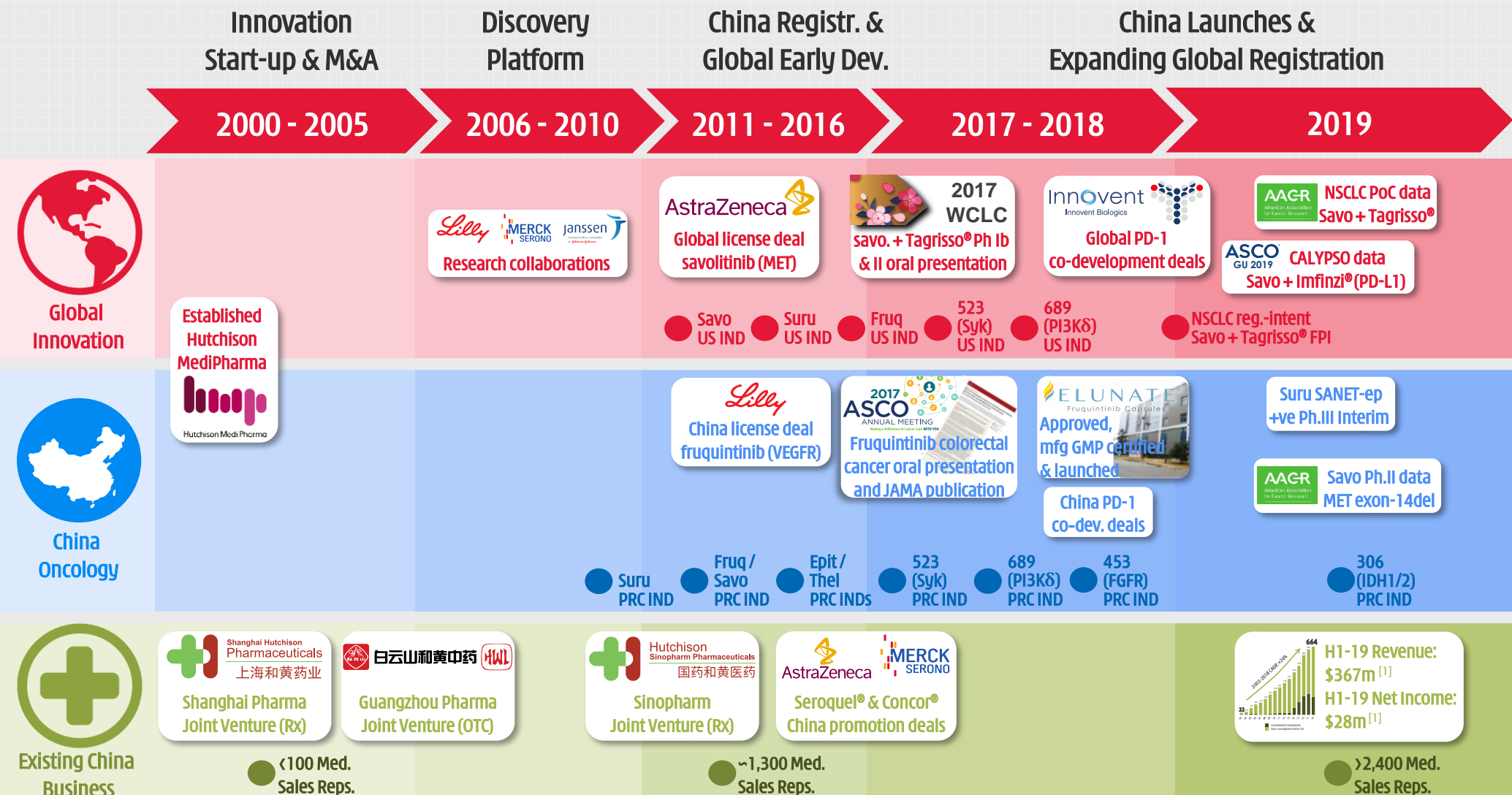


A3

Further Corporate Information

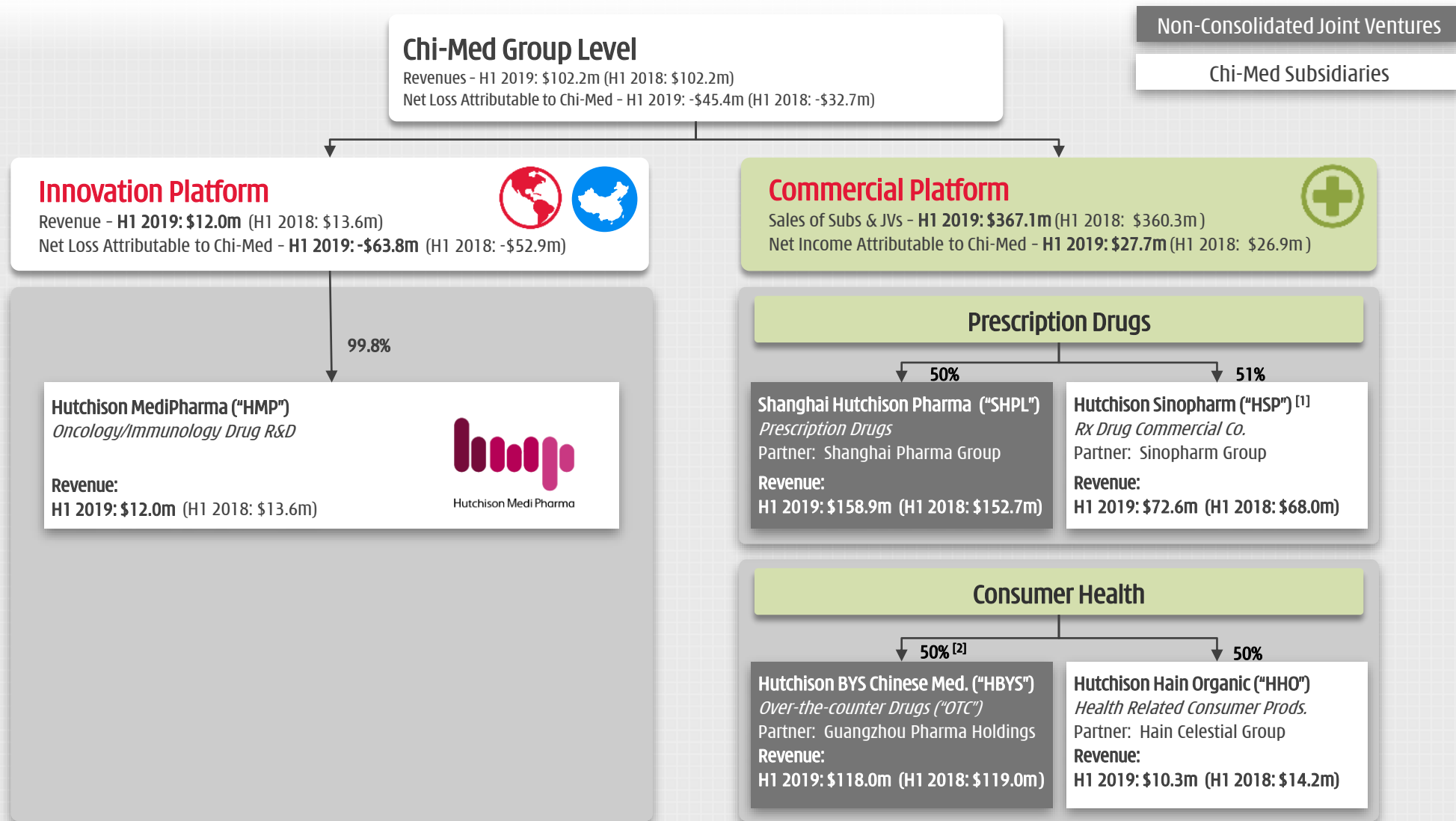


# Important milestones in Chi-Med's evolution



[1] Based on aggregate Non-GAAP revenues and net income / (loss) of consolidated subsidiaries and non-consolidated joint ventures of Commercial Platform.

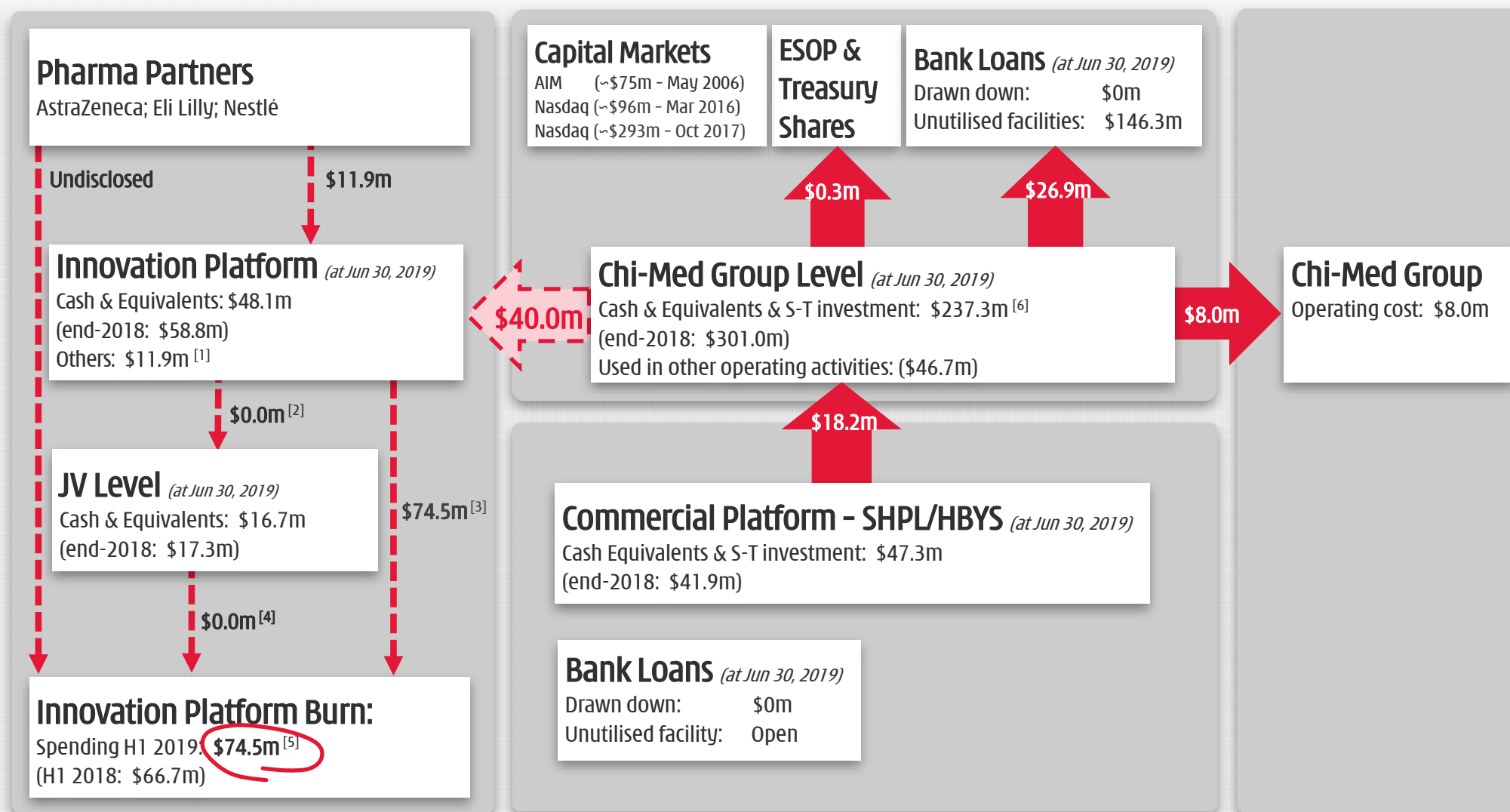
# Chi-Med Group Structure - Major Entities



[1] Excluded HSP's Zhi Ling Tong & Topfer infant nutrition business; [2] Held through an 80% owned subsidiary.

# FY2019 H1 Inter-group cash flow

\$237.3m cash (Jun 30, 2019); \$146.3m in undrawn bank facilities



[1] Others represent changes in working capital, capital expenditure spending and other non-cash items; [2] No capital injection to NSP and no service income received from NSP; [3] Including research & development cost and general & admin. expenses; [4] Share of NSP operating loss; [5] Please see appendix "Non-GAAP Financial Measures and Reconciliation" for a Reconciliation of GAAP to adjusted research and development expenses; [6] Including \$153.9m short-term investment (deposits over 3 months) as at June 30, 2019.

(US\$ millions)

# Non-GAAP Financial Measures and Reconciliation (1/3)



## Reconciliation of Adjusted Group net cash flows and Adjusted Group net cash flows excluding financing activities:

	Jun 30, 2019	2019 Current Guidance	2019 Previous Guidance
Cash and cash equivalents and short-term investments at end period	237.3	180-210 <sup>[1]</sup>	150-180 <sup>[1]</sup>
Less: cash and cash equivalents and short-term investments at beginning of year	(301.0)	(300)	(300)
<b>Adjusted Group net cash flows</b>	<b>(63.7)</b>	<b>(90) - (120)</b>	<b>(120) - (150)</b>
Add: Net cash used in financing activities for the period	29.5	— <sup>[1]</sup>	— <sup>[1]</sup>
<b>Adjusted Group net cash flows excluding financing activities</b>	<b>(34.2)</b>	<b>(90) - (120)</b>	<b>(120) - (150)</b>

## Reconciliation of Adjusted Research and Development Expenses:

	H1 2018	H1 2019
Segment operating loss - Innovation Platform	(53.1)	(63.9)
Less: Segment revenue from external customers - Innovation Platform	(13.6)	(12.0)
Add: Costs of goods & service - third parties	—	1.4
<b>Adjusted R&amp;D expenses</b>	<b>(66.7)</b>	<b>(74.5)</b>

[1] For the purposes of this reconciliation, 2019 guidance for net cash used in or generated from financing activities for the year is not provided and as such, cash and cash equivalents and short-term investments at the end of year excludes the effect of any net cash used in or generated from financing activities for the year.



# Non-GAAP Financial Measures and Reconciliation

## (2/3)



### Reconciliation of GAAP growth to CER growth

\$'Million (except %)	Six Months Ended		Growth Amount			Growth %		
	June 30, 2019	June 30, 2018	Actual	at CER	Exchange effects	Actual growth %	CER growth %	Exchange effect %
<b>Consolidated sales</b>	<b>102.2</b>	<b>102.2</b>	<b>-</b>	<b>5.1</b>	<b>(5.1)</b>	<b>0%</b>	<b>5%</b>	<b>-5%</b>
<b>Commercial Platform</b>	<b>90.2</b>	<b>88.6</b>	<b>1.6</b>	<b>6.4</b>	<b>(4.8)</b>	<b>2%</b>	<b>7%</b>	<b>-5%</b>
— Prescription Drugs subsidiary	72.6	68.0	4.6	9.1	(4.5)	7%	13%	-6%
— Consumer Health subsidiaries	17.6	20.6	(3.0)	(2.7)	(0.3)	-15%	-13%	-2%
<b>Non-consolidated joint venture sales</b>	<b>276.9</b>	<b>271.7</b>	<b>5.2</b>	<b>22.3</b>	<b>(17.1)</b>	<b>2%</b>	<b>8%</b>	<b>-6%</b>
— SHPL	158.9	152.7	6.2	15.8	(9.6)	4%	10%	-6%
— HBYS	118.0	119.0	(1.0)	6.5	(7.5)	-1%	5%	-6%
<b>Total Commercial Platform (Non-GAAP)</b>	<b>367.1</b>	<b>360.3</b>	<b>6.8</b>	<b>28.7</b>	<b>(21.9)</b>	<b>2%</b>	<b>8%</b>	<b>6%</b>
<b>Consolidated net income attributable to Chi-Med</b>	<b>(45.4)</b>	<b>(32.7)</b>	<b>(12.7)</b>	<b>(15.6)</b>	<b>2.9</b>	<b>-39%</b>	<b>-48%</b>	<b>9%</b>
<b>Innovation Platform</b>	<b>(63.8)</b>	<b>(52.9)</b>	<b>(10.9)</b>	<b>(15.4)</b>	<b>4.5</b>	<b>-21%</b>	<b>-29%</b>	<b>8%</b>
<b>Commercial Platform</b>	<b>27.7</b>	<b>26.9</b>	<b>0.8</b>	<b>2.4</b>	<b>(1.6)</b>	<b>3%</b>	<b>9%</b>	<b>-6%</b>
— Prescription Drugs	21.8	20.8	1.0	2.3	(1.3)	5%	11%	-6%
— Consumer Health	5.9	6.1	(0.2)	0.1	(0.3)	-4%	2%	-6%
<b>Sales of SXXB pill</b>	<b>141.0</b>	<b>129.8</b>	<b>11.2</b>	<b>19.7</b>	<b>(8.5)</b>	<b>9%</b>	<b>15%</b>	<b>-6%</b>

# Non-GAAP Financial Measures and Reconciliation (3/3)



## Reconciliation of Non-GAAP Sales and Non-GAAP Net (loss)/income after tax<sup>[1]</sup>

- Prescription Drugs: includes our Consolidated subsidiary (Hutchison Sinopharm) and Non-consolidated joint venture (SHPL);
- Consumer Health: includes our Consolidated subsidiaries (HHO, HHL and HCP) and Non-consolidated joint venture (HBYS).

	IFRS										US GAAP								H1'18- H1'19 Growth
(US\$ millions)	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	H1'18	H1'19	Growth
Sales (Non-GAAP)	21.9	27.9	65.1	101.4	119.0	155.8	197.0	236.4	278.6	360.7	402.3	465.4	518.9	627.4	677.2	664.4	360.3	367.1	2%
Prescription Drugs	17.2	21.8	23.3	23.2	28.1	39.5	54.4	71.2	92.4	116.5	138.2	204.9	286.6	372.3	411.0	408.5	220.7	231.5	5%
- Consolidated subsidiary	-	-	-	-	-	-	-	-	-	-	-	50.2	105.5	149.9	166.4	132.8	68.0	72.6	7%
- Non-consolidated joint venture	17.2	21.8	23.3	23.2	28.1	39.5	54.4	71.2	92.4	116.5	138.2	154.7	181.1	222.4	244.6	275.7	152.7	158.9	4%
Consumer Health	4.7	6.1	41.8	78.2	90.9	116.3	142.6	165.2	186.2	244.2	264.1	260.5	232.3	255.1	266.2	255.9	139.6	135.6	-3%
- Consolidated subsidiaries	4.7	6.1	9.3	8.9	3.7	5.5	7.0	14.1	14.9	15.5	16.5	16.8	20.7	31.0	38.8	40.1	20.6	17.6	-15%
- Non-consolidated joint venture	-	-	32.5	69.3	87.2	110.8	135.6	151.1	171.3	228.7	247.6	243.7	211.6	224.1	227.4	215.8	119.0	118.0	-1%
Total Sales Growth	n/a	27%	133%	56%	17%	31%	26%	20%	18%	29%	n/a	16%	11%	21%	8%	-2%		2%	
- GuanBao divested in Sept'2017	-	-	-	-	-	-	-	-	(11.4)	(50.5)	(51.6)	(49.7)	(40.7)	(45.0)	(38.6)	0.0	0.0	0.0	n/a
Adjusted Consumer Health	4.7	6.1	41.8	78.2	90.9	116.3	142.6	165.2	174.8	193.7	212.5	210.8	191.6	210.1	227.6	255.9	139.6	135.6	-3%
- Adjusted Non-consolidated joint venture	0.0	-	32.5	69.3	87.2	110.8	135.6	151.1	159.9	178.2	196.0	194.0	170.9	179.1	188.8	215.8	119.0	118.0	-1%
Adjusted Sales (Non-GAAP)	21.9	27.9	65.1	101.4	119.0	155.8	197.0	236.4	267.2	310.2	350.7	415.7	478.2	582.4	638.6	664.4	360.3	367.1	2%
Total Adjusted Sales Growth	n/a	27%	133%	56%	17%	31%	26%	20%	13%	16%	13%	19%	15%	22%	10%	4%		2%	
Net (loss)/Income after tax (Non-GAAP)	(10.7)	(3.6)	2.2	6.7	11.2	14.7	21.5	27.9	30.1	33.1	39.7	48.8	54.1	63.3 <sup>[3]</sup>	77.3 <sup>[4]</sup>	83.6	55.1	57.0	3%
Prescription Drugs	(0.4)	1.3	1.9	1.3	1.9	2.8	6.0	11.9	14.2	17.7	22.4	26.5	31.9	41.4	53.0	63.9	41.5	43.7	5%
- Consolidated subsidiary	-	-	-	-	-	-	-	-	-	-	-	0.1	0.6	1.6	2.4	4.1	2.7	1.6	-41%
- Non-consolidated joint venture	(0.4)	1.3	1.9	1.3	1.9	2.8	6.0	11.9	14.2	17.7	22.4	26.4	31.3	39.8	50.6	59.8	38.8	42.1	9%
Consumer Health	(10.3)	(4.9)	0.3	5.4	9.3	11.9	15.5	16.0	15.9	15.4	17.3	22.3	22.2	21.9	24.3	19.7	13.6	13.3	-2%
- Consolidated subsidiaries	(10.3)	(4.9)	(2.9)	(2.4)	0.2	-	0.8	1.0	(0.4)	(1.1)	0.1	1.5	0.8	1.5	3.5	2.8	1.6	1.1	-29%
- Non-consolidated joint venture	-	-	3.2	7.8	9.1	11.9	14.7	15.0	16.3	16.5	17.2	20.8	21.4	20.4	20.8	16.9	12.0	12.2	2%
% Margin	-48.9%	-12.9%	3.4%	6.6%	9.4%	9.4%	10.9%	11.8%	10.8%	9.2%	9.9%	10.5%	10.4%	10.1%	11.4%	12.6%	15.3%	15.5%	
Net (loss)/Income attrib. to Chi-Med	(5.7)	(3.7)	(0.5)	1.2	4.5 <sup>[2]</sup>	5.9 <sup>[2]</sup>	9.3 <sup>[2]</sup>	12.6 <sup>[2]</sup>	13.6 <sup>[2]</sup>	14.6 <sup>[2]</sup>	18.2 <sup>[2]</sup>	22.8 <sup>[2]</sup>	25.2 <sup>[2]</sup>	29.9 <sup>[3]</sup>	37.5 <sup>[4]</sup>	41.4	26.9	27.7	3%
Prescription Drugs	(0.2)	0.6	1.0	0.7	0.9	1.4	3.0	5.9	7.1	8.8	11.2	13.2	15.9	20.7	26.5	32.1	20.8	21.8	5%
Consumer Health	(5.5)	(4.3)	(1.5)	0.5	3.6	4.5	6.3	6.7	6.5	5.8	7.0	9.6	9.3	9.2	11.0	9.3	6.1	5.9	-4%
Net (loss)/income attrib. to Chi-Med growth	n/a	-35%	-86%	340%	275%	31%	58%	35%	8%	7%	n/a	26%	10%	19%	25%	10%		3%	

[1] 2003-2006 incl. disco. operation; [2] Continuing Operations; [3] Excludes the land compensation in SHPL of \$80.8 million from net income after tax and \$40.4 million from net income attributable to Chi-Med for 2016;

[4] Excludes SHPL's R&D related subsidies of \$5.0 million from net income after tax and \$2.5 million from net income attributable to Chi-Med for 2017.

# China Commercial Platform has substantial value

- Chi-Med's Commercial Platform continues to perform well relative to our peer group.
- The market value, based on China Pharma **median PE multiples** is approximately **\$1.8 billion**.<sup>[1]</sup> Given our share in the JVs, Chi-Med's share of this value is approximately **\$0.9 billion**.

	Code	NET SALES			NET INCOME				VALUATION <sup>[4]</sup>	
		2017 Jan-Dec	2018 Jan-Dec	FY17-18 Growth	2017 Jan-Dec	2018 Jan-Dec	FY17-18 Growth	FY2018 Margin	Market Cap.	P/E
<b>CHI-MED Commercial Platform -- Subsidiaries/JVs<sup>[2]</sup></b>		<b>638.6 <sup>[3]</sup></b>	<b>664.4</b>	<b>4%</b>	<b>77.3</b>	<b>83.6</b>	<b>8%</b>	<b>13%</b>	<b>n/a</b>	<b>n/a</b>
Li Zhu Pharma	000513	1,292.6	1,342.5	4%	124.2	179.0	44%	13%	3,590	16
Shandong Dong E E Jiao	000423	1,117.0	1,111.9	0%	309.7	316.2	2%	28%	3,384	12
Kunming Pharma	600422	886.7	1,076.1	21%	50.8	51.8	2%	5%	1,247	23
Zhejiang Kang En Bai Pharma	600572	802.1	1,028.3	28%	110.6	122.5	11%	12%	2,655	24
Tianjin Zhong Xin Pharma	600329	862.0	963.4	12%	71.7	86.0	20%	9%	1,560	18
Zhangzhou Pien Tze Huang	600436	562.7	722.1	28%	118.2	171.0	45%	24%	9,654	52
Jiangsu Kang Yuan	600557	496.2	579.4	17%	57.3	66.3	16%	11%	1,333	20
Zhuzhou Qian Jin Pharma	600479	482.2	504.3	5%	37.4	45.8	23%	9%	618	15
Jiu Zhi Tang	000989	581.3	473.1	-19%	109.3	49.0	-55%	10%	1,113	27
Wuhan Jian Min Pharma	600976	410.8	327.5	-20%	13.9	12.3	-11%	4%	356	29
<b>Peer Group -- Median (10 Comps. excl. Chi-Med)</b>		<b>691.7</b>	<b>842.8</b>	<b>22%</b>	<b>90.5</b>	<b>76.2</b>	<b>-16%</b>	<b>9%</b>	<b>1,446</b>	<b>21</b>
<b>All 61 Listed China Pharma. Companies -- Median</b>		<b>515.1</b>	<b>579.4</b>	<b>12%</b>	<b>50.8</b>	<b>49.6</b>	<b>-2%</b>	<b>9%</b>	<b>1,247</b>	<b>21</b>

Peer Group: 10 companies (excl. Chi-Med) selected as ALL listed and profitable mainland Chinese OTC/RX pharma manufacturing companies, with a focus on similar product types, and 2018 Net Sales in the ~\$300-1,400 million range.

Source: Company data, Deutsche Bank, FactSet

[1] Peer group/China Pharma multiple of 21x 2018 actual Net income after tax of \$83.6 million; [2] Total aggregate PRC domestic results of Chi-Med's 6 Commercial Platform companies (HBYS, SHPL, Hutchison Sinopharm, HHO, HHL & HCPL); [3] Excluding Guanbao (divested); [4] Market Capitalization and Price Earnings Ratios as at **July 26, 2019**: Trailing Twelve Month PE weighted averaged based on market capitalization.

(US\$ millions)

# National Reimbursement Drug List Pricing ("NRDL")

## July'17 update - 15 new drugs in oncology<sup>[1]</sup> added to NRDL



Brand (generic)	Company	Unit Pricing (US\$) <sup>[3]</sup>				Approximate Monthly Pricing (US\$) <sup>[3]</sup>			Indication coverage
		Dosage	Avg. Tender	Reimbursed	Δ%	Dosage	Avg. Tender	Reimbursed	
Herceptin® (trastuzumab)	Roche	440mg:20ml	\$3,298.81	\$1,125.93	-66%	Breast: 4mg/kg wk 1, 2mg/kg weekly. <sup>[2]</sup>	\$4,500	\$1,540	Breast: Her2+; Her2+ meta. Her2+ late-stage meta. gastric.
Avastin® (bevacizumab)	Roche	100mg:4ml	\$772.74	\$296.00	-62%	10mg/kg Q2W.	\$11,590	\$4,440	Late-stage meta. CRC or advanced non-squamous NSCLC.
TheraCIM® <sup>[4]</sup> (nimotuzumab)	Biotech Pharma	50mg:10ml	\$435.26	\$251.85	-42%	100mg weekly.	\$3,730	\$2,160	Combo with radiotherapy for EGFR+ Stage III/IV nasopharyngeal carcinoma.
Rituxan® (rituximab)	Roche	500mg:50ml <sup>[2]</sup>	\$2,544.74	\$1,228.15	-52%	375 mg/m <sup>2</sup> weekly.	\$13,090	\$6,320	Restorative or resistant follicular central type lym.; CD20+ stage III-IV follicular NHL, CD20+ DLBCL.
Tarceva® (erlotinib)	Roche	150mg <sup>[2]</sup>	\$68.15	\$28.89	-58%	150mg QD.	\$2,040	\$870	Advanced NSCLC with limited EGFR gene mutation.
Nexavar® (sorafenib)	Bayer	0.2g	\$60.44	\$30.07	-50%	400mg BID.	\$7,250	\$3,610	Unresectable RCC. Unresectable HCC. meta. Diff. thyroid after radio-iodine therapy.
Tykerb® (lapatinib)	GSK	250mg	\$17.63	\$10.37	-41%	1,500mg QD.	\$3,170	\$1,870	Adv./meta. breast cancer with Her2 O/E, after anthracycline, paclitaxel, trastuzumab.
AiTan® (apatinib)	Hengrui	425mg <sup>[2]</sup>	\$47.85	\$30.22	-37%	850mg QD.	\$2,870	\$1,810	3L gastric adenocarcinoma or esophageal junction with adenocarcinoma.
Velcade® (bortezomib)	J&J	3.5mg <sup>[2]</sup>	\$1,873.78	\$906.07	-52%	1.3mg/m <sup>2</sup> quartic every 3 wks.	\$6,360	\$3,080	Myeloma; recurring or refractory mantle cell lymphoma.
EnDu® (rh-endostatin)	Simcere	15mg	\$132.15	\$93.33	-29%	7.5mg/m <sup>2</sup> iv QD 2-wks- on / 1-week-off.	\$2,110	\$1,490	Late-stage NSCLC.
Epidaza® (chidamide)	Chipscreen	5mg	\$81.48	\$57.04	-30%	30mg QD, 2x per wk.	\$4,190	\$2,930	2L+ Recurring or refractory peripheral T-cell lymphoma (PTCL).
Zytiga® (abiraterone)	J&J	250mg	\$45.63	\$21.48	-53%	1,000mg QD.	\$5,480	\$2,580	Metastatic or ovariectomized prostate cancer.
Faslodex® (fulvestrant)	AstraZeneca	250mg:5ml	\$806.81	\$355.56	-56%	500mg per month.	\$1,610	\$710	Advanced ER/PR+ breast can., failing aromatase inhibitor.
Afinitor® (everolimus)	Novartis	5mg <sup>[2]</sup>	\$36.44	\$21.93	-40%	10mg QD.	\$2,190	\$1,320	Adv. RCC after sunitinib or sorafenib. Adv./meta. pancreatic NETs. Tuberous sclerosis with renal angiomyolipoma.
Revlimid (lenalidomide)	Celgene	25mg <sup>[2]</sup>	\$413.93	\$163.26	-61%	25mg QD 3-wks-on / 1-wk-off.	\$9,310	\$3,670	2L+ Recurring myeloma.

Source: Ministry of Human Resources and Social Security (MOHRSS); Yaozhi; BofA Merrill Lynch Global Research.

[1] Excluding 3 botanical oncology drugs; [2] Reference SKU or reference recommended dosage for monthly pricing calculation; [3] Calculation assumes an exchange rate of CN¥6.75 per US\$1; [4] Marketed as Tai Xin Sheng® in China.

# National Reimbursement Drug List Pricing ("NRDL")

## Oct'18 update - 17 new drugs in oncology added to NRDL



Brand (generic)	Company	Dosage	Unit Pricing (US\$) [2]			Approximate Monthly Pricing (US\$) [2]			Indication coverage
			Avg. Tender	Reimbursed	Δ%	Dosage [1]	Avg. Tender	Reimbursed	
Focus V <sup>®</sup> (anlotinib)	Sino Biopharm	12mg	\$127	\$70	-45%	12mg QD (2 wks-on/1-wk-off)	\$1,783	\$981	3L NSCLC
Oncaspar <sup>®</sup> (pegaspargase)	Hengrui	5ml:3750 IU	\$560	\$429	-23%	≤2ml every 14 days	\$1,231	\$943	1L ALL
Vidaza <sup>®</sup> (azacitidine)	Celgene	100mg	\$378	\$152	-60%	1 <sup>st</sup> cycle: 75mg QD for 7 days; 4wk cycle. After 2 cycles increase dose to 100mg, min of 4-6 cycles	\$14,022	\$5,636	Refractory anemia (RA) or RA with ringed sideroblasts (RARS), RA with excess blasts (RAEB / RAEB-T), and chronic myelomonocytic leukemia (CMML)
Inlyta <sup>®</sup> (axitinib)	Pfizer	5mg	\$99	\$30	-70%	5mg BID	\$5,957	\$1,787	2L Advanced renal cell carcinoma
Tagrisso <sup>®</sup> (osimertinib)	AstraZeneca	80mg	\$253	\$73	-71%	80mg QD	\$7,597	\$2,201	EGFR TKI refractory T790M+ NSCLC
Ninlaro <sup>®</sup> (ixazomib)	Takeda	4mg	\$3,234	\$710	-78%	4mg on Days 1, 8, 15 (28 day cycle)	\$12,934	\$2,839	2L Multiple myeloma
Xalkori <sup>®</sup> (crizotinib)	Pfizer	250mg	\$123	\$37	-70%	250mg BID	\$7,407	\$2,245	Locally adv. or meta. ALK+ or ROS1+ NSCLC
Gilotrif <sup>®</sup> (afatinib)	Boehringer	40mg	\$116	\$29	-75%	40mg QD	\$3,483	\$863	NSCLC with EGFR
Tasigna <sup>®</sup> (nilotinib)	Novartis	200mg	\$39	\$14	-65%	400mg BID	\$4,645	\$1,635	CML
Votrient <sup>®</sup> (pazopanib)	Novartis	200mg	\$66	\$23	-65%	800mg QD	\$7,891	\$2,348	RCC
Sutent <sup>®</sup> (sunitinib)	Pfizer	12.5mg	\$49	\$22	-55%	GIST & RCC: 50mg QD pNET: 37.5mg QD	\$5,544 \$4,455	\$2,498 \$2,007	RCC, GIST, pNET
Stivarga <sup>®</sup> (regorafenib)	Bayer	40mg	\$52	\$28	-46%	160mg QD, 3-wks-on/1-wk-off *	\$4,368	\$2,352	Meta. CRC, GIST, HCC
Zykadia <sup>®</sup> (certinib)	Novartis	150mg	\$108	\$28	-74%	450mg QD	\$9,699	\$2,564	NSCLC
Zelboraf <sup>®</sup> (vemurafenib)	Roche	240mg	\$30	\$16	-47%	960mg BID	\$7,252	\$2,369	Melanoma
Erbitux <sup>®</sup> (cetuximab)	Merck	100mg	\$571	\$186	-67%	400mg/m2 initial dose, 250mg weekly	\$10,446	\$3,074	Colorectal cancer, head and neck cancer
Sandostatin LAR <sup>®</sup> (octreotide)	Novartis	20mg	\$1,169	\$835	-29%	20mg Q4W	\$1,169	\$835	GEP-NENS
Imbruvica <sup>®</sup> (ibrutinib)	JNJ	140mg	\$78	\$27	-65%	MCL: 560mg QD CLL & WM: 420mg QD	\$9,324 \$6,993	\$3,263 \$2,447	MCL, CLL/SLL

Source: Ministry of Human Resources and Social Security (MOHRSS); Yaozhi; China Merchants Securities Research; Citi Global Research.

[1] Reference SKU or reference recommended dosage for monthly pricing calculation; [2] Calculation assumes an exchange rate of CN¥6.95 per US\$1.

\* Price amended to account for 3-weeks on, 1 week off regimen.





HUTCHISON CHINA MEDITECH

Thank you