

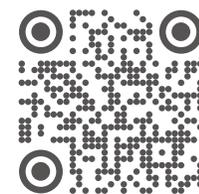


HUTCHISON CHINA MEDITECH

# 2018 Full Year Results

March 11, 2019

AIM/Nasdaq: HCM



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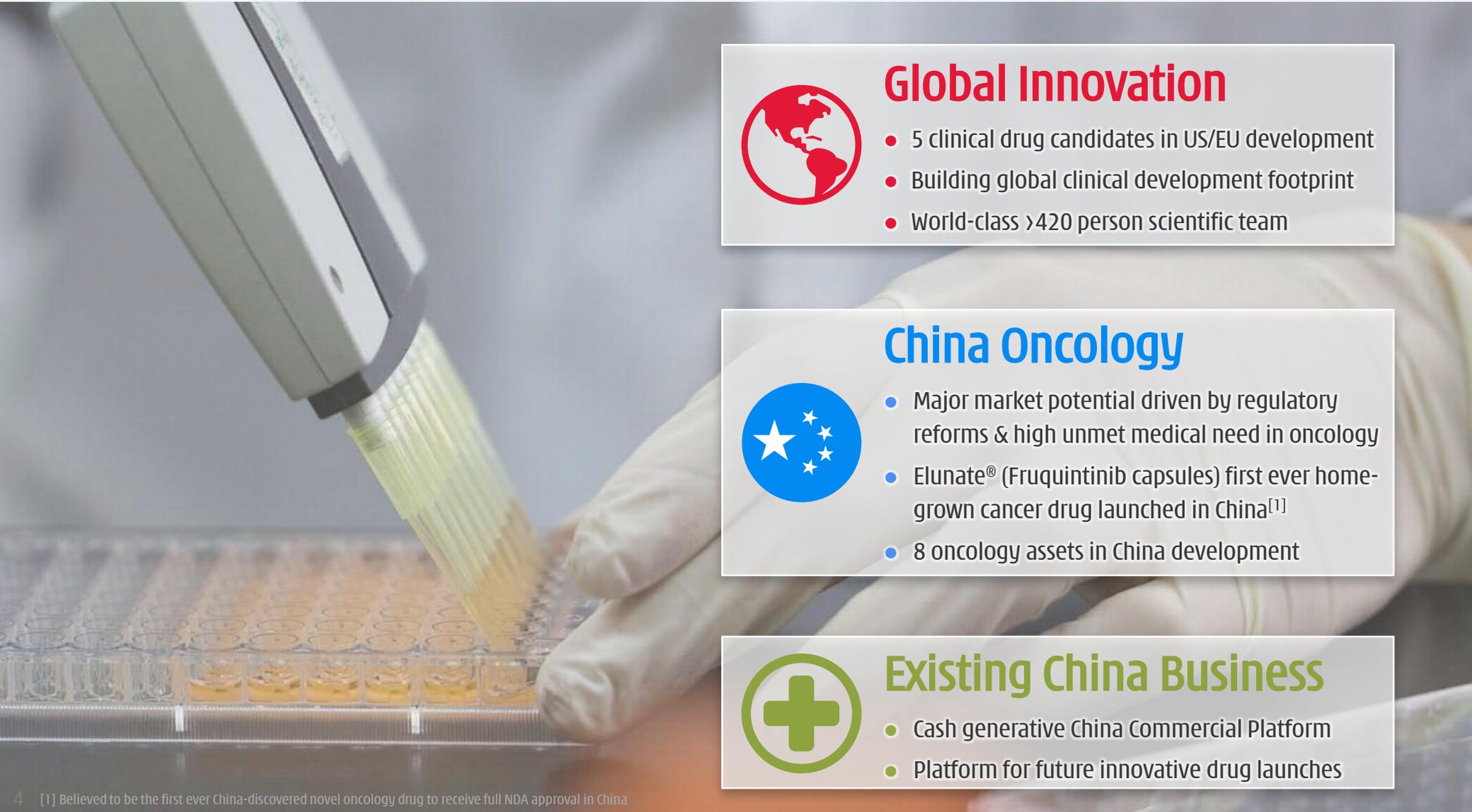
*Use of Non-GAAP Financial Measures* - Certain financial measures used in this presentation are based on non-GAAP financial measures. Please see the appendix slides titled "Non-GAAP Financial Measures and Reconciliation" for further information relevant to the interpretation of these financial measures and reconciliations of these financial measures to the most comparable GAAP measures.



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# 2018 Financial Results

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



## Global Innovation

- 5 clinical drug candidates in US/EU development
- Building global clinical development footprint
- World-class >420 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

# 2018 Financial Results



Global  
Innovation



China  
Oncology

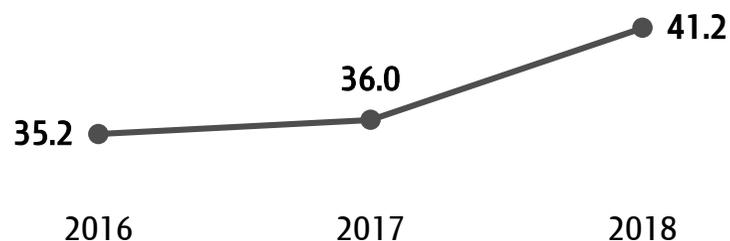


Existing China  
Business

	2016	2017	2018	2018 Guidance <sup>[3]</sup>
<b>GROUP REVENUES</b>	<b>216.1</b>	<b>241.2</b>	<b>214.1</b>	<b>155 - 175</b>
<i>Unconsolidated JV Revenues <sup>[1]</sup></i>	<i>401.5</i>	<i>433.3</i>	<i>491.5</i>	<i>460 - 480</i>
<b>SEGMENT NET INCOME/(LOSS) <sup>[2]</sup></b>				
<b>INNOVATION PLATFORM</b>	<b>(40.7)</b>	<b>(51.9)</b>	<b>(102.4)</b>	<b>(92) - (112)</b>
<b>COMMERCIAL PLATFORM</b>	<b>29.9</b>	<b>37.5</b>	<b>41.4</b>	<b>41 - 43</b>
<i>Prescription Drugs Business</i>	<i>20.7</i>	<i>26.5</i>	<i>32.1</i>	
<i>Consumer Health Business</i>	<i>9.2</i>	<i>11.0</i>	<i>9.3</i>	
<b>Chi-Med Group Costs</b>	<b>(17.9)</b>	<b>(14.8)</b>	<b>(13.8)</b>	<b>(16) - (18)</b>
<b>Land Comp. &amp; Subsidies</b>	<b>40.4</b>	<b>2.5</b>	<b>-</b>	<b>-</b>
<b>GROUP NET INCOME/(LOSS) <sup>[2]</sup></b>	<b>11.7</b>	<b>(26.7)</b>	<b>(74.8)</b>	<b>(71) - (84)</b>
<i>EPS Attrib. to Ord. S-H (Basic) (US\$)</i>	<i>0.20</i>	<i>(0.43)</i>	<i>(1.13)</i>	

# 2018 Financial Results - Innovation Platform

## Revenues



## Net Loss <sup>[1]</sup>



## ■ \$26.9m revenues from Lilly:

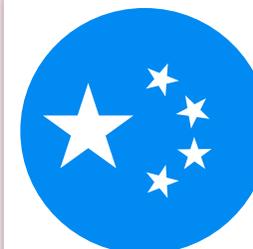
- CRC approval milestone & service fees (\$23.3m);
- Last 5 weeks of 2018 - Elunate<sup>®</sup> manufacturing revenue & royalty (\$3.6m).

## ■ R&D expenses of \$142.2m (non-GAAP):

- Development of 8 drug candidates (5 in U.S./International);
- Established GMP small molecule manufacturing (formulation) in China;
- Expanded U.S./International C&R operation in New Jersey.



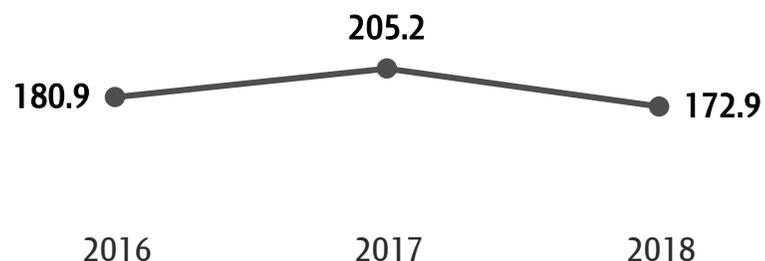
Global  
Innovation



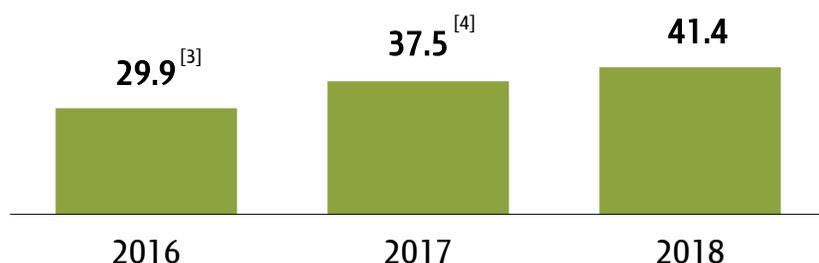
China  
Oncology

# 2018 Financial Results - Commercial Platform

## Revenues <sup>[1]</sup>



## Net Income <sup>[2]</sup>



## ■ Net income up +10% to \$41.4m (non-GAAP):

- SXBX pill (cardiovascular Prescription drug) sales up +11% to \$233.1m;
- Seroquel® & Concor® service fees up +61% to \$21.2m.

## ■ China Two-Invoice System implemented:

- HSP sales lower due to move to fee-for-service model - from revenue consolidation - on some 3<sup>rd</sup> party drugs; No impact on net income;
- Restructure of Prescription Drugs distrib./logistics network under SHPL.



Existing China  
Business

# Portfolio Summary: (1) Step-change global assets; (2) near-term China NDAs targeted; & (3) marketed drugs



Dose Finding / Safety	Dose Expansion / Proof-of-Concept	Registration	Marketed
Fruquintinib + Tyvyt® (PD-1) Solid Tumors <sup>[1]</sup>	Savo / Savo + Imfinzi® (CALYPSO) x2: PRCC & ccRCC	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 + Taxotere® (VIKTORY) MET+ gastric cancer	Savolitinib MET Exon 14 deletion NSCLC	SXBX <sup>[3]</sup> Pill Coronary artery disease (FY'18: \$233m)
HMPL-523 (Syk) Indolent non-Hodgkin's Lymph. (NHL) <sup>[1][2]</sup>	Savolitinib (CTG 1234B) 1L/2L MET+ prostate cancer	Fruquintinib + Taxol® (FRUTIGA) 2L gastric cancer	Seroquel® & Seroquel® XR Schizophrenia/biopolar (FY'18: \$17m fees)
HMPL-689 (PI3Kδ) Indolent NHL <sup>[1]</sup>	Fruquintinib 3L/4L colorectal cancer <sup>[1]</sup>	Surufatinib (SANET-p) Pancreatic NET	Concor® Hypertension (FY'18: \$4m fees)
Fruquintinib + Tyvyt® (PD-1) Solid Tumors <sup>[1]</sup>	Surufatinib 2L pancreatic NET	Surufatinib (SANET-ep) Non-pancreatic NET	> 10 other Rx/OTC drugs (FY'18: >\$250m)
Fruquintinib + GB226 (PD-1) Solid Tumors <sup>[1]</sup>	Fruquintinib + Iressa® 1L EGFRm+ NSCLC		
Surufatinib + Tuoyi® (PD-1) Solid Tumors <sup>[1]</sup>	Surufatinib 2L biliary tract cancer		
Surufatinib + HX008 (PD-1) TBD <sup>[1]</sup>	HMPL-523 B-cell malignancies; AML; ITP <sup>[1]</sup>		
HMPL-453 (FGFR1/2/3) Solid tumors	HMPL-689 Indolent NHL		
Epitinib Glioblastoma			

-  Global Innovation
-  China Oncology
-  Existing China Business

[1] In planning/imminent; [2] Proof-of-concept in Australia; [3] SXBX = She Xiang Bao Xin pill (cardiovascular).  
 Targets: savolitinib = c-MET; fruquintinib = VEGFR1/2/3; surufatinib = VEGFR/FGFR1/CSF-1R; HMPL-523 = Syk; HMPL-689 = PI3Kδ; epitinib (HMPL-813) = EGFR with brain metastases; Theliatinib (HMPL-309) = EGFR wild-type; HMPL-453 = FGFR1/2/3; NET = Neuroendocrine tumors; NSCLC = Non-small cell lung cancer; RCC = Renal cell carcinoma; AML = Acute myeloid leukemia; ITP = Immune thrombocytopenia.

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## Global Innovation

*Pushing the envelope on our most valuable assets*

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



## Global step-change innovation

- *Multiple potential first-in-class assets*



## Kinase selectivity - enable combos

- *Dial out off-target toxicity & address TKI resistance*



## Building broad range of assets against novel targets

- *2nd generation I/O & expanding to mAbs*



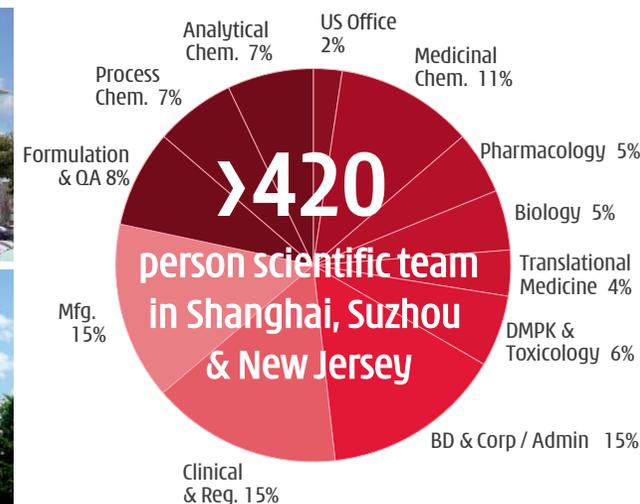
# Proven innovation & commercial operations

## 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. 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

Commercial Team (subsidiaries):

- >200** staff covering:
  - Drug distribution operations; &
  - New Oncology Business Dept.

50/50 Joint Ventures:

- >2,400** Rx medical sales reps.;
- >950** person OTC sales team; &
- >1,500** staff in two major factories

# Global clinical drug portfolio (1/2)

## Savolitinib

Potential First-in-class small molecule selective c-MET inhibitor

**Point of Differentiation:** No kidney toxicity (no 2-quinolinone metabolite)

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

**Dosed to-date:** [2] ~900 patients

**Summary Data:** NSCLC - Tagrisso® EGFR TKI refractory combinations:

Post 1<sup>st</sup>-gen TKI (n=34): ORR 55-61%

Post 3<sup>rd</sup>-gen TKI (n=30): ORR 33%

PRCC (n=44): ORR 18%; mPFS 6.2mo.

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

## Fruquintinib

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

**Point of Differentiation:** No off-target toxicity; full & sustained target coverage

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

**Dosed to-date:** ~1,550 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 16%; mPFS 3.8mo. vs 1.1mo. (SoC)

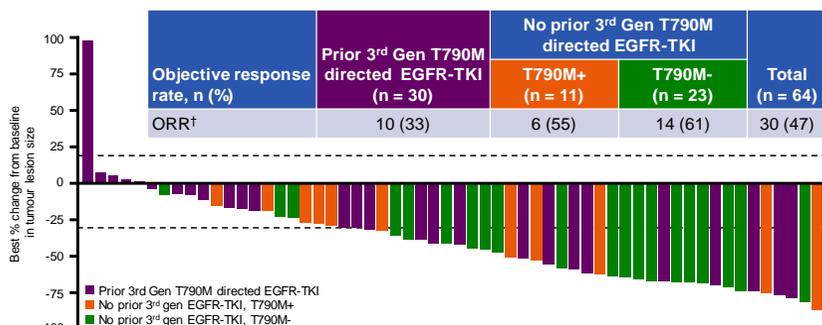
1L NSCLC (Iressa® combo) (n=50): ORR 77% [1]

2L Gastric (Taxol® combo) (n=28): ORR 36%

## IASLC 18TH WORLD CONFERENCE ON LUNG CANCER

October 15-18, 2017 | Yokohama, Japan

### Preliminary anti-tumour activity in all MET-positive patients\*, n = 64

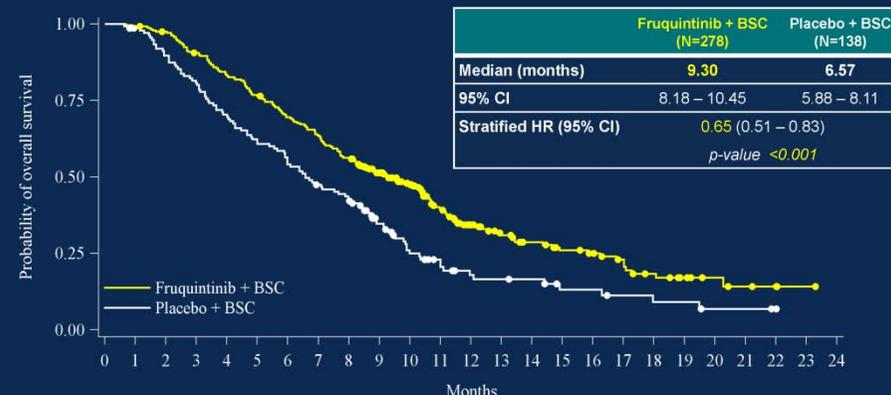


Waterfall plot based on evaluable patients (n = 64); all patients dosed and with on-treatment assessment or discontinuation prior to first tumour assessment  
Data cut-off 31 Aug 2017  
\*17 patients did not have central FISH confirmation of MET-positive status (n = 6 MET-negative; n = 11 unknown by central lab); †Confirmed by a later scan performed at least 4 weeks after initial response observed  
TATTON Part B NCT02143466

## PRESENTED AT: ASCO ANNUAL MEETING '17

### Overall Survival (Primary Endpoint)

FRESCO clearly succeeded in meeting the primary efficacy endpoint of OS



# Global clinical drug portfolio (2/2)

## Surufatinib

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

**Point of Differentiation:** Angio-immuno kinase profile; angiogenesis & TAM <sup>[1]</sup> inhibition

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

**Dosed to-date:** <sup>[2]</sup> ~700 patients

**Step-change efficacy in NET**

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

## HMPL-523

Potential First-in-class small molecule selective Syk inhibitor

**POD:** No off-target toxicity; full & sustained target coverage

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

**Dosed to-date:** ~110 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

**POD:** No off-target toxicity; full & sustained target coverage

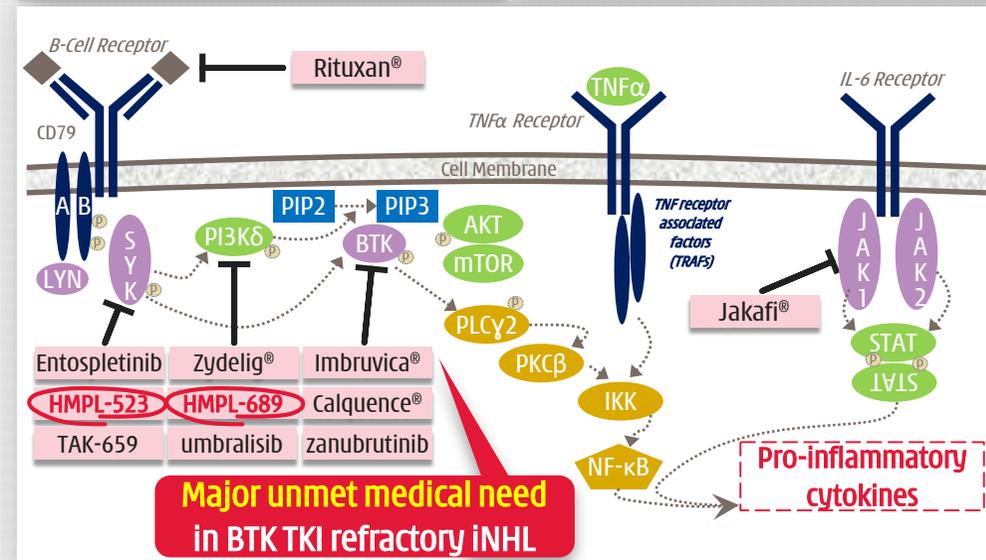
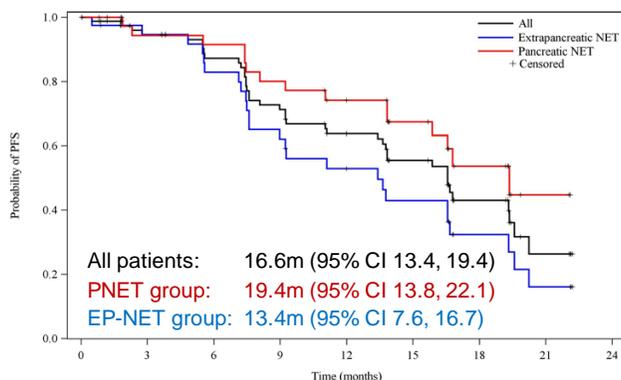
**Indications:** Indolent non-Hodgkin's lymphoma

**Dosed to-date:** ~30 pts. & ~48 healthy vols.

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

**ENETS** 14<sup>th</sup> Annual ENETS Conference | 8-10 March 2017  
Neuroendocrine Tumor Society

### Progression free survival in ITT patients as of 20 Jan 2017



[1] TAM = Tumor Associated Macrophages; [2] Dosed to-date = patients in all clinical trials (treatment & placebo); [3] 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, PI3Kδ = Phosphatidylinositol-3-Kinase delta, Syk = spleen tyrosine kinase, TAM = tumor associated macrophages, pNET = pancreatic neuroendocrine tumors, ep-NET = non-pancreatic neuroendocrine tumors, POD = point of differentiation, 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> c-MET	Savolitinib + Tagrisso®	NSCLC	2L/3L EGFRm; Tagrisso® ref.; MET+	SAVANNAH	Global	Oxnard/Ahn - DF/SMC		Full Ph.II data at AACR Apr 2019
	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		Prelim. PoC at ASCO GU Feb 2019
	Savolitinib + Imfinzi® (PD-L1)	Clear cell RCC	VEGFR TKI refractory	CALYPSO	UK/Spain	Powles - Queen Mary's		
	Savolitinib	Gastric cancer	MET+	VIKTORY	South Korea	Lee - Samsung Med. Ctr		
	Savolitinib + Taxotere®	Gastric cancer	MET+	VIKTORY	South Korea	Lee - Samsung Med. Ctr [1]		
	Savolitinib + Taxotere®	Gastric cancer	MET over expression	VIKTORY	South Korea	Lee - Samsung Med. Ctr [1]		Prelim. PoC mid 2019
	Savolitinib	Prostate cancer	MET+	CCGT 1234B	Canada	Kolinsky/MukJee/Ong/Chi		
<b>Fruquintinib</b> VEGFR 1/2/3	Fruquintinib	Colorectal cancer	3L/4L; Stivarga®/Lonsurf® ref./intol.		US	Eng/Desari - MD And. [2]		Planning US/EU registr. study based on FRESCO/US Ph.Ib
	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		Planning US/EU registr. study based on China Ph.II/US Ph.Ib
	Surufatinib + Tuoyt® (PD-1)	Solid tumors				In planning		
<b>HMPL-523</b> Syk	HMPL-523	Indolent NHL			Australia	N/A		Global Ph.I/PoC data-set now at n >110
	HMPL-523	Indolent NHL			US	Fowler - MD Anderson [3]		
<b>HMPL-689</b> PI3Kδ	HMPL-689	Healthy volunteers			Australia			Data-set now emerging in China Ph.I (n ~31)
	HMPL-689	Indolent NHL			US	Ghosh/Cohen - Levine/Emory [3]		

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

Note: c-MET = mesenchymal epithelial transition receptor, VEGFR = vascular endothelial growth factor receptor, EGFR = 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, DF = Dana-Farber, SMC = Samsung Medical Center, 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<sup>®</sup> combo approval & launch**

 **Build out US/EU development operation**

- US/EU C&R operation set up in Florham Park, NJ in 2018; expected to reach ~30 staff by end 2019



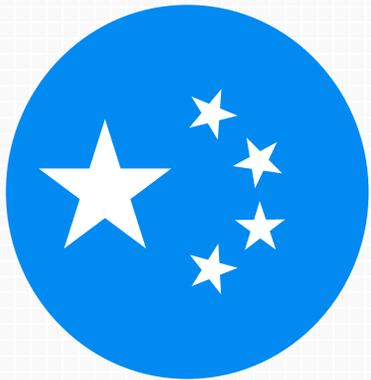
 **Accelerate development of 4 un-partnered global assets**

- 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 move ~1 novel drug candidate into global development per year**

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2b

## China Oncology

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

# China oncology - ~24% of world's cancer patients



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

- *Regulatory reforms in China - addressing low SoC [1]*
- *Major investment inflow*



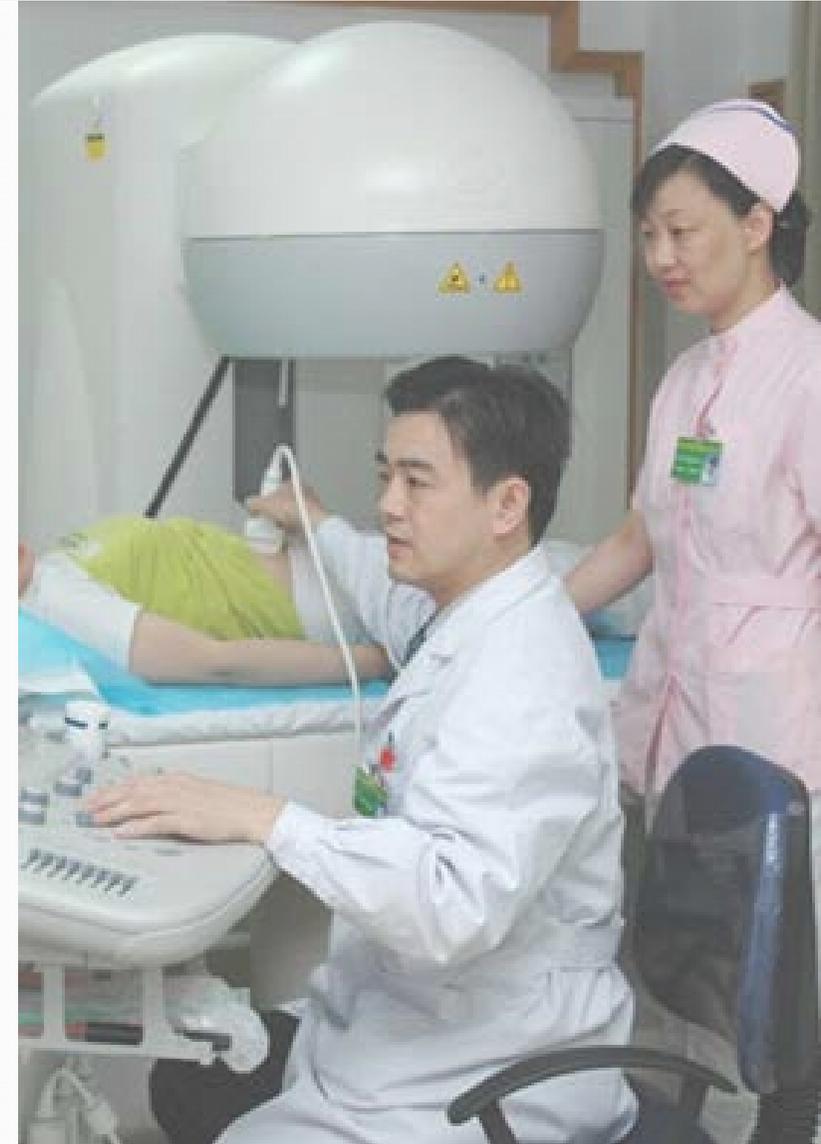
## Chi-Med is a first mover

- *Elunate® launch in 3L mCRC; First ever in China [2]*
- *Deep pipeline - 8 clinical drug candidates with 5 registration studies underway/set to start in China*



## Major commercial opportunity

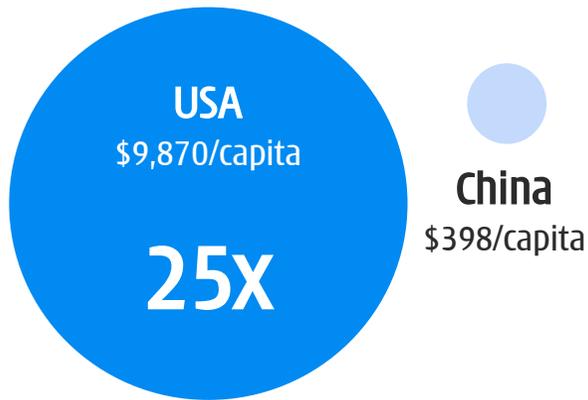
- *National Drug Reimbursement; Medical coverage*



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

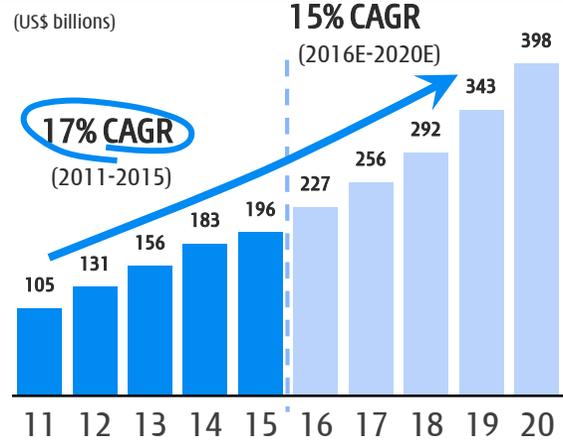
## ...investment, approvals & access all accelerating rapidly

### Per Capita Healthcare Spending [1]



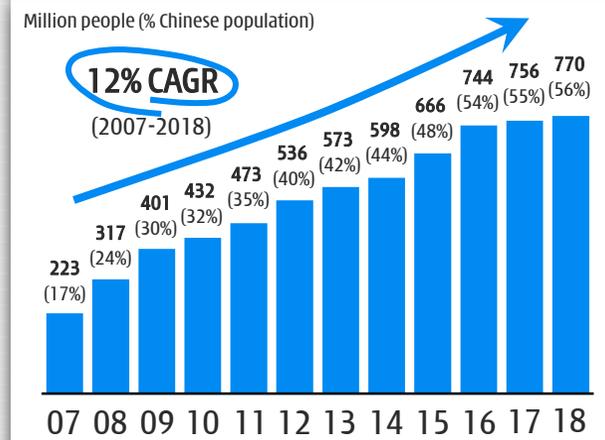
Source: WHO Global Health Expenditure Database (2016 data)

### PRC Pharmaceutical Market Size



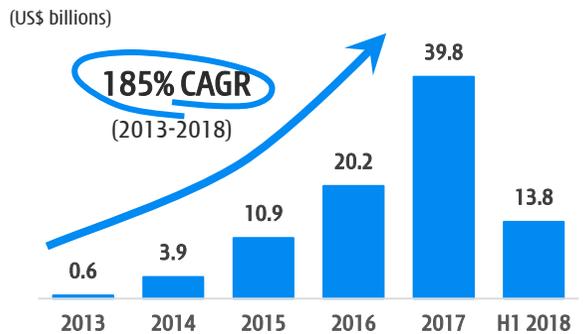
Source: Frost & Sullivan

### Medical Insurance Coverage [2]



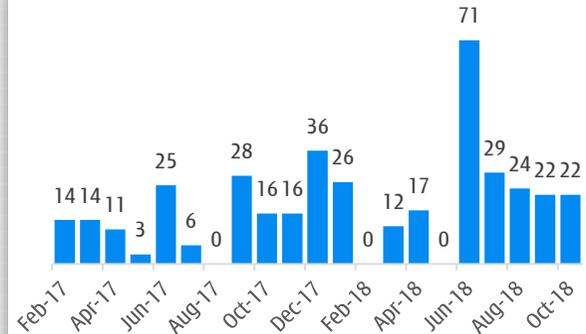
Source: National Bureau of Statistics (2017)

### PRC Healthcare VC/PE Funds [3]



Source: McKinsey; ChinaBio 2018 report

### Number of Priority Review NDAs [4]



Source: McKinsey; National Medical Products Administration

### Improved Access since 2017

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

Source: McKinsey

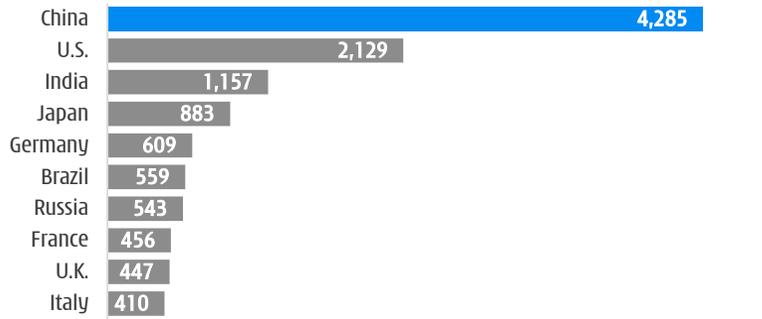
[1] Current health expenditure by revenues of health care financing schemes (in current US\$ per capita); [2] Urban Basic Medical Care Insurance (for both employees & residents) - total persons covered at year-end; [3] Funds raised; [4] NDA = New Drug Application. Note: CAGR = Compound annual growth rate.

# Cancer is a major unmet need in China

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



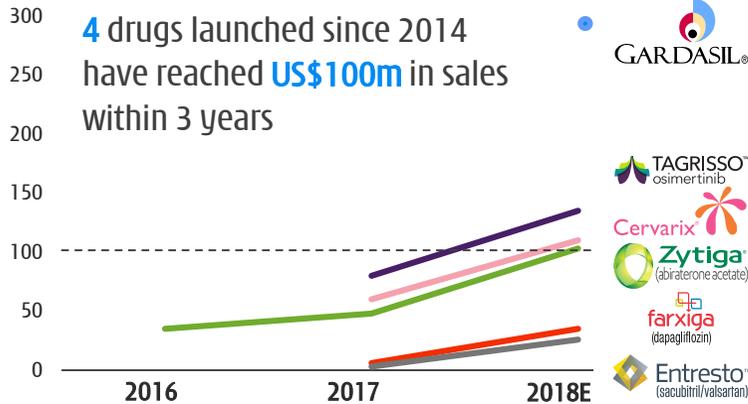
## Cancer Incidence in China (2018)



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 NDRL inclusion - approx. 4x penetration<sup>[1]</sup>



**Herceptin**  
trastuzumab

(Bar Chart US\$ millions; Price per Cycle US\$)



**AVASTIN**  
bevacizumab

Price per cycle: US\$ 11,590 -62% US\$ 4,440



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

[1] Estimated volume/penetration increase assumes change in headline prices per cycle approximate change in average sales prices before and after NDRL inclusion, i.e. minimal in discounting and/or patient access programs.

Major Increases in Access, Volume & Penetration

# 8 assets in China development

...fruq launched - savo/ suru NDAs & Syk/ PI3Kδ PoC ahead



Program	Treatment	Indication	Target patient	Study name	Sites	Dose finding / safety run-in	Proof-of-concept	Registration
Savolitinib c-MET	Savolitinib	NSCLC	MET Exon 14 deletion		China	Lu Shun - SH Chest Hosp.		n ~60
	Savolitinib + Iressa®	NSCLC	2L EGFRm; Iressa® ref.; MET+		China	Wu Yilong - GD General		Launched Nov 2018
	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.		Interim Early 2019
	Fruquintinib + Taxol®	Gastric cancer	2L	FRUTIGA	China	Xu Ruihua - Sun Yat Sen		
	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	In planning		Interim Late 2019
	Fruquintinib + Tyvyt® (PD-1)	Solid tumors			China	In planning		Interim Early 2019
Surufatinib VEGFR 1/2/3; FGFR1; CSF-1R	Surufatinib	Pancreatic NET	All	SANET-p	China	Xu Jianming - #5 Med. Ctr.		Planning China Ph.II/III Based on Ph.Ib data
	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. [1]		Planning China Ph.II/III in several iNHL types Ph.Ib data now n >110
	Surufatinib + HX008 (PD-1)	Solid tumors			China	In planning		Data-set emerging in China Ph.I (n ~31)
HMPL-523 Syk	HMPL-523 + azacitidine	Acute Myeloid Leuke.	1L		China	Wang/Qi - CN Hem. Hosp.		
	HMPL-523	B-cell malignancies	All		China	Multiple leads by sub-types		
	HMPL-523	ITP	All		China	Yang - CN Hem. Hosp. [1]		
HMPL-689 PI3Kδ	HMPL-689	Indolent NHL			China	Cao/Zhou - Fudan/ Tongji		
Epitinib EGFR	Epitinib	NSCLC	EGFRm with brain metastasis		China	Wu Yilong - GD General		
	Epitinib	Glioblastoma	EGFR gene amplified		China	Ying Mao - SH Huashan		
Theletinib EGFR wt	Theletinib	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		

### **Establish Elunate<sup>®</sup> 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 potentially in late 2019;
- Expand Oncology Commercial Org. from current ~30 people to ~200 by end 2020

### **Savolitinib NDA in MET Exon 14 NSCLC potentially in early 2020**

### **Progress development pipeline**

- Syk & PI3K $\delta$  into registration studies & aim to establish PoC for epitinib, theliatinib & FGFR;
- Aim for 2-3 further novel drug candidates into early development by 2021

CHI-

MED



2c

## 2018 Innovation Platform Highlights

# 2018 Operating Highlights

## ■ Fruquintinib (Elunate®)

- Received China NDA approval for fruquintinib & launched in Nov 2018 for colorectal cancer;
- Completed an agreement with Lilly to amend the original 2013 license & collaboration agreement.

## ■ Savolitinib

- Initiated two studies with potential for registration in lung cancer;
- Presented Phase II data of Imfinzi® / savolitinib combo in papillary renal cell carcinoma.

## ■ Hematological malignancies

- Australia & China Phase Ib expansion in lymphoma for HMPL-523 (Syk) & HMPL-689 (PI3Kδ);
- Cleared U.S. IND applications (523/689). U.S. and E.U. clinical development set to start in H1 2019.

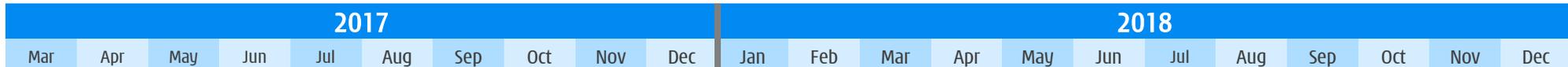
## ■ Immunotherapy combinations

- Signed 4 co-development collaborations for fruquintinib & surufatinib PD-1 antibodies.

## ■ Global clinical development

- Expansion of U.S. & international C&R operations. 5 Chi-Med drug candidates in global development.

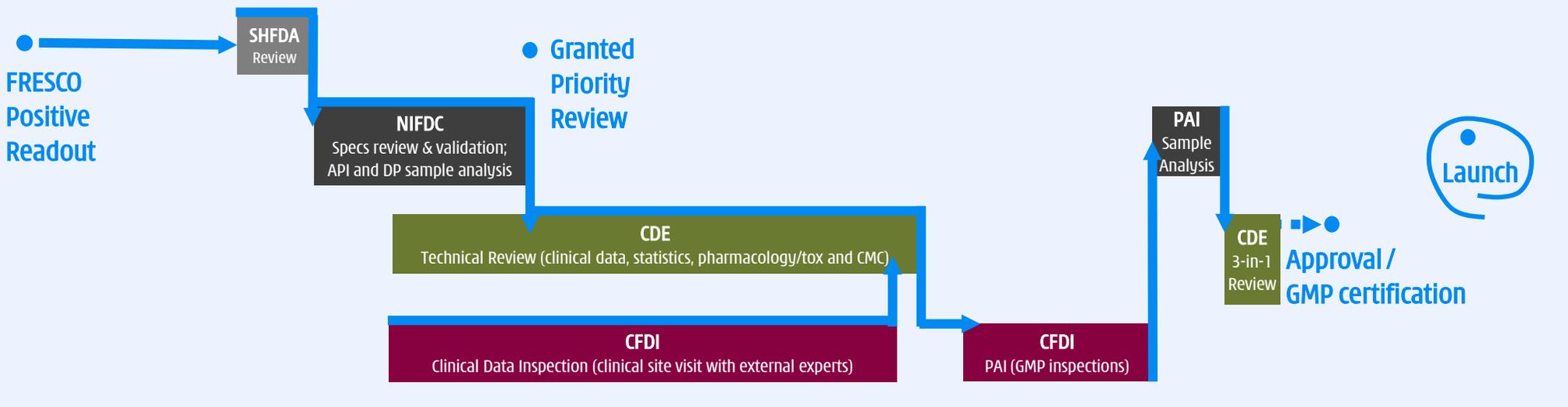
# Many "Firsts" for China biotech



● Oral Presentation



2018 ASCO ANNUAL MEETING  
● Presentation of further analyses



Shanghai Food and Drug Administration (SHFDA)



National Institutes for Food and Drug Control (NIFDC)



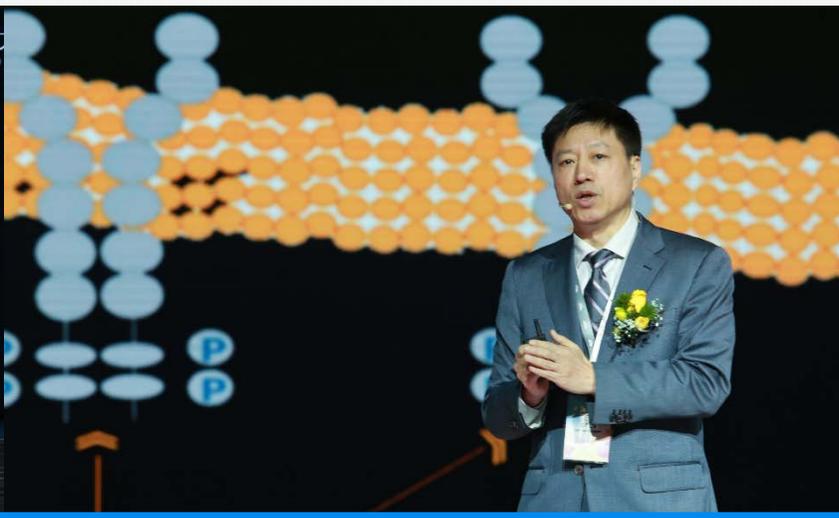
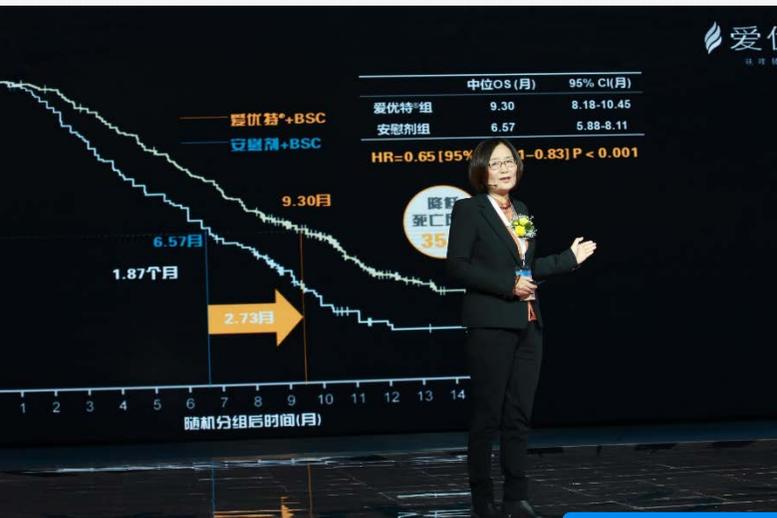
Center for Drug Evaluation (CDE)



Center for Food and Drug Inspection (CFDI)



Critical Path

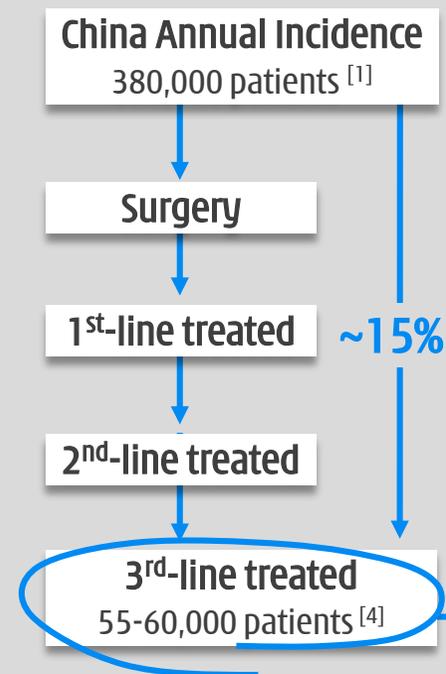


**First ever oncology drug discovered & launched in China [1]**

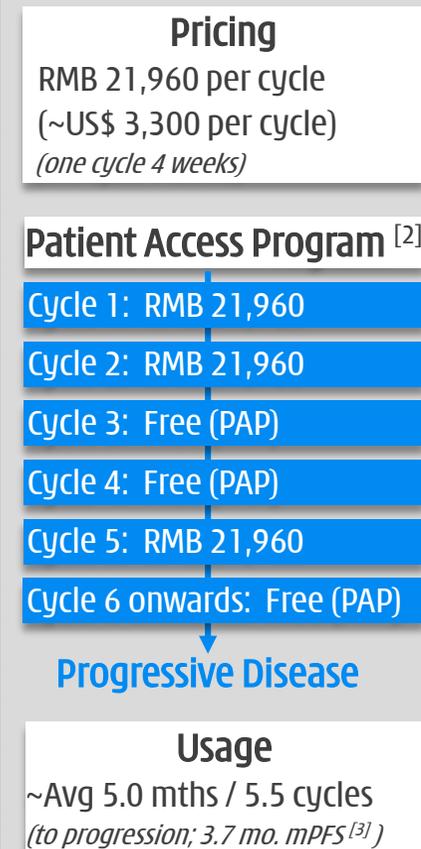


# 3<sup>rd</sup>-line colorectal cancer ("CRC")

## 1. Epidemiology



## 2. Price / Usage



## 3. Latest status

- **Launch of Elunate<sup>®</sup> underway & doing well**
  - In 5 weeks in Nov/Dec 2018: Revenues of \$3.3m from product purchases (manufacturing); & royalty of \$0.3m (15% of ~\$2.0m external sales);
  - Encouraging month-to-month growth trajectory.

# 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;
- **Freedom to collaborate with any third-party** in clinical development; and
- **Possible promotion rights in 30-40% of China for Elunate®.** 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>[2]</sup>	12.5	↗	20.0
Royalty Payments - Paid to Chi-Med <sup>[3]</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**

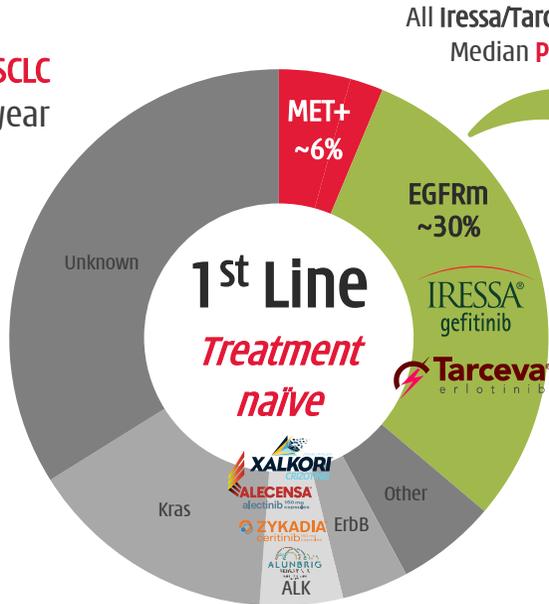
# Savolitinib

Biggest opportunity is MET+ NSCLC



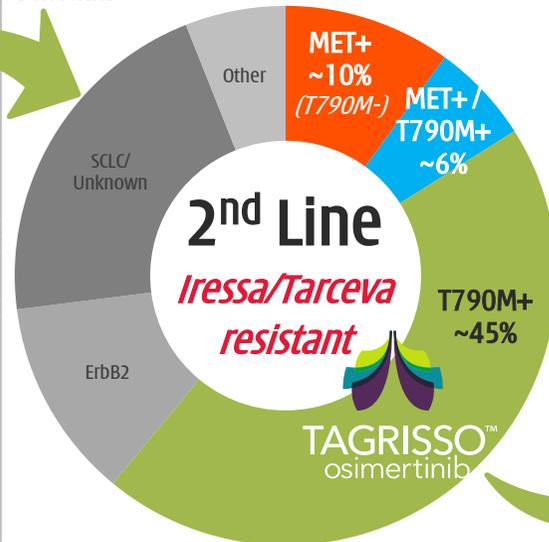
## Primary NSCLC

1.7 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)	Est. <sup>[1]</sup> Pts Treated/yr.
Iressa	EGFRm	2003	518	~20,000
Tarceva	EGFRm	2004	550	~20,000
Tagrisso	EGFRm / T790M	2015	1,860	
Xalkori	ALK / ROS1 / MET	2011	524	
Zykadia	ALK	2015	Not disc.	
Alecensa	ALK	2015	650	
<b>Total Sales</b>			<b>&gt; 4.1b</b>	

Launch	2016 (\$m)	2017 (\$m)	2018 (\$m)	Est. <sup>[3]</sup> Pts Treated/yr.
Dec-15	423	955	1,860	~10-20,000
	423	955	1,860	

**Est. global peak sales ~\$4-5 bn<sup>[4]</sup>.**

# Savolitinib - MET Exon 14 deletion NSCLC

Prelim data AACR 2019; Potential China NDA submission in 2020



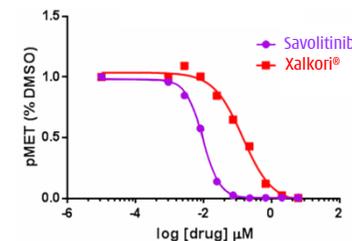
## 1. Competitive landscape outside China:

			Line of treatment	N	Investigator ORR	95% CI	BICR ORR	95% CI
Capmatinib (Novartis/ Incyte)	ESMO 2018 #LBA52	Selective MET	2/3L	69	42.0% (29/69)	30.2%, 54.5%	39.1% (27/69)	27.6%, 51.6%
Capmatinib	ESMO 2018 #LBA52	Selective MET	1L	25	68.0% (17/25)	46.5%, 85.1%	72.0% (18/25)	50.6%, 87.9%
Tepotinib (Merck Serono)	WCLC 2018 #12896	Selective MET	35% 1L, 65% ≥2L	40	57.5% (23/40)	40.9%, 73.0%	42.9% (12/28) <sup>[3]</sup>	24.5%, 62.8%
Xalkori® (Pfizer)	WCLC 2018 #13453	Multi-kinase	38% 1L	65	32% (21/65)	21%, 45%	na	na
Xalkori®	WCLC 2018 #12937	Multi-kinase	[Median 1 (range 0-4)]	25	na	na	40% (10/25)	21%, 61%

## 2. Xalkori® a multi-kinase TKI - probably will be the first approval in MET Exon14 deletion patients outside China.

IC <sub>50</sub> (nM)	Savolitinib	Xalkori® (crizotinib)	Savolitinib vs. Xalkori®
EBC1 Viability	2	19	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>[2]</sup>



## 4. Savolitinib aim to be first approved drug in China in MET Exon14 deletion NSCLC:

- Preliminary China Phase II data<sup>[1]</sup> to be presented at the 2019 AACR conference (March 31);
- Registration study primary data completion expected in 2020;
- 2-3% of NSCLC - estimated incidence of approximately 10,000 new patients per year in China.

[1] The trial is focused on patients with MET Exon 14 mutation who have failed prior systemic therapy, or are unwilling or unable to receive chemotherapy, however the target patient population is intended to be all MET Exon 14 mutation patients;

[2] 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; [3] previous DCO.

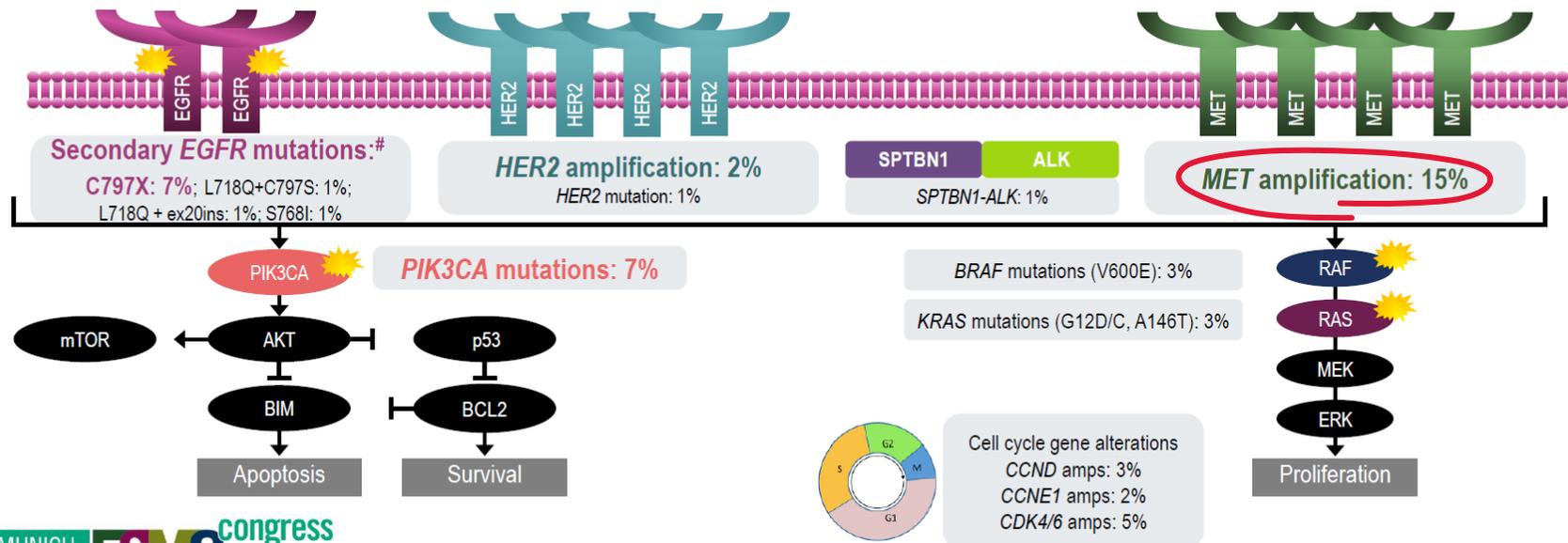
# Savolitinib - EGFR TKI Refractory NSCLC

## MET the main resistance mechanism for Tagrisso® 1L failure

Analysis from **plasma samples from FLAURA patients** who progressed or discontinued Tagrisso® (osimertinib) treatment. Frequency of MET amplification may be higher in tissue samples.

### 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



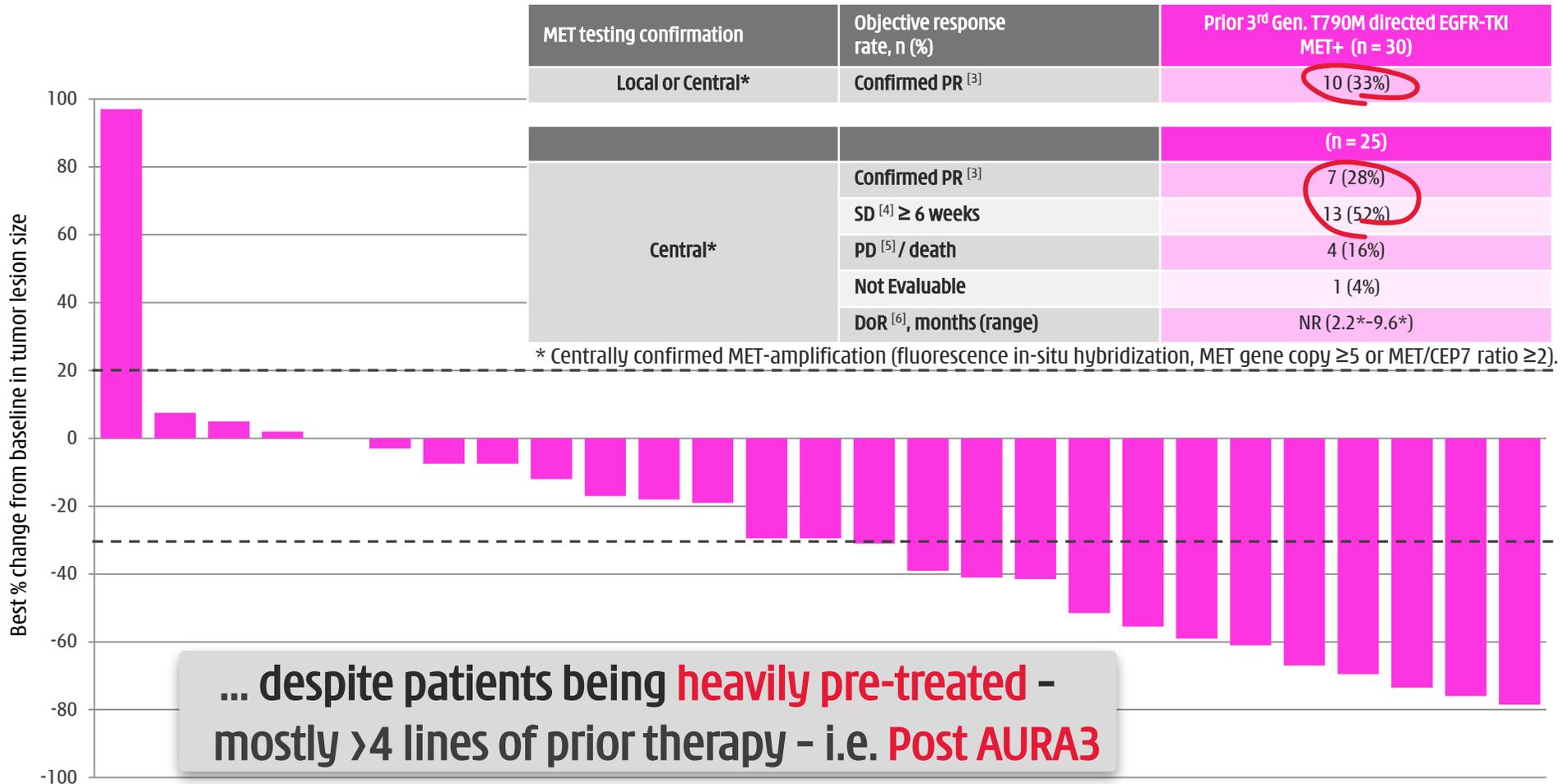
\*Resistance mechanism reported may overlap with another; #Two patients had *de novo* T790M mutations at baseline of whom one acquired C797S at progression

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

## TATTON Study - Full data oral presentation at AACR - April 2019



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



[1] EGFRm NSCLC; [2] WCLC 2017 - Ahn M-J, *et al.* TATTON Phase Ib expansion cohort; Waterfall plot based on evaluable patients (n=30): all patients dosed and with on-treatment assessment or discontinuation prior to first tumour assessment; Data cut-off 31 Aug 2017; [3] PR = Partial Response; [4] SD = Stable Disease; [5] PD = Progressive Disease; [6] DoR = Duration of Response.

# Safety & tolerability

Tagrisso® & savo both highly selective/tolerable monotherapies



US FDA Approval Date	Treatment	Disease setting	n	Efficacy		Discontinuations as % Enrolled		
				ORR	Median PFS (mo.)	Due to AE	Withdrawn / Other	Total [5]
<b>Monotherapy - Tagrisso® / savolitinib</b>								
30-Mar-17	Tagrisso® (osimertinib)	2L EGFRi-refractory T790M+ NSCLC (AURA3)	279	71%	10.1	6%	6%	13%
	savolitinib 600mg QD monotherapy [3]	All-lines Papillary RCC -- <i>FOR REFERENCE ONLY NOT NSCLC</i>	109 [1]	18%	6.2	9%	5%	14%
<b>Combination - Tagrisso® + savolitinib</b>								
	savolitinib 600mg QD + Iressa® (gefitinib) [4]	≥2L EGFRm+ c-MET+ T790M- NSCLC after 1 <sup>st</sup> -gen EGFR TKI (expansion)	51 [2]	52%	ND	20%	14%	33%
	savolitinib 600mg QD + Tagrisso® [4]	≥2L EGFRm+ c-MET+ T790M-/+ NSCLC after 1 <sup>st</sup> -gen EGFR TKI (TATTON B)	34	59%	ND	30%	3%	33%
	savolitinib 600mg QD + Tagrisso® [4]	≥3L EGFRm+ c-MET+ NSCLC after 3 <sup>rd</sup> -gen EGFR TKI (TATTON B)	30	33%	ND			
<b>Approved treatments in NSCLC</b>								
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] TATTON Study - Efficacy data for noted molecular subsets; Tolerability data from all patients (n=64); [3] September 2017 Journal of Clinical Oncology; [4] 2017 World Conference on Lung Cancer; [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

#### Approved therapies in RCC [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 - not yet approved) [6]	59.3%	15.1	NR
Bavencio® + Inlyta® (PD-L1/VEGFR combo - not yet approved) [6]	51.4%	13.8	NR

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

### 2. RCC est. ~\$3.3 bn. market by 2020 [1]

Clear-cell RCC (~\$2.7b)

~80% of RCC  
 ~ 270k new patients/yr.[2]

Non-Clear-cell RCC (~\$0.6b)

~20% of RCC  
 ~ 70k new patients/yr.[2]

### 3. Unmet medical need:

**MET+**  
**Papillary RCC**  
 (~\$0.2-0.3b)

~7% of RCC  
 ~ 25k new patients/yr.[2]

**MET-**  
**Papillary RCC**  
 (~\$0.2-0.3b)

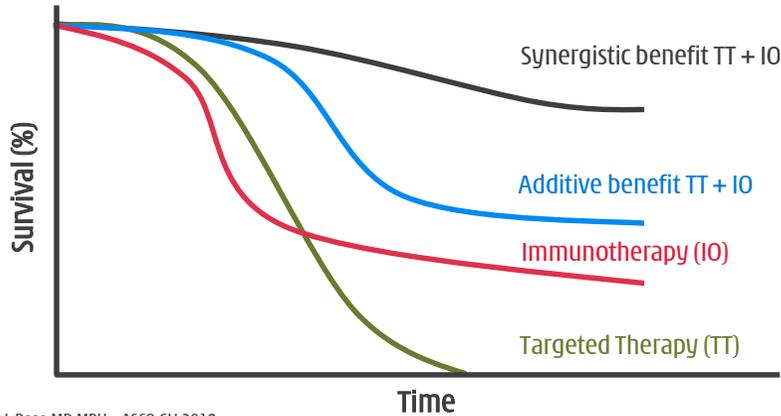
~7% of RCC  
 ~ 25k new patients/yr.[2]

**Other non-ccRCC**  
 (~\$0.1-0.2b)

~5% of RCC  
 ~ 20k new patients/yr.[2]

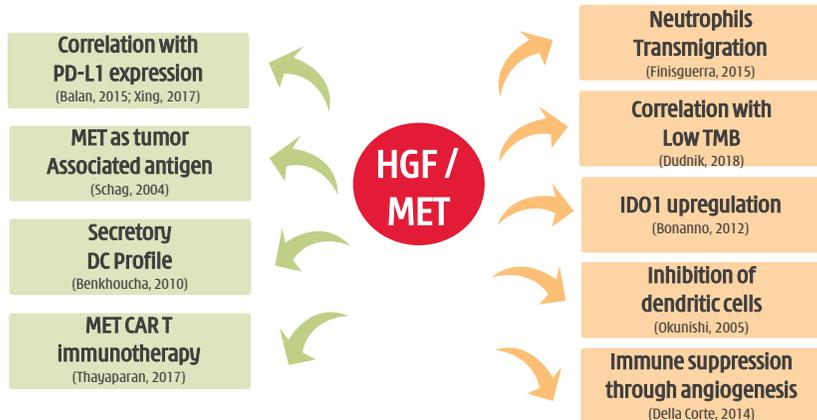
# Savolitinib + Imfinzi<sup>®</sup> combination

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



Tracy L Rose MD MPH - ASCO GU 2019

## 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]

<p><b>MET+ Papillary RCC</b>                  (~\$0.2-0.3b)                  ~7% of RCC                  ~ 25k new patients/yr.</p>	<p><b>Savo mono.</b>                  All lines: (n=44)                  ORR 18.2%                  DCR 73.2%                  mPFS 6.2 mo.</p>
<p><b>MET- Papillary RCC</b>                  (~\$0.2-0.3b)                  ~7% of RCC                  ~ 25k new patients/yr.</p>	<p><b>Keytruda<sup>®</sup> mono.</b>                  All lines: (n=118)                  ORR 25.4%                  DCR 43.2%                  mPFS na</p> <p><b>Savo + Imfinzi<sup>®</sup></b>                  All lines: (n=41)                  ORR 26.8%                  DCR na                  mPFS 5.3 mo.                  First line: (n=28)                  ORR 32.1%                  DCR na                  mPFS na  <i>Interim Data</i></p>
<p><b>Other non-ccRCC</b>                  (~\$0.1-0.2b)                  ~5% of RCC                  ~ 20k new patients/yr.</p>	<p><b>Tecentriq<sup>®</sup> + Avastin<sup>®</sup></b>                  All lines: (n=39)                  ORR 25.6% **                  DCR na                  mPFS na  <i>Not confirmed ORR</i></p> <p><b>Keytruda<sup>®</sup> mono.</b>                  All lines: (n=165)                  ORR 24.8%                  DCR 40.6%                  mPFS 4.1 mo.</p>

# 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 > 110 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**

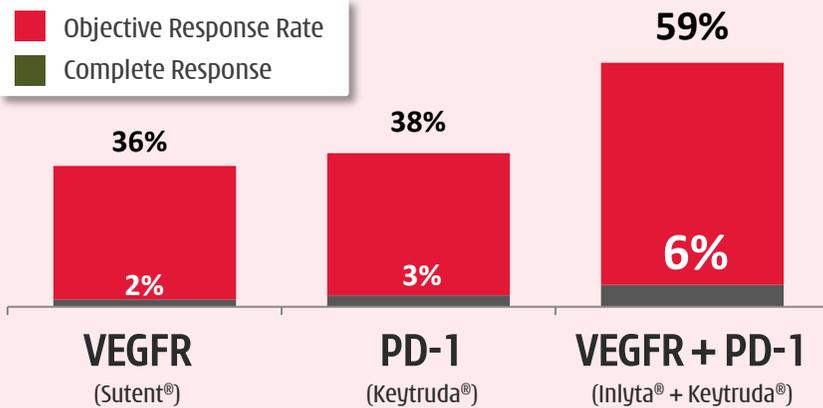
**600mg QD**

until disease progression, death, intolerable toxicity, etc.

# Immunotherapy combinations... our assets are 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 TkrB
<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



savolitinib + Imfinzi® (PD-L1)

ccRCC/PRCC

Jointly managed by Chi-Med & partners



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] Source: 1. 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; 2. 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; [2] BTD = Breakthrough Therapy Designation.

CHI-

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2d

## Strategy – Existing China Business

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

# 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 & >950 OTC sales people in over 320 [1] cities & towns in China.

Drugs in ~24,900 hospitals detailing ~108,000 doctors.

Sold ~4.8 billion doses of medicine in 2018.

### Leadership Market Shares

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

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

### JVs with 3 Major China Pharmas



[1] 320 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.

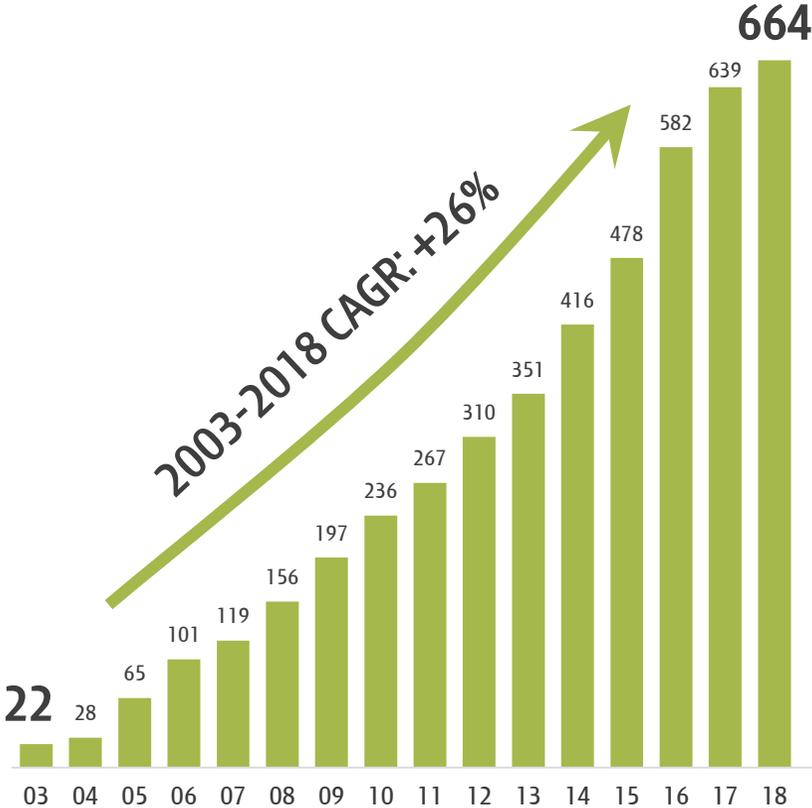
# Chi-Med's Commercial Platform in China

Proven track record of success - important source of cash



## Sales (Non-GAAP) [1][2]

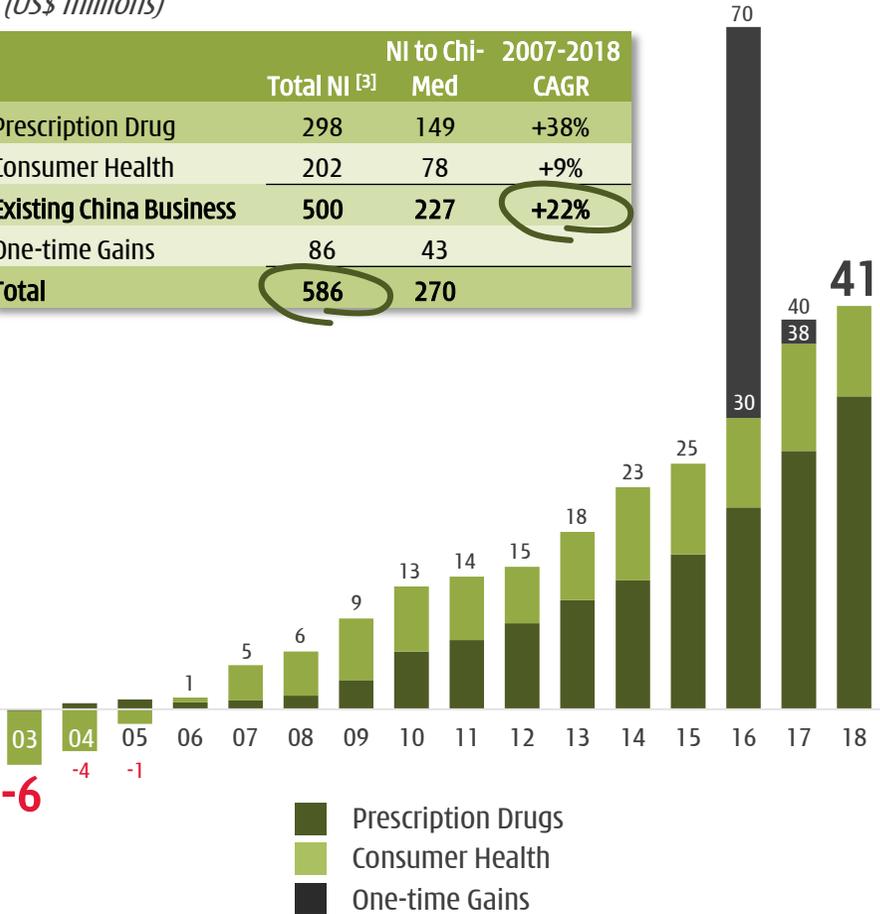
(US\$ millions)



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

(US\$ millions)

	NI to Chi- 2007-2018		
	Total NI [3]	Med	CAGR
Prescription Drug	298	149	+38%
Consumer Health	202	78	+9%
<b>Existing China Business</b>	<b>500</b>	<b>227</b>	<b>+22%</b>
One-time Gains	86	43	
<b>Total</b>	<b>586</b>	<b>270</b>	



[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".

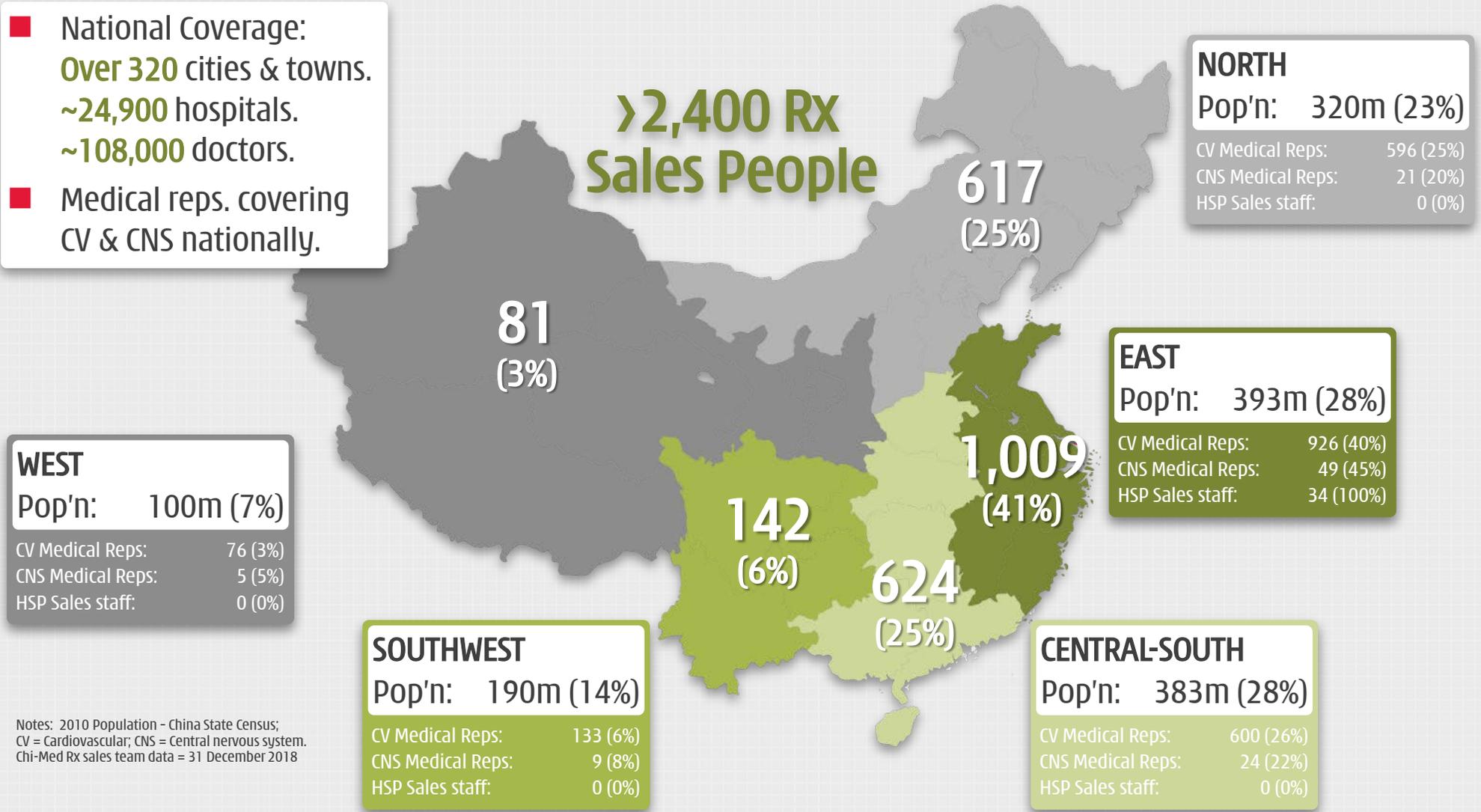
# A powerful Rx Commercial Platform in China....

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



- National Coverage:  
**Over 320** cities & towns.  
**~24,900** hospitals.  
**~108,000** doctors.
- Medical reps. covering  
 CV & CNS nationally.

**>2,400 Rx Sales People**



Notes: 2010 Population - China State Census;  
 CV = Cardiovascular; CNS = Central nervous system.  
 Chi-Med Rx sales team data = 31 December 2018

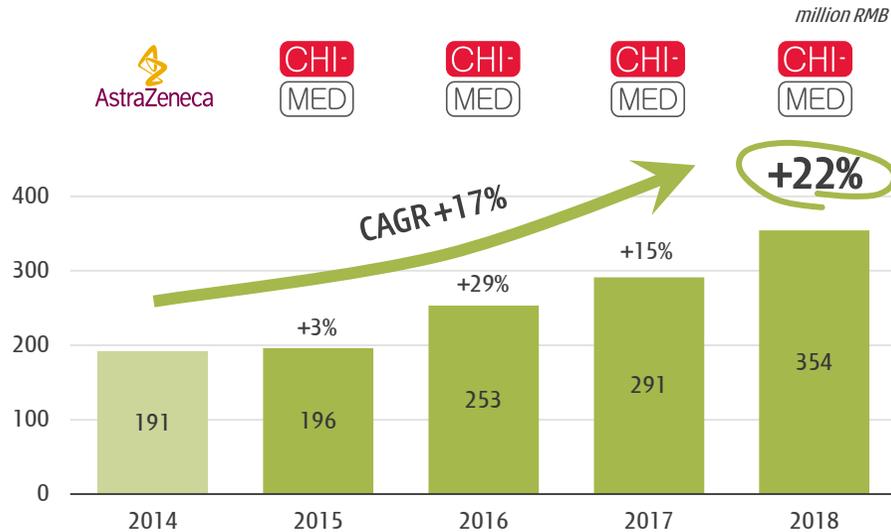
# ...highly adaptable commercial platform

3<sup>rd</sup> party products - sales of Seroquel® & Concor® up significantly



Seroquel®, or quetiapine, is a second generation antipsychotic approved for the treatment of schizophrenia, bipolar disorder and as adjunct treatment of major depressive disorder.

- Chi-Med holds **exclusive all China commercial rights** - full service commercial role (fee-for-service<sup>[1][2]</sup>).
- Luye acquisition. **Chi-Med retain rights through 2025 if we hit sales targets.** 2018 target RMB354m or **+22%** & +15% p.a. thereafter.



Year	Service fees (US\$ million)
2014	\$4.9m
2015	\$9.3m
2016	\$11.4m
2017	\$17.2m

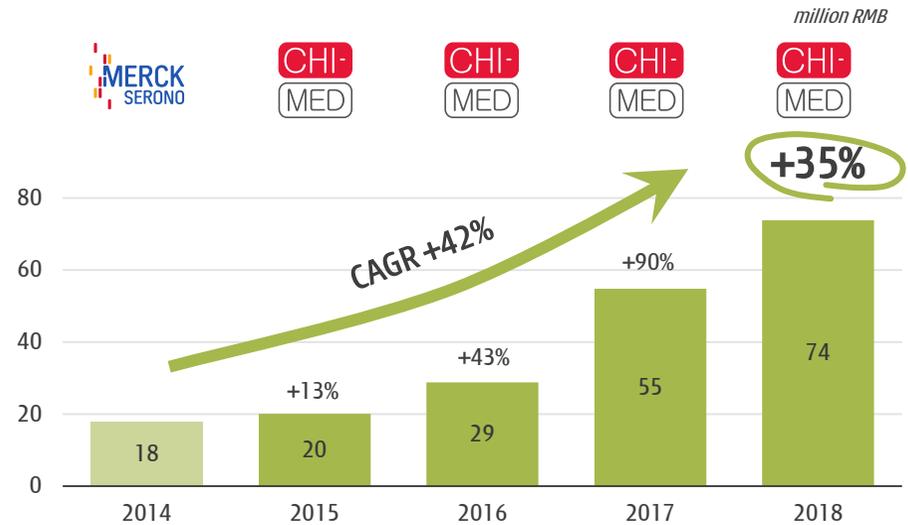
(Paid to Chi-Med, non-GAAP)

[1] In Oct 2017, as a result of the new NMPA Two-Invoice System policy, the Seroquel® operating model changed to a "fee-for-service" model vs. the prior model in which Chi-Med consolidated the sales of Seroquel® -- the change has no material impact on net income earned;  
 [2] 2014 full year and Q1 2015 were managed by AstraZeneca. Chi-Med took over commercial function for Seroquel® across all-China in April 2015.



Concor®, or bisoprolol hemifumarate, is a beta-blocker approved for the treatment of hypertension.

- Chi-Med runs **nine core territories covering ~600m people** - full service commercial role (fee-for-service).
- Took over from MS Jan-2015<sup>[3]</sup>.
- Leverages SHPL's existing **>2,300 cardiovascular medical reps.**



Year	Service fees (US\$ million)
2014	\$0.9m
2015	\$1.4m
2016	\$1.8m
2017	\$4.0m

(Paid to Chi-Med, non-GAAP)

[3] 2014 full year was managed by Merck Serono. Chi-Med took over commercial function for Concor® in 3 original territories on fee-for-service basis in Jan 2015.

# Existing China Business

Plans for 2019-2021



- + Continue organic growth;**
  - Focus on proprietary prescription drug products. Mid- to long-term target of high single-digit percentage growth.
  
- + Build out synergies with China Oncology Organization**
  
- + Strategically evaluate potential for M&A**
  - Expand the scope & scale of our joint ventures
  - Continue to evaluate potential for divestment of certain non-strategic assets
  
- + Focus on cash generation**



3

Cash, Guidance & News Flow

# Cash position & 2019 Guidance

\$420 million in cash resources <sup>[1]</sup>



## Cash Position

- **\$301 million cash / cash equiv. / ST inv.** <sup>[2]</sup>
  - **\$119 million** additional unutilized banking facilities <sup>[3]</sup>
  - **\$42 million** additional cash in Commercial JVs
- 
- **\$27 million** in bank borrowings
  - ✓ Avg. cost 2.8%



	2019 Guidance
Research & Development Expenses	(160) - (200)
Adj. (non-GAAP) Group Net Cash Flows <sup>[4]</sup>	(120) - (150)

- **Innovation Platform:**
  - Elunate<sup>®</sup> revenues ramp-up in coming years - gradual start in 2019;
  - Increase in R&D investment. U.S./E.U. expansion.
- **Commercial Platform:**
  - China reforms <sup>[5]</sup> could narrow 2019 growth before seeing mid- to long-term benefit;
  - RMB 5% weaker vs. US\$ than first half 2018.

[1] Including cash, cash equivalents, short-term investments & unutilized banking facilities; [2] Short-term investments: deposits over 3 months; [3] From Scotiabank, Bank of America Merrill Lynch, Deutsche Bank, Hong Kong Shanghai Banking Corporation; [4] Adjusted (non-GAAP) Group net cash flows excluding financing activities; [5] Two-Invoice System leading to change in SHPL distribution/logistics network & 4+7 Quality Consistency Evaluation System affects some of Hutchison Sinopharm's third-party products.

# Major targets/news flow in 2019



## Global Innovation

**Savo + Imfinzi®**  
PRCC (CALYPSO) ✓  
**Phase II Data**

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

**Savo / Taxotere®** ★  
2L gastric (VIKTORY)  
**Phase II Data**

**Fruq**  
3L/4L colorectal cancer  
**Phase II/III Start (US)**

**Savo + Tagrisso®** ★  
NSCLC (TATTON)  
**Phase Ib Data (AACR)**

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

**Savo Lung Cancer**  
Anticipate announcing plans for further Ph.II/III studies in 2019

**Fruq / Suru PD-1 combos**  
Anticipate initiating U.S / E.U. development



## China Oncology

**Savo** ★  
NSCLC Exon14d  
**Phase II Data (AACR)**

**Suru**  
2L Biliary tract  
**Ph.II/III Start**

**Savo**  
NSCLC Exon14d  
**Reg. Study enrolled**

**Suru** ★  
Pancr. NET (SANET-p)  
**Ph.III Interim (late)**

**Fruq / Suru**  
PD-1 combos  
**Phase I Start**

**Suru** ★  
Non-Pan NET (SANET-ep)  
**Ph.III Interim (late)**

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

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

**Fruq + Taxol®**  
2L gastric (FRUTIGA)  
**Ph.III Interim (early)**

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



HUTCHISON CHINA MEDITECH

Thank you



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## Appendix 1

*Discovery Research Strategy*

# Attack cancer from multiple angles at same time

## Immune Desert

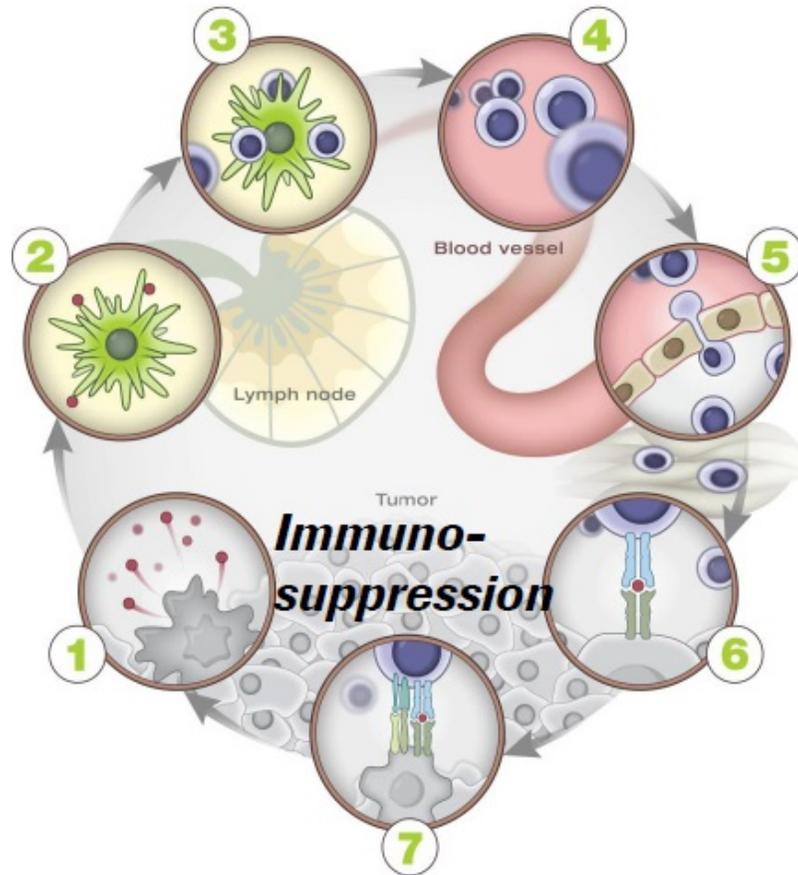
Insufficient T cell response

- 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

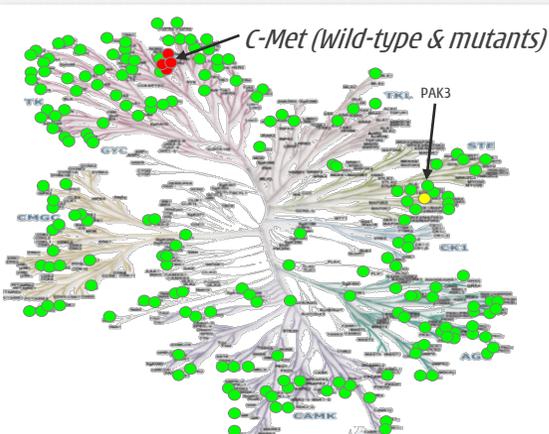
## Inflamed

Inactivated T cell response

- Immunotherapies (address negative regulators)
- Vaccines

Need combinations of potent, yet tolerable drugs against specific targets

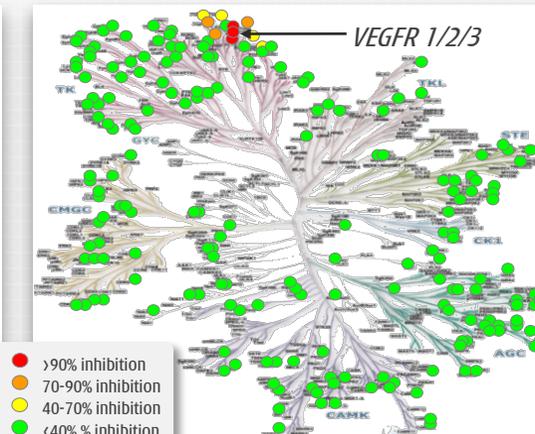
# Our advanced medicinal chemistry provides superior selectivity & safety profiles...



## Savolitinib

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

Screening at 1 μM against 253 Kinases



~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]
<i>Monotherapy - Tagrisso® / savolitinib</i>			
Tagrisso® (osimertinib)	6%	6%	13%
savolitinib 600mg QD monotherapy [2]	9%	5%	14%
<i>Combination - Tagrisso® + savolitinib</i>			
savolitinib 600mg QD + Tagrisso® [3]	30%	3%	33%
savolitinib 600mg QD + Tagrisso® [3]	30%	3%	33%
<i>Approved treatments in NSCLC</i>			
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%

3 <sup>rd</sup> -Line Metastatic CRC	FRESCO Study Mainland China		CONCUR Study (China, HK, Taiwan) [4]	
	Elunate®	Placebo	Stivarga®	Placebo
<i>Treatment arms</i>				
<i>VEGFR on-target related AEs:</i>				
Hypertension ≥G3	21.2%	2.2%	12.5%	8.3%
Hand-Foot Syndrome (Palmar-plantar), ≥G3	10.8%	0.0%	17.0%	0.0%
<i>Off-target (i.e. non-VEGFR) related AEs:</i>				
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%
<i>Hepatic function (Liver function) AEs:</i>				
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%
<i>Tolerability:</i>				
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] 2017 World Conference on Lung Cancer; [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.

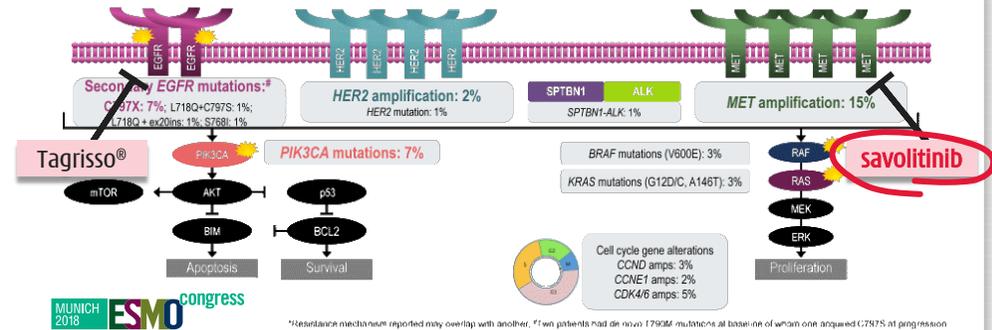
# ...superior safety allows for combinations TKI + TKI combos to address acquired resistance



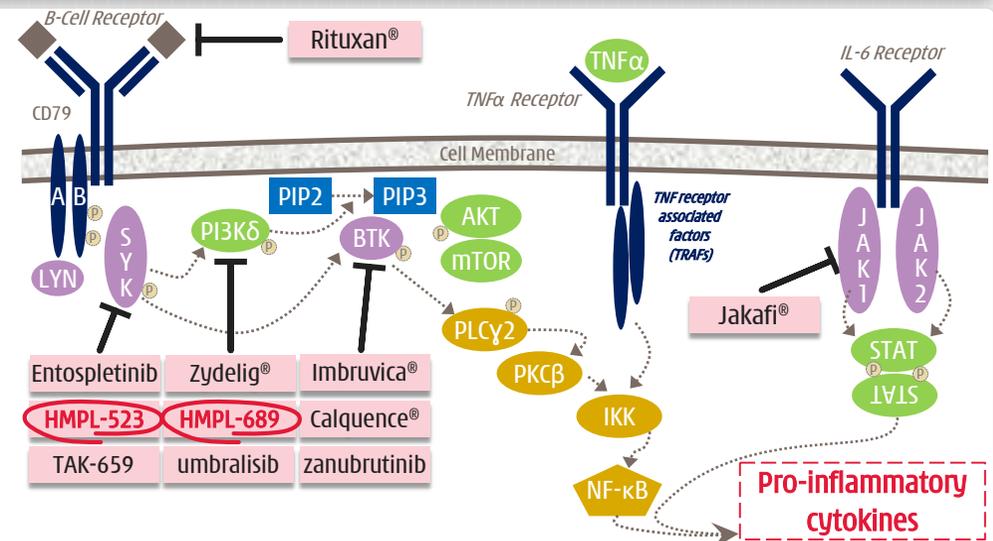
- **MET amplification** is the most common resistance mechanism for Tagrisso®;
- Requires addition of **MET inhibitor - savolitinib** - in combo with Tagrisso®

## 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**



# What is next from discovery?

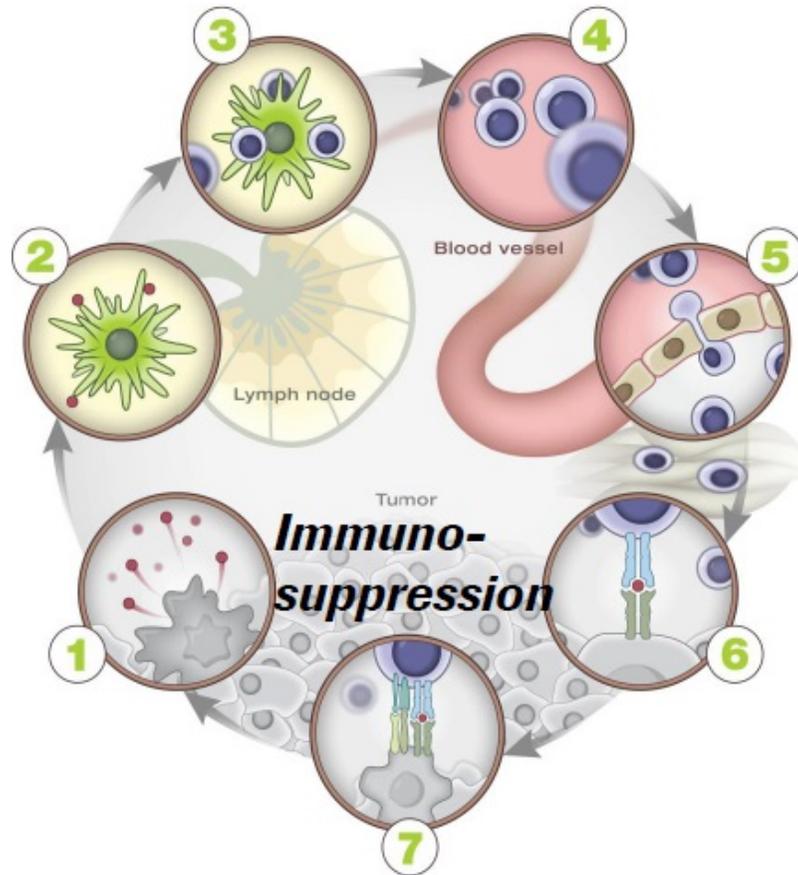
Differentiated assets against multiple targets to emerge 2019-22

## Priming & activations

- aOX40
- 4-1BB

## Antigen release

- c-MET (savolitinib)
- EGFR (epitinib/theliatinib)
- Syk (HMPL-523)
- PI3K $\delta$  (HMPL-689)
- FGFR (HMPL-453)
- ERK
- RIP1K
- IDH



## 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



5

## Appendix 2

*Further details on each drug candidate*



5a

## Savolitinib (AZD6094)

*Potential first-in-class selective c-Met inhibitor*

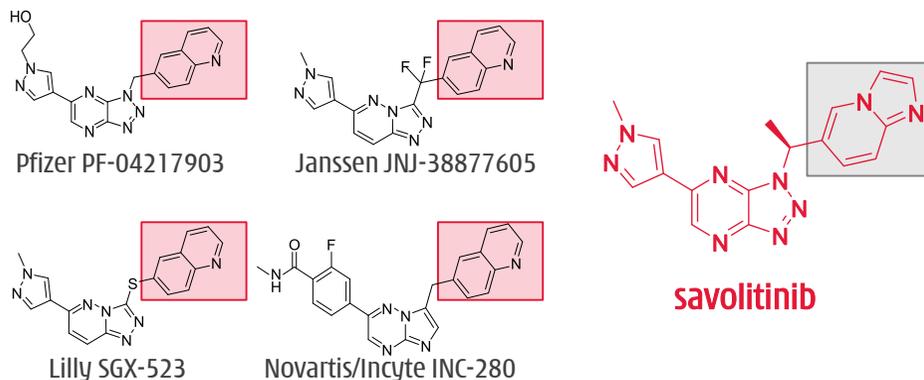
# Savolitinib (AZD6094)

## Potential first-in-class selective c-Met inhibitor

### 1. Strong potential to become first selective c-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) & molecular selection.**

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



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

### 2. c-Met is aberrant in many tumor settings. [3]

Indication	c-MET			New Cases (2015)	
	Amplification	Mutation	Over-Expression	Global	China
Gastric	10%	1%	41%	1,034,000	679,100
Lung	8-10% [1]	8%	67%	1,690,000	733,300
Head & Neck		11%	46%	740,000	135,000
Colorectal	10%		65%	1,477,000	376,300
Renal cell Carcinoma (Papillary)	40-70%	100% [2]		50,000	7,000
Renal cell Carcinoma (Clear cell)			79%	270,000	60,000
Esophagus	8%		92%	496,000	477,900
Prostate [4]			54-83%	1,100,000	60,300

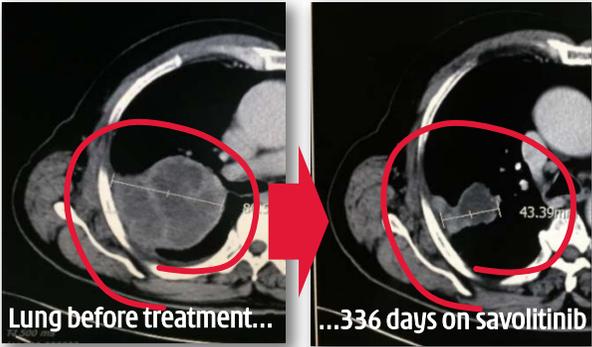
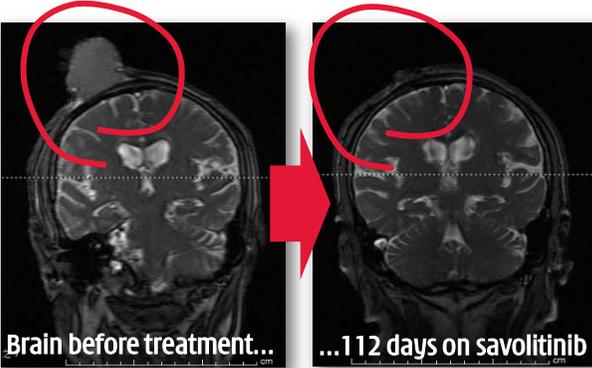
### 4. AstraZeneca collaboration & 2016 amendment.

- \$20m received upfront (Dec 2011);
- \$120m in development/approvals milestones (\$25m received as of Dec 2018);
- 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%);
- **14-18% tiered royalty ex-China [5]** & 30% flat rate China royalty on all product revenues.

[1] Range includes (i) approximately 4% of c-Met+ naive non-small cell lung cancer patients and (ii) 10 - 30% of EGFR+ non-small cell lung cancer patients, which 15 to 20% develop EGFR+ tyrosine kinase inhibitor resistance pathway as c-Met+; [2] Hereditary papillary renal cell carcinoma only; [3] Company estimates considering Frost & Sullivan data, National Central Cancer Registry of China and publicly available epidemiology data; [4] By IHC, c-Met overexpression in 54% of lymph node disease and 83% of bone metastases. Varkaris et al, Expert Opin Investig Drugs. 2011 Dec; 20(12): 1677-1684; [5] Subject to approval in the papillary renal cell carcinoma (PRCC) indication and 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%.

# Savo standout efficacy in all MET+ NSCLC subsets...

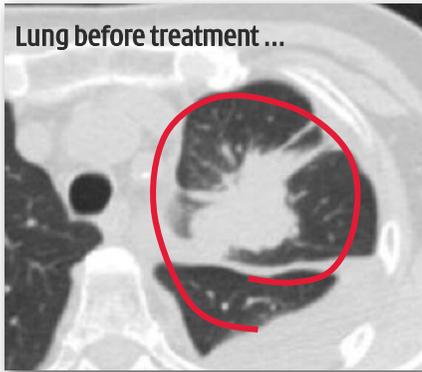
## 1L NSCLC [1]



## 2L post Iressa® / Tarceva®



## 2L/3L post Tagrisso®



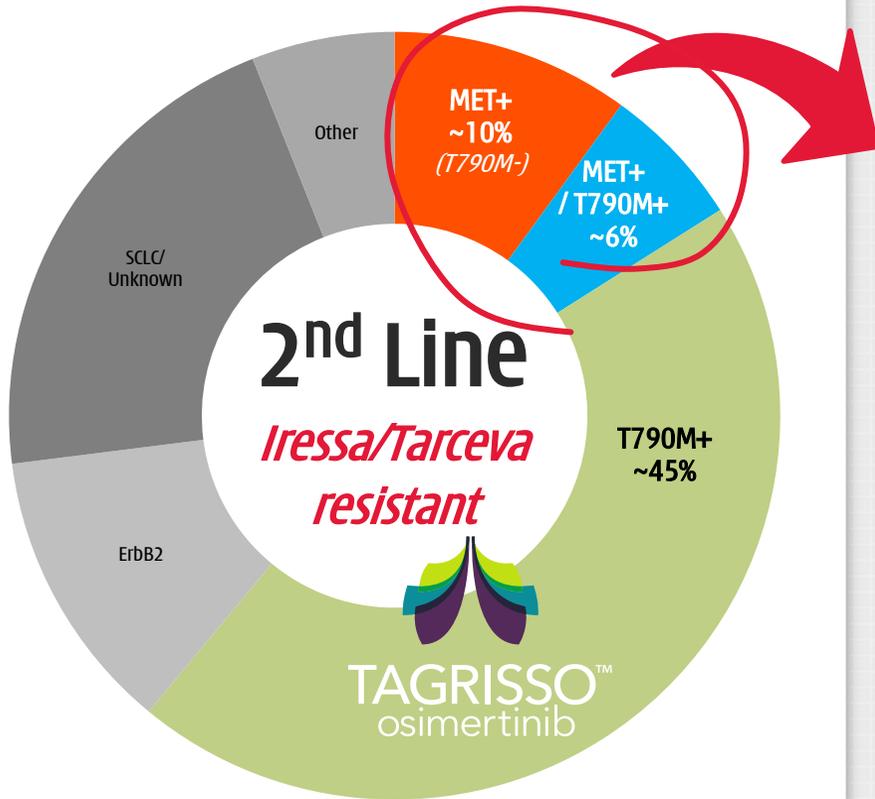
56 [1] The trial is focused on patients with MET Exon 14 mutation who have failed prior systemic therapy, or are unwilling or unable to receive chemotherapy, however the target patient population is intended to be all MET Exon 14 mutation patients.

# Savolitinib - 2L EGFRm NSCLC

Very strong preclinical rationale for combination w/ EGFR-TKIs

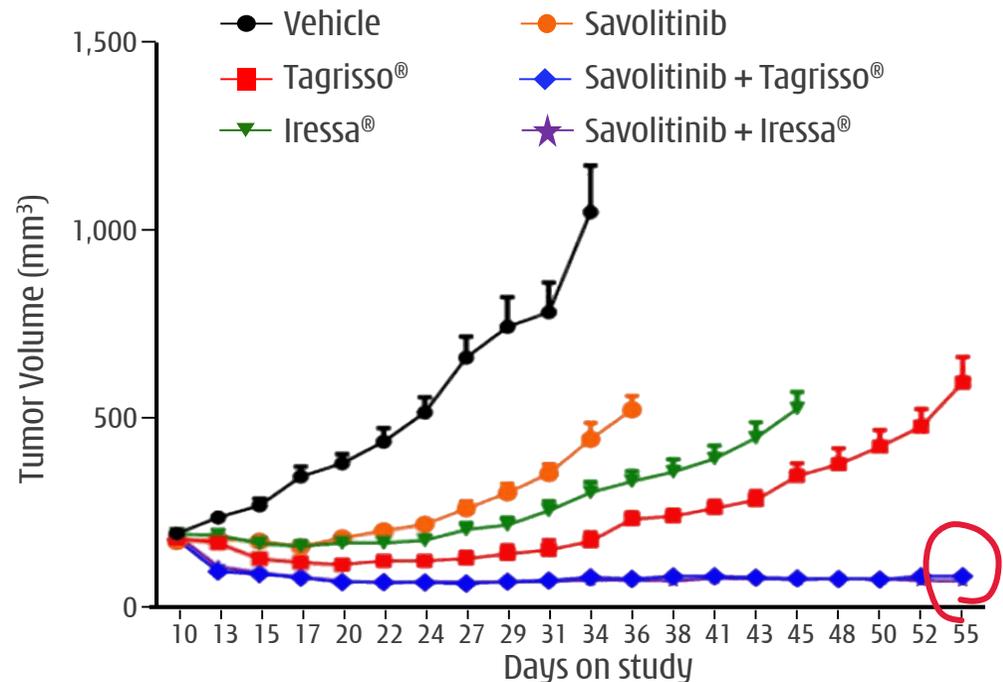


1. 2<sup>nd</sup> Line NSCLC is a **fast and attractive indication for savolitinib** to go after. Also important unmet medical need and potential **Breakthrough Therapy** area.



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 - EGFR TKI Refractory NSCLC

MET also the main resistance mechanism for Tagrisso<sup>®</sup> ≥2L failure

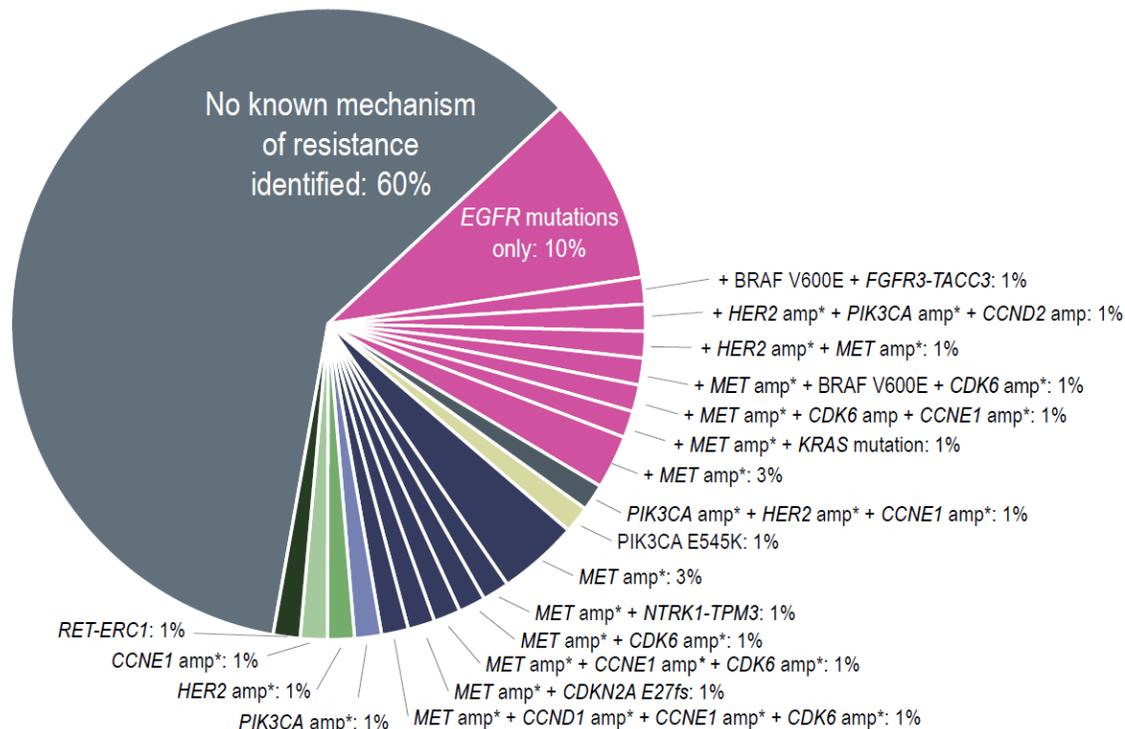


Analysis from **plasma samples from AURA3** patients who progressed or discontinued Tagrisso<sup>®</sup> (osimertinib) treatment. Frequency of MET amplification may be higher in tissue samples.

## Acquired resistance mechanisms post-osimertinib (n=73)

### Summary

- ◆ Acquired *EGFR* mutations: 21%
- ◆ **MET amp\*<sup>\*</sup>: 19%**
- ◆ Cell cycle gene alterations: 12%
- ◆ *HER2* amp\*<sup>\*</sup>: 5%
- ◆ *PIK3CA* amp\* / mutation: 5%
- ◆ Oncogenic fusion: 4%
- ◆ BRAF V600E: 3%

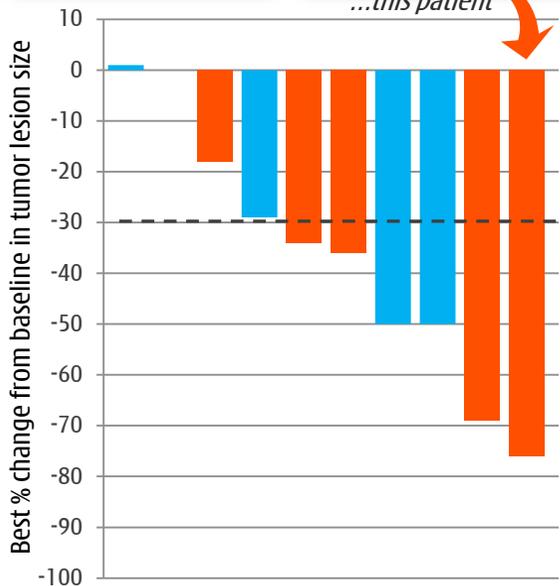


### TATTON A <sup>[2]</sup> - **signal...**

MET testing confirmation	Objective response rate, n (%)	Total (n = 10)
Local or Central	Confirmed PR <sup>[4]</sup>	<b>6 (60%)</b>



...this patient

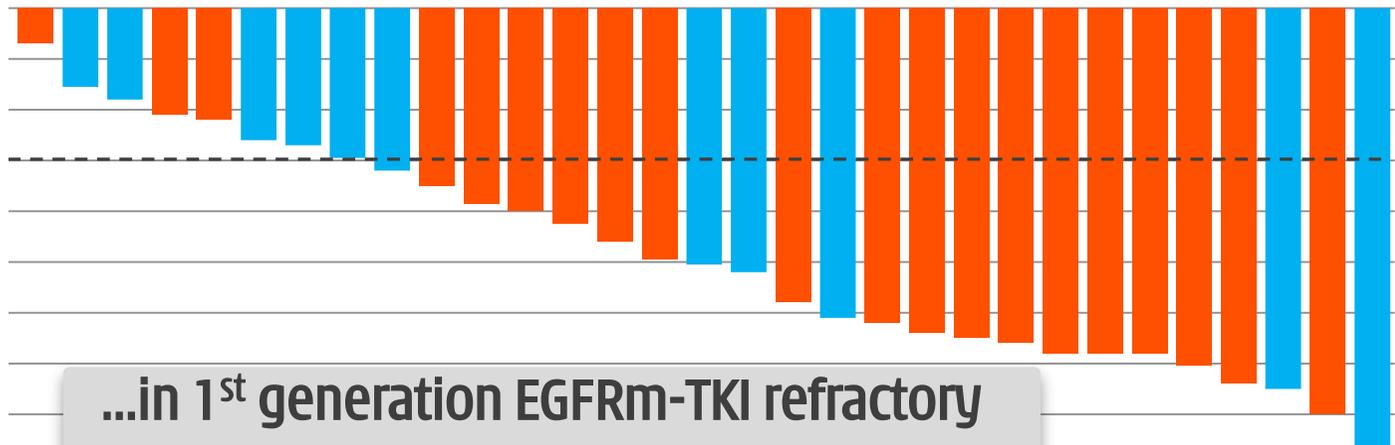


### ...TATTON B <sup>[3]</sup> - ...**interim data** from WCLC Oct 2017

MET testing confirmation	Objective response rate, n (%)	MET+ / T790M+ (n = 11)	MET+ (T790M-) (n = 23)	Total (n = 34)
Local or Central	Confirmed PR <sup>[4]</sup>	<b>6 (55%)</b>	<b>14 (61%)</b>	<b>20 (59%)</b>

		(n = 7)	(n = 15)	(n = 22)
Central *	Confirmed PR <sup>[4]</sup>	4 (57%)	8 (53%)	<b>12 (55%)</b>
	Stable Disease ≥6 weeks	3 (43%)	6 (40%)	<b>9 (41%)</b>
	Progressive Disease/death	0	1 (7%)	1 (5%)
	Not Evaluable	0	0	0 (0)
	DoR, months (range)	<b>9.7 (2.8*-9.7)</b>	NR (1.6*-5.9*)	NR (1.6*-9.7)

\* Centrally confirmed MET-amplification (fluorescence in-situ hybridization, MET gene copy ≥5 or MET/CEP7 ratio ≥2) <sup>[5]</sup>



...in 1<sup>st</sup> generation EGFRm-TKI refractory NSCLC patients **regardless of T790M status.**

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

Compelling in MET+ / T790M-, next step under discussion



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

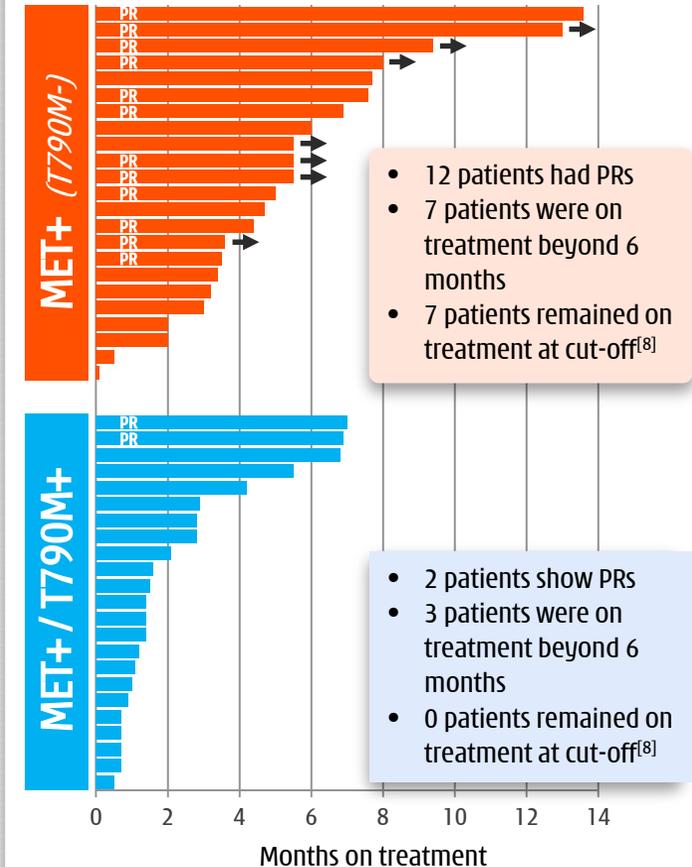
MET testing confirmation	Objective response rate, n (%)	MET+ / T790M+ (n = 23)	MET+ (T790M-) (n = 23)	MET+ / T790M unk. (n = 5)	Total (n = 51)
Central *	Confirmed PR <sup>[3]</sup>	2 (9%)	12 (52%)	2 (40%)	16 (31%)
	SD <sup>[4]</sup> ≥ 6 weeks	9 (39%)	7 (30%)	2 (40%)	18 (35%)
	PD <sup>[5]</sup> / death	7 (30%)	3 (13%)	0	10 (20%)
	Not Evaluable	5 (22%)	1 (4%)	1 (20%)	7 (14%)

## ...vs. TATTON B data (savo / Tagrisso<sup>®</sup> combo)<sup>[6]</sup>

MET testing confirmation	Objective response rate, n (%)	MET+ / T790M+ (n = 11)	MET+ (T790M-) (n = 23)	MET+ / T790M unk. (n = 0)	Total (n = 34)
Local or Central	Confirmed PR <sup>[3]</sup>	6 (55%)	14 (61%)	0	20 (59%)
Central *		(n = 7)	(n = 15)	(n = 0)	(n = 22)
	Confirmed PR <sup>[3]</sup>	4 (57%)	8 (53%)	0	12 (55%)
	SD <sup>[4]</sup> ≥ 6 weeks	3 (43%)	6 (40%)	0	9 (41%)
	PD <sup>[5]</sup> / death	0	1 (7%)	0	1 (5%)
	Not Evaluable	0	0	0	0 (0)

\* Centrally confirmed MET-amplification (fluorescence in-situ hybridization, MET gene copy ≥ 5 or MET/CEP7 ratio ≥ 2)<sup>[9]</sup>.

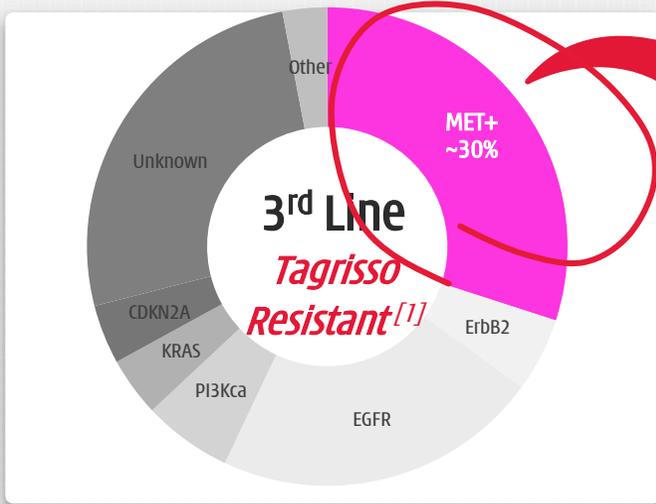
## ...Iressa<sup>®</sup> combo - ~6mo. DoR<sup>[7]</sup> in MET+ / T790M- patients



[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] PR = Partial Response; [4] SD = Stable Disease; [5] PD = Progressive Disease; [6] WCLC 2017 - Ahn M-J, et al. TATTON Phase Ib exp. cohort; [7] DoR = Duration of Response; [8] Aug 21, 2017; [9] On TATTON B, some local MET-status determined via IHC+3 in ≥ 50% of tumor cells.

# 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		<i>MET</i> amp, T790 WT	<i>MET</i> amp, T790M ND
2	Del19	1		-	T790M ND
3	Del19	2	Y	-	T790M ND
4	L858R (de novo T790M)	2	Y	<i>MET</i> amp, <i>EGFR</i> amp T790M (germline)	-
5	L858R	3	Y	T790wt, <i>EGFR</i> amp	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	-	<i>PIK3CA</i> E545K, <i>PIK3CA</i> amp, T790M ND
11	Del19	2	Y	<i>MET</i> amp, <i>EGFR</i> amp, 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	<i>FGFR1</i> D60N, <i>FGFR1</i> amp, T790M ND
16	L858R	2		<i>MET</i> amp, T790 WT	<i>MET</i> , <i>EGFR</i> amp, T790M ND
17	L858R	3	Y	T790 WT	T790M ND
18	Del19 (de novo T790M)	3		SCLC, T790 WT	T790M ND, <i>EGFR</i> amp
19	Del19	3	Y	T790 WT	T790M/C797S, <i>MET</i> amp, <i>EGFR</i> amp
20	L858R	2		<i>MET</i> amp, <i>EGFR</i> amp, T790 WT	-
21	L858R	3		-	T790M/C797S, <i>EGFR</i> amp
22*	L858R	1		<i>MET</i> 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

[1] Based on rociclitinib/Tagrisso data published at 2016/2017 ASCO; [2] In xenograft model H820, with EGFRm, T790M+ and MET CN gain. D'Cruz CM et al; #761 Preclinical data for changing the paradigm of treating drug resistance in NSCLC: Novel combinations of AZD6094, a selective MET inhibitor, and AZD9291 an irreversible, selective (EGFRm and T790M) EGFR TKI; American Association of Cancer Research Annual Meeting; April 19, 2015.

# Safety - savolitinib plus

**IRESSA<sup>®</sup>**  
gefitinib

or

**TAGRIS<sup>®</sup>**  
osimertinib



## Adverse event profiles of combinations - manageable & tolerable

	IPASS Phase III 1 <sup>st</sup> -Line EGFRm NSCLC			FLAURA Phase III 1 <sup>st</sup> -Line EGFRm NSCLC		AURA3 Phase III 2 <sup>nd</sup> -Line EGFRm NSCLC		
Grade ≥3 AEs, Preferred term, n (%)*	IPASS Iressa <sup>®</sup> (N=607)	IPASS carbo. + Taxol <sup>®</sup> (N=589)	≥ 2 <sup>nd</sup> -Line [2] Savo + Iressa <sup>®</sup> (N=51)	Tagrisso <sup>®</sup> (N=279)	Iressa <sup>®</sup> or Tarceva <sup>®</sup> (N=277)	Tagrisso <sup>®</sup> (N=279)	Chemo-doublet (plat. + pemetrex.) (N=136)	≥ 2 <sup>nd</sup> -Line [1] Savo + Tagrisso <sup>®</sup> (N=66)
<b>Any Grade ≥3 AE</b>	<b>29% (Gr. 3-4)</b>	<b>61% (Gr. 3-4)</b>	<b>17 (33%)</b>	<b>94 (34%)</b>	<b>124 (45%)</b>	<b>63 (23%)</b>	<b>64 (47%)</b>	<b>33 (50%)</b>
Vomiting	1 (<1%)	16 (3%)		0	4 (1%)	1 (<1%)	3 (2%)	5 (8%)
Rash or acne	19 (3%)	5 (1%)		3 (1%)	19 (7%)	2 (1%)		4 (6%)
AST/ALT increase			8 (16%)	3 (1%)	37 (13%)	6 (2%)	2 (2%)	4 (6%)
Nausea	2 (<1%)	9 (1%)	1 (2%)	0	0	2 (1%)	5 (4%)	3 (5%)
Decreased appetite				7 (3%)	5 (2%)	3 (1%)	4 (3%)	3 (5%)
Fatigue				2 (1%)	2 (1%)	3 (1%)	1 (1%)	3 (5%)
Neutropenia	22 (4%)	387 (67%)				4 (1%)	16 (12%)	3 (5%)
ALP increased			11 (22%)					
Neurotoxic effects	2 (<1%)	29 (5%)						
Anemia	13 (2%)	61 (11%)		3 (1%)	3 (1%)	2 (1%)	16 (12%)	
Leukopenia	9 (1%)	202 (35%)					5 (4%)	
Thrombocytopenia						1 (<1%)	10 (7%)	

Sources: [1] TATTON B - Figures where any grade AE ≥10% patients. Ahn M-J, et al. Abstract #8985. Presented at the World Lung Cancer Congress (WCLC) 2017, Japan, October 2017;

[2] Phase Ib/II study - Figures where any grade AE ≥10% patients. Yang J-J, et al. Abstract #8995. Presented at WCLC 2017, Japan, October 2017.

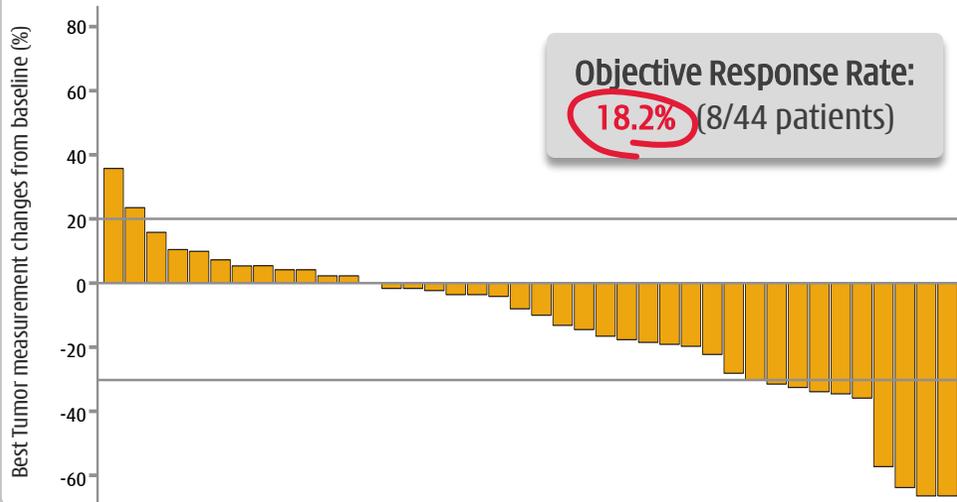
AST = aspartate aminotransferase; ALT = alanine aminotransferase; ALP = alkaline phosphatase.

# Savolitinib - PRCC Phase II

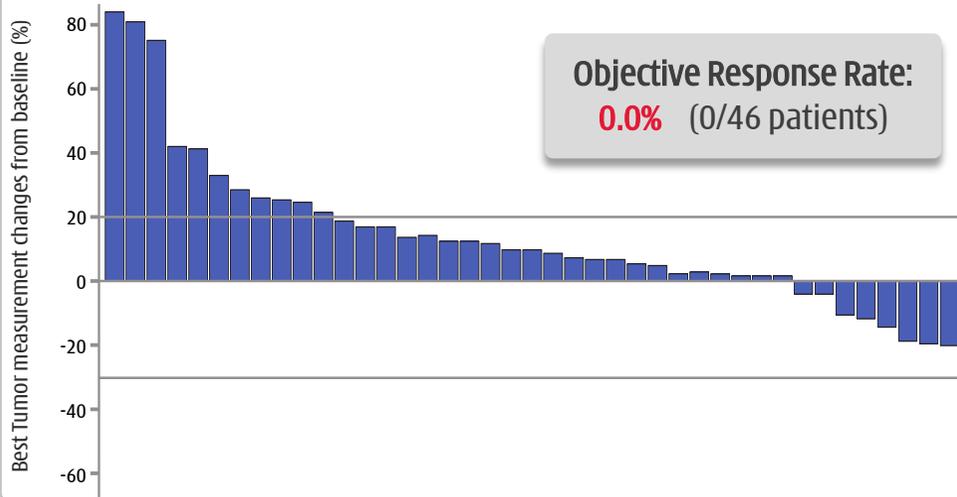
## Clear efficacy & durable response in MET+ PRCC patients



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



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



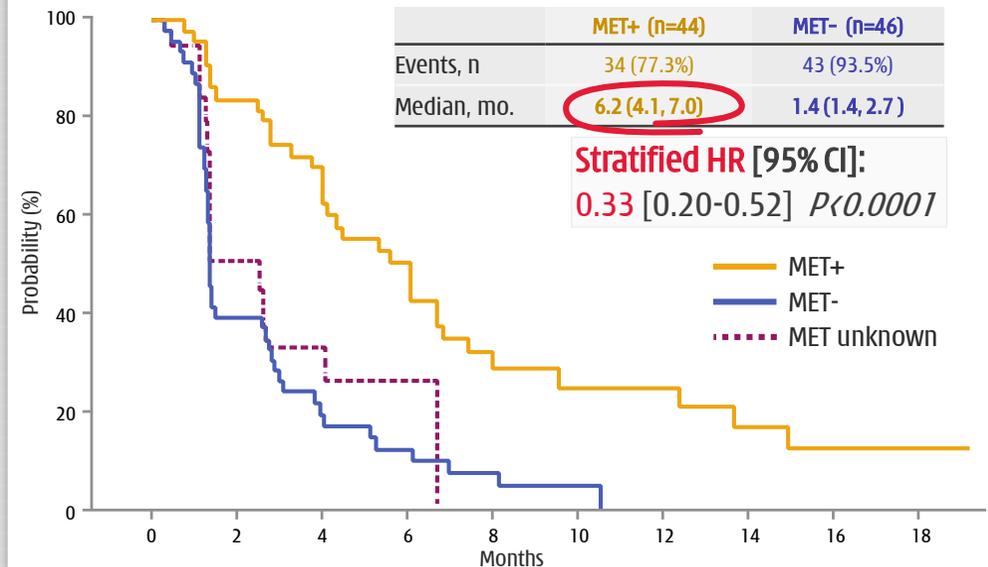
### 3. Disease Control Rate ("DCR") - big advantage in MET+ with **DCR 73.2%** vs. MET- **28.2%**.<sup>^</sup>

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.



# Highest selectivity delivers better tolerability

		PRCC PHASE II	COMPARZ PHASE III [1]		METEOR PHASE III [2]		SINGLE-ARM PHASE III [3]
		Savolitinib 1L/2L (n=109)	Sunitinib 1L (n=548)	Pazopanib 1L (n=554)	Cabozantinib 2L (n=331)	Everolimus 2L (n=322)	Sunitinib 2L (n=106)
<b>MSKCC Risk Group</b>	Favorable	14%	27%	27%	45%	46%	58%
	Intermediate	45%	59%	58%	42%	41%	42% <sup>[6]</sup>
	Poor	9%	9%	12%	12%	13%	0%
	Missing	32%	4%	3%	0%	0%	0%
<b>Number of prior systemic therapies</b>	0	55%	100%	100%	0%	0%	0%
	1	23%	0%	0%	71%	70%	100%
	≥2	22%	0%	0%	29%	30%	0%
<b>Grade ≥3 AEs:</b>	Any AE	47%			68%	58%	
	Any treatment-related AE [4]	19%	77% <sup>[5]</sup>	76% <sup>[5]</sup>			
<b>All Grade ≥3 AEs with ≥5% incidence (AND selected savolitinib AEs for comparison)</b>		<b>TRAES</b>	<b>TRAES</b>	<b>TRAES</b>	<b>All AEs</b>	<b>All AEs</b>	
	Hypertension	0%	15%	15%	15%	3%	6%
	Fatigue	2%	17%	11%	9%	7%	11%
	Hand-foot-syndrome	0%	12%	6%	8%	<1%	7%
Diarrhea	0%	8%	9%	11%	2%		
<b>Hematologic Abnormalities Grade ≥3 AEs with ≥5% incidence:</b>	Neutropenia	0%	20%	5%	0%	0%	16%
	Thrombocytopenia	0%	24%	4%	0%	0%	6%
	Lymphocytopenia	0%	14%	5%	0%	0%	
	Leukopenia	0%	6%	1%	0%	0%	
	Anemia	<1%	7%	2%	5%	16%	6%
<b>Lab Abnormalities Grade ≥3 AEs with ≥5% incidence:</b>	Increased ALT	5%	4%	17%	2%	<1%	
	Increased AST	3%	3%	12%	2%	<1%	
	Hypophosphatemia	0%	9%	4%	4%	2%	
	Hyponatremia	3%	7%	7%	0%	0%	
	Hypokalemia	0%	1%	3%	5%	2%	
	Hyperglycemia	0%	4%	5%	<1%	5%	
<b>Tolerability</b>	Treatment discontinuation due to any AE [7]	8%	20%	24%	12%	11%	11%
	Dose reduction due to AE:	13%	51%	44%	62%	25%	

Better safety data despite higher risk patient population:

✓ Only 14% "favorable" vs. 27-58%.

Superior safety profile vs. other TKIs - Most ≥3 G3 AEs ≈ 0-2%:

- ✓ Hypertension: 0% vs. 6~17%.
- ✓ Fatigue: 2% vs. 6~12%.
- ✓ Diarrhea: 0% vs. ~10%.
- ✓ Anemia: <1% vs. 7~16%.
- ≈ ALT/AST Increase: 3-5% vs. 0~17%.
- ✓ Other Lab Abnorm: 0% vs. ≤9%.

Highly tolerable vs. other TKIs:

- ✓ Discontinued: 8% vs. 10~24%.
- ✓ Dose reduction: 13% vs. 44-62%.

# Savolitinib - Gastric cancer

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

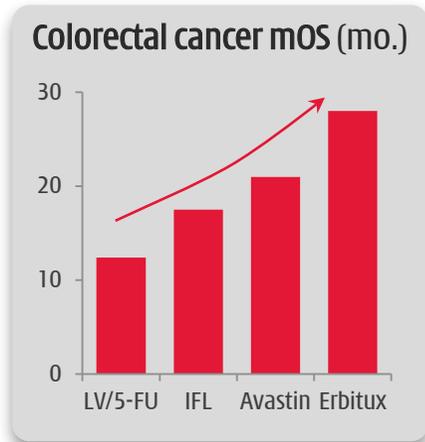
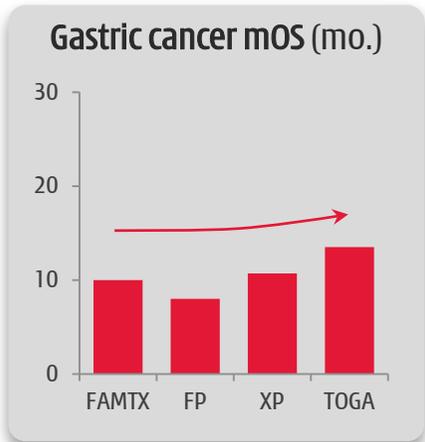


1. Gastric (stomach) cancer is the 5<sup>th</sup> most common cancer globally - **723,000 deaths/year**.

	Est. Age Standardised Rates (cases/100,000)	New cases ('000)	Deaths ('000)	5-year Prevalence ('000)
World	17.0	952	723	1,538
South Korea	41.8	22	17	32
Japan	29.9	38	29	56
China	22.7	405	325	594
EU-28	9.0	82	58	119
USA	6.8	21	12	32

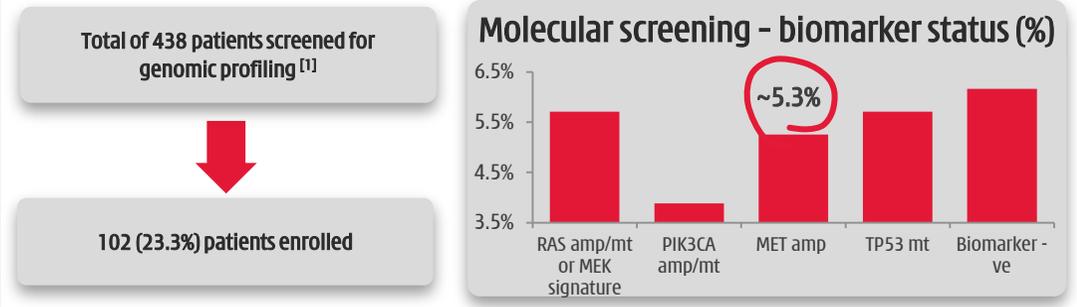
Jeeyun Lee, AACCR 2016; IARC, WHO 2012; Jung KW, Cancer Research Treatment 2013; World Cancer Research Fund International.

2. Little progress in gastric cancer<sup>[2]</sup> in improving overall survival ("OS") in first-line palliative setting.

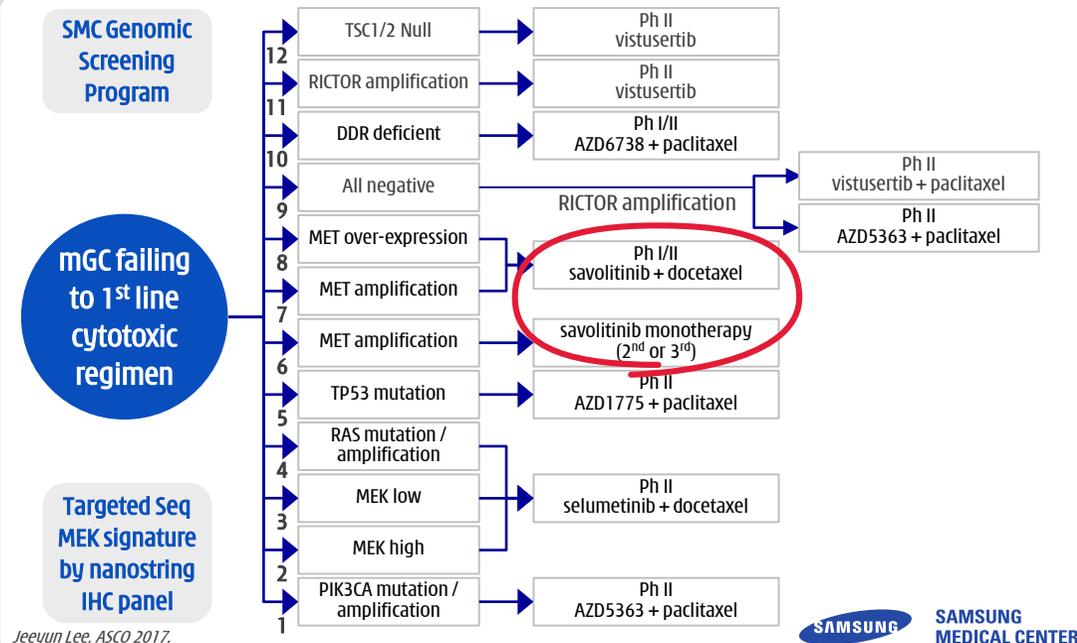


Jeeyun Lee, AACR 2016; Mayer RJ, J Clin Oncol 2015.

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



Jeeyun Lee, ASCO 2017



Jeeyun Lee, ASCO 2017.



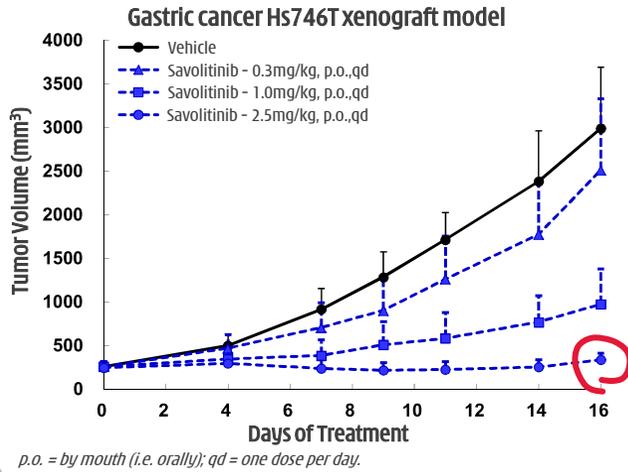
[1] Since June 2014; [2] FAMTX = 5-FU + doxorubicin + methotrexate; FP = cisplatin + 5-FU; XP = capecitabine + cisplatin; TOGA = trastuzumab + chemo; LV/5-FU = leucovorin + 5-FU; IFL = irinotecan + 5-FU + leucovorin.

# Savo potential not only in NSCLC...

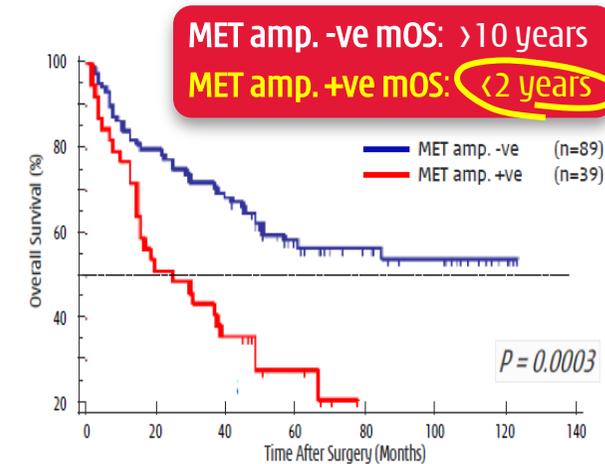
...highly promising efficacy in MET+ gastric cancer (...& kidney)



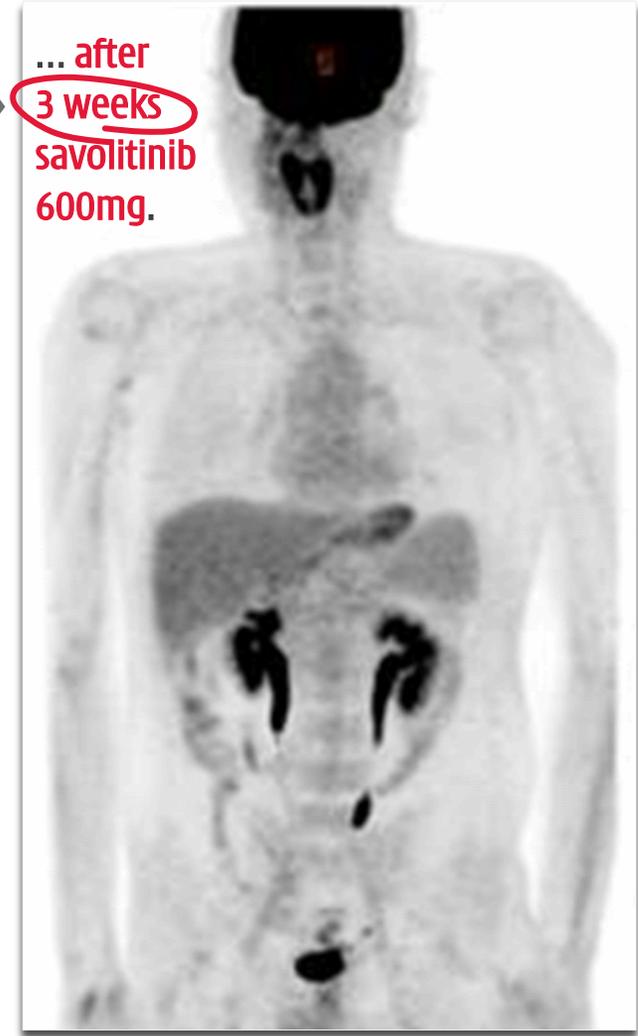
## Strong preclinical efficacy.



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



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





5b

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

*Highly selective anti-angiogenesis inhibitor*

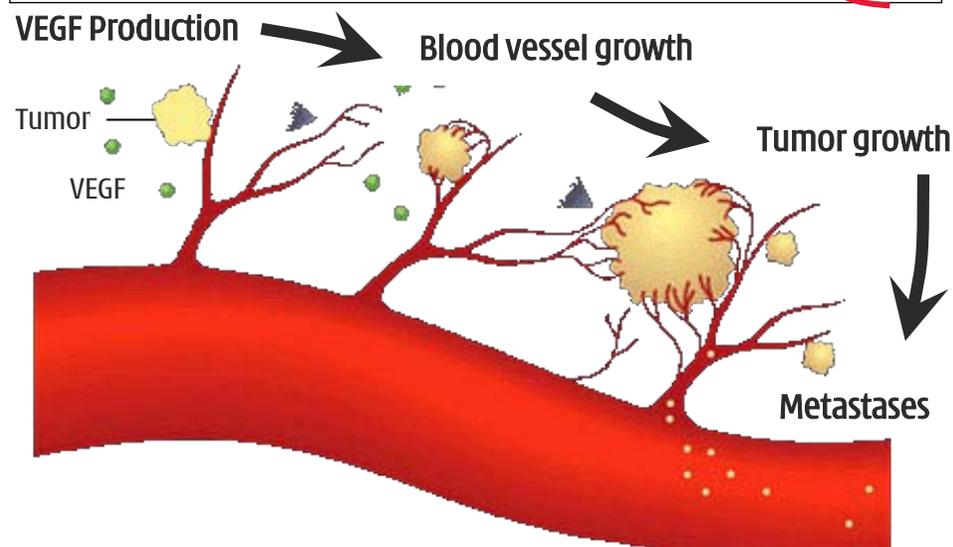
# Fruquintinib best-in-class VEGFR TKI

Cutting off blood flow a **\$16+ bn** market in **~30 tumor settings**



Company	Drug (INN Name)	FDA Approved Indications		2018 Sales
		Indication	Year	
Roche	Avastin® (Bevacizumab)	2L bevacizumab-pretreated mCRC	2013	\$6,890m
		1/2L mCRC	2004	
		1L non-sq NSCLC	2006	
		2L GBM	2009	
		1L ccRCC	2009	
		1L Cervical Ca.	2014	
		1L Ovarian Ca.	2018	
		1/2L platinum-sensitive Ovarian Ca.	2016	
Pfizer	Sutent® (Sunitinib)	2L GIST	2006	\$1,049m
		≥1L pNET	2011	
		adjuvant RCC	2017	
		1L RCC	2007	
		≥2L cytokine-ref. ccRCC	2006	
Boehringer Ingelheim	Vargatef® Ofev® (Nintedanib)	2L adeno-NSCLC (by EMA)	2014	\$1,076m <sup>[1]</sup>
Bayer	Nexavar® (Sorafenib)	≥1L RCC	2005	\$788m
		1L HCC	2007	
		Iodine-ref. DTC	2013	
Novartis	Votrient® (Pazopanib)	1/2L RCC	2009	\$828m
		2L STS	2012	
Lilly	Cyramza® (Ramucirumab)	2L GC	2014	\$821m
		2L NSCLC	2014	
		2L mCRC	2015	
Exelixis/Ipsen	Cometriq® Cabometyx® (Cabozantinib)	≥1L MTC	2012	\$783m
		1L ccRCC	2017	
		≥2L ccRCC	2016	
Bayer	Stivarga® (Regorafenib)	3L mCRC	2012	\$348m
		2L GIST	2013	
		2L HCC	2017	
Pfizer	Inlyta® (Axitinib)	2L ccRCC	2012	\$298m

Company	Drug (INN Name)	FDA Approved Indications		2018 Sales
		Indication	Year	
Merck/Eisai	Lenvima® (Lenvatinib)	Iodine-ref. DTC	2015	\$575m
		2L ccRCC	2016	
		1L HCC	2018	
Hengrui	AiTan® (Apatinib)	3L GC (by CFDA)	2015	\$255m
Sanofi	Zaltrap® (Ziv-Aflibercept)	2L mCRC	2012	\$101m
Simcere	Endu® (rh-Endostatin)	≥1L NSCLC (by CFDA)	2005	NA
Sanofi	Caprelsa® (Vandetanib)	≥1L MTC	2011	NA
Aveo	Fotivda® (Tivozanib)	1/2L ccRCC (by EMA)	2017	NA
Sino Biopharm	FocusV® (Anlotinib)	3L NSCLC (by CFDA)	2018	NA



Note: \* Active indications in US as of July 3, 2018. Some indications have been approved for frontline therapy. Sources: FDA approved label; Medtrack; Corporate annual reports; D. Ribatti, Oncotarget 2017 8(24) 38080-1, Sales for anti-angiogenic drugs.

[1] 2017 sales, includes sales for idiopathic pulmonary fibrosis

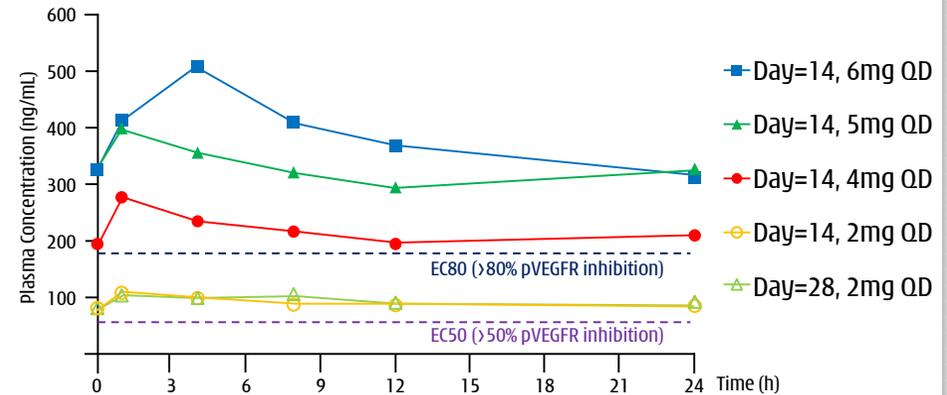
# Fruquintinib - 24hr full target coverage

The most selective VEGFR inhibitor in clinical trials globally [1]

## 1. Fruquintinib Approved by NMPA Sept 2018.

- ✓ Validation of R&D approach - designed to only inhibit VEGFR1,2,3, facilitating **full target coverage & combinations**.
- ✓ **Approval and launch for 3L CRC**.
- ✓ **Pivotal Phase III Taxol® combo in 2L gastric cancer - initiated Oct 2017**.
- ✓ **Phase II Iressa® combo in 1L EGFRm+ NSCLC - early data at WCLC 2017**.
- ✓ **Phase I in solid tumors in US - initiated Q4 2017**.
- ✓ China GMP **facility built and certified** to support launch.
- ✓ **PD-1 combination collaborations**.

## 2. Only inhibits VEGFR - limits off-target toxicity & allows for full & sustained target inhibition.



## 3. 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 [2] 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.

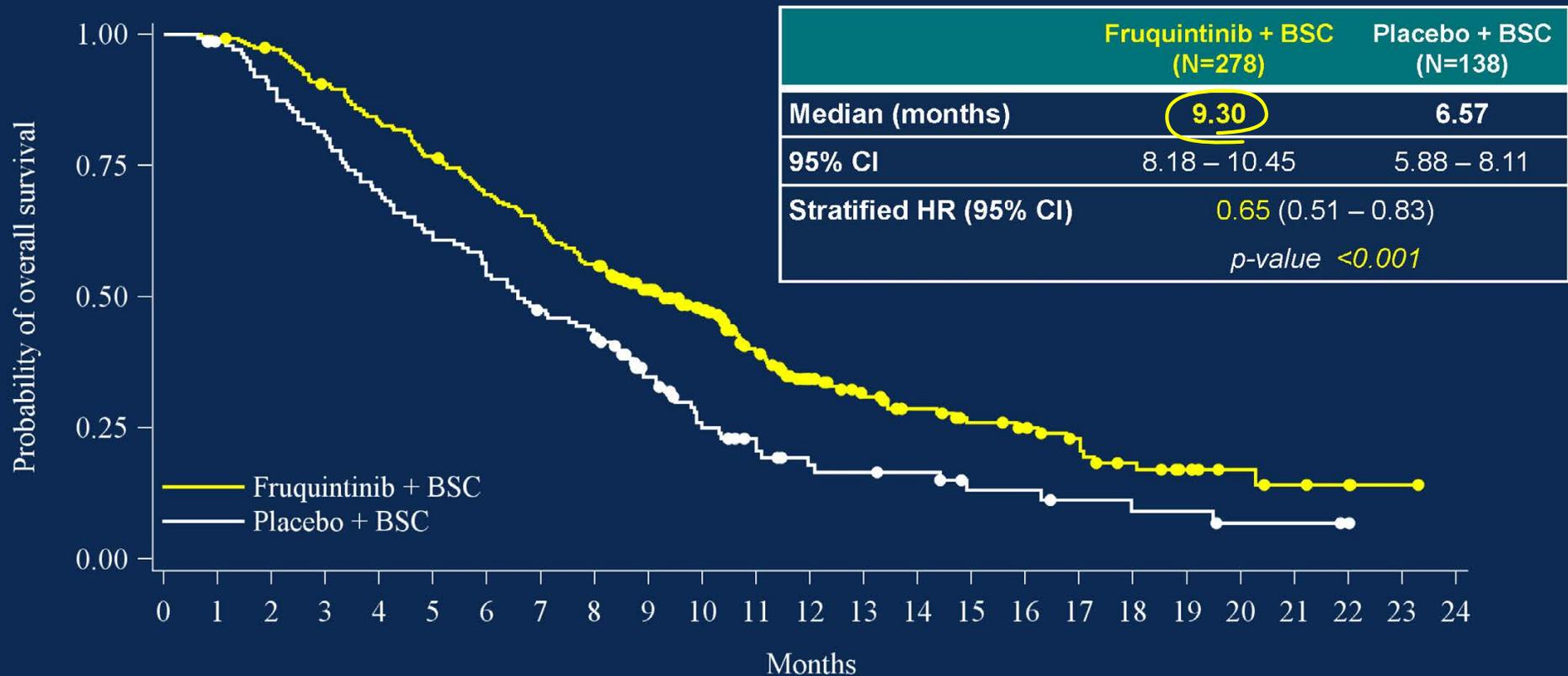
# Fruquintinib - 3L/4L colorectal cancer

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

Presented by: Jin Li, MD PhD

June 5, 2017

10

[1] ASCO = American Society of Clinical Oncology Annual Meeting.

# Better tolerability = Better efficacy

Third-Line Metastatic Colorectal cancer	Fruquintinib		Regorafenib		Regorafenib		Regorafenib		
	FRESCO		CONCUR		CONCUR		CORRECT		
	Mainland China		Chinese Patients (Mainland China, Hong Kong, Taiwan) [1]		Mainland China, Hong Kong, Taiwan, Vietnam, South Korea		Global		
Treatment arms	Fruquintinib	Placebo	Regorafenib	Placebo	Regorafenib	Placebo	Regorafenib	Placebo	
Patients (n)	278	138	112	60	136	68	505	255	
Complete Response, n (%)	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	
Partial Response, n (%)	4.3%	0.0%	3.6%	0.0%	4.4%	0.0%	1.0%	0.4%	
Stable Disease, n (%)	57.6%	12.3%	40.2%	6.7%	45.6%	7.4%	42.8%	14.5%	
Disease Control Rate, n (%)	62.2%	+49.9	45.5%	+38.8	51.5%	+44.1	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
mPFS p-value	<0.001		not published		<0.0001		<0.000001		
mPFS Hazard Ratio	0.26		0.32		0.31		0.49		
Median Overall Survival (mOS) (mo.)	9.3	+2.7	6.6	8.4	+2.2	6.2	8.8	+2.5	6.3
mOS p-value	<0.001		not published		0.0002		0.0052		
mOS Hazard Ratio	0.65		0.56		0.55		0.77		

- **Good fruquintinib efficacy over regorafenib in Chinese patients** - specifically in terms of Disease Control Rate; median Progression-Free Survival and median Overall Survival.
- **FRESCO is a fully-powered Phase III registration study (n=416)** whereas **CONCUR was an under-powered Asia region study (n=204, including only 129 mainland Chinese patients [2])**.
- **CONCUR results should be regarded as directional only - China approval resulted from CORRECT study (n=760)**.

[1] Efficacy & safety of regorafenib monotherapy in Chinese patients with previously treated metastatic colorectal cancer: subgroup analysis of the CONCUR trial; R Xu; [2] China FDA website.

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<sup>®</sup> 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]	
	Elunate <sup>®</sup>	Placebo	Stivarga <sup>®</sup>	Placebo
Treatment arms				
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<sup>®</sup> higher selectivity; lower off-target toxicity; superior tolerability**

# FALUCA - Third-line NSCLC

## FALUCA Phase III

- 527 NSCLC (3<sup>rd</sup>-line) patients enrolled;
- Topline results released Nov 2018;
- **Anticipate presenting full data set and analysis at scientific conference in 2019.**

## FALUCA Phase III - Topline Results

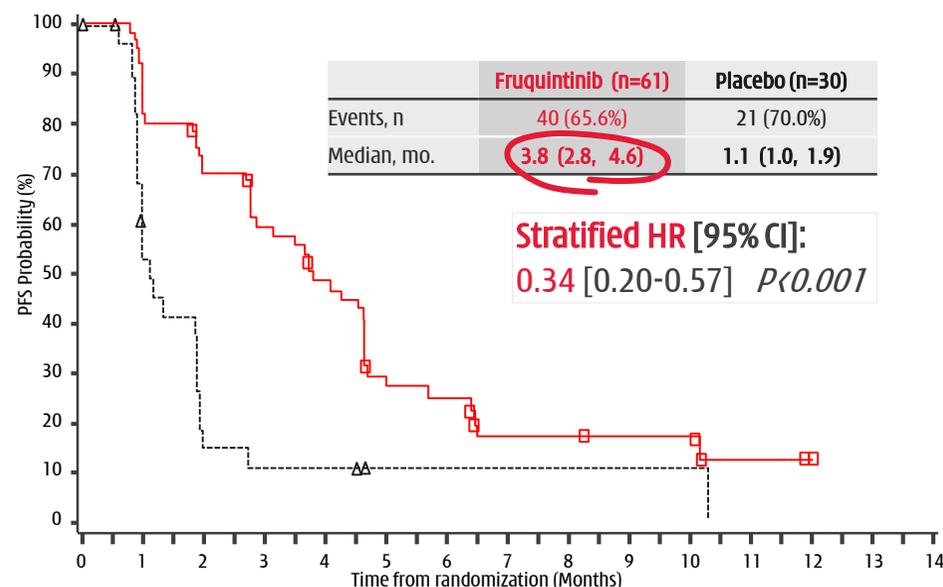
- **Did not achieve Primary Endpoint** of median Overall Survival;
- **Clearly met all Secondary Endpoints:** mPFS; ORR; DCR; & Duration of Response vs. placebo <sup>[1]</sup>;
- **AEs consistent** with those observed in prior clinical studies.

## Phase II Study (reported May 2015)

- 91 NSCLC (3<sup>rd</sup>-line) patients enrolled;
- **Clearly met Primary Endpoint:** mPFS vs. placebo;
- **AEs consistent & more tolerable than ≥3L CRC** <sup>[2]</sup>.

Patients, %	Fruquintinib (n=61)	Placebo (n=30)
All AEs, any grade	61 (100%)	27 (90.0%)
All AEs, grade ≥3	20 (32.8%)	6 (20.0%)
Hypertension, grade ≥3	5 (8.2%)	1 (3.3%)
Hand-foot syndrome ("HFS"), grade ≥3	3 (4.9%)	0
All other AEs, grade ≥3 (each)	≤2 (≤3.3%)	0
Leading to dose interruption	9 (14.8%)	0
Leading to dose reduction	8 (13.1%)	0
Leading to treatment discontinuation	6 (9.8%)	1 (3.3%)

## Phase II - Median PFS

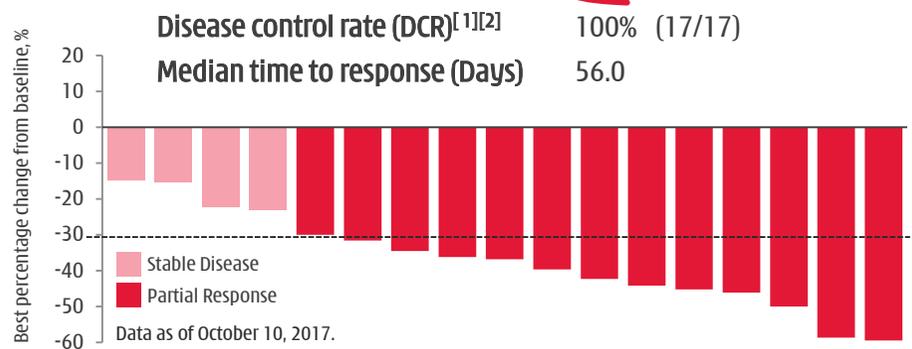


# Fruquintinib - 1L NSCLC combo w/ IRESSA<sup>®</sup> gefitinib

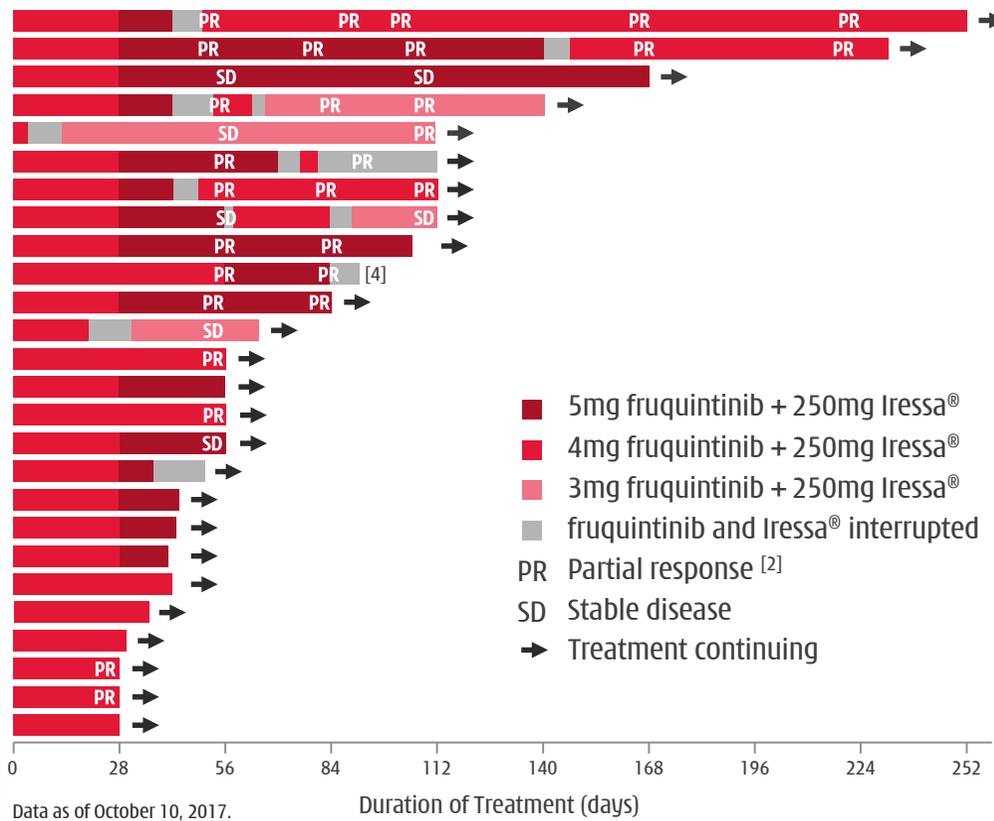
## Two small molecule TKIs allow for better management of tox.



### 1. Promising efficacy in first line - 76% ORR (13/17). [1,2,3]



### 3. Combination of highly selective TKIs vs. mAbs: daily dose flexibility improves tolerability. This enables maintained drug exposure, leading to more durable response. [2,3]



### 2. Prelim. safety data: fruquintinib vs. other VEGFRis.

Adverse Events ("AEs")	Iressa <sup>®</sup> or Tarceva <sup>®</sup> FLAURA <sup>[5]</sup> N = 277, n (%)	Avastin <sup>®</sup> + Tarceva <sup>®</sup> <sup>[6]</sup> N = 75, n (%)	Fruquintinib + Iressa <sup>®</sup> 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

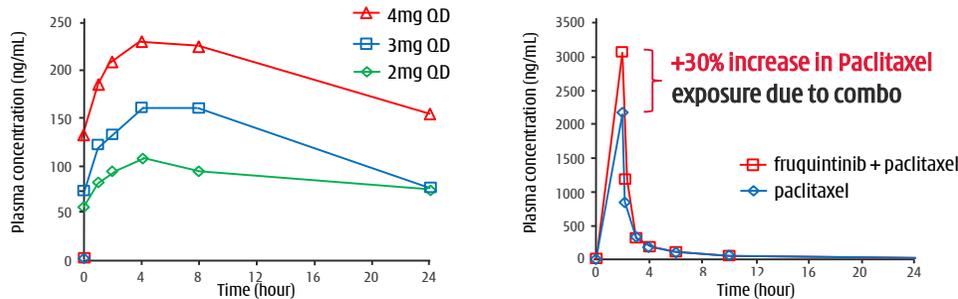
[1] Best tumor response for efficacy evaluable patients (patients who had both baseline and post-baseline tumor assessments); ORR = objective response rate; [2] Four PRs not yet confirmed at the time of data cut-off date; mAb = Monoclonal Antibody; [3] Lu, S., et al, "A Phase II study of fruquintinib in combination with gefitinib in stage IIIB/IV NSCLC patients harboring EGFR activating mutations", ID 10907 IASLC 18<sup>th</sup> World Conference on Lung Cancer, Yokohama, Japan, October 15-18, 2017; [4] Drug discontinuation due to Grade 3 proteinuria and Grade 3 QTC prolonged; [5] Ramalingam S. et al, "LBA2 PR Osimertinib 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 harbouring EGFR mutations (J025567); an open-label, randomised, multicenter, phase 2 study", The Lancet 2014, 15 (11) 1236-1244.

# Fruquintinib - Gastric combo with paclitaxel

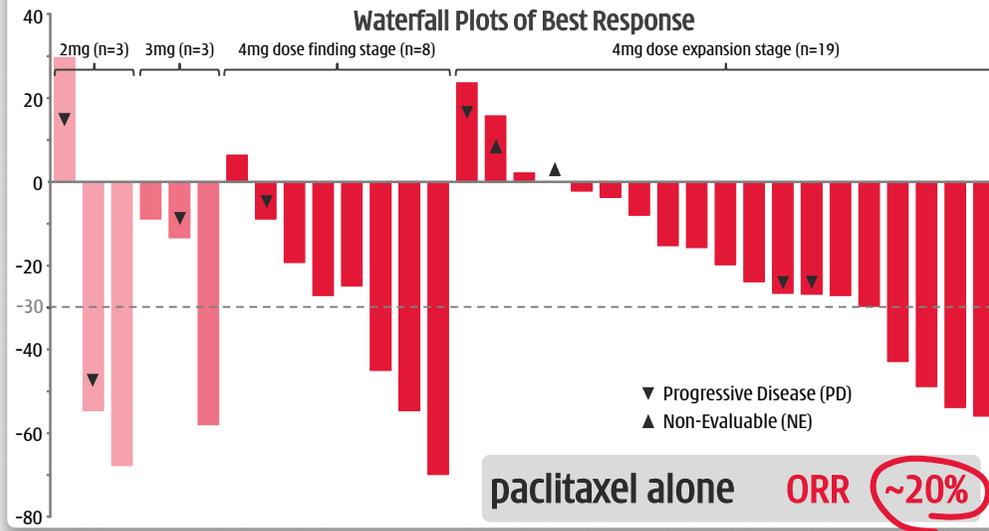


Phase III initiated Oct 2017 - Interim analysis planned early 2019

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).

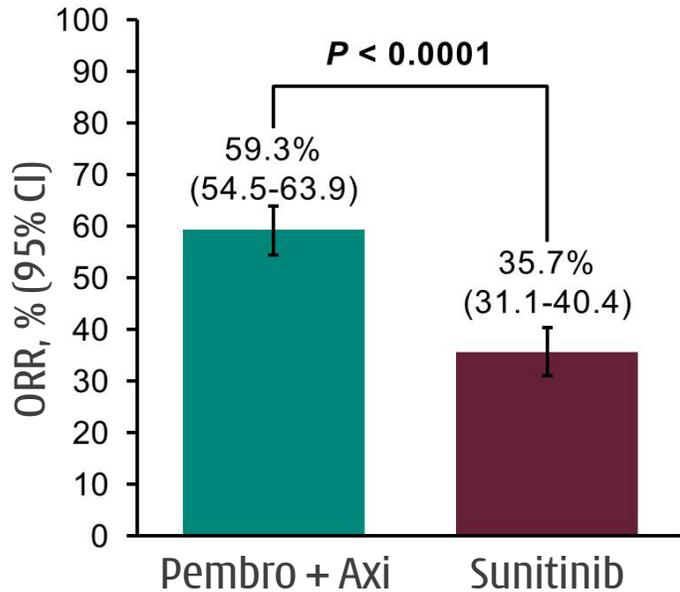
Characteristics (Unit)	Drug Expansion Stage (N=19)	
	Fruquintinib 4 mg + paclitaxel 80 mg/m <sup>2</sup> Drug interruption	Drug reduction
Dose modification with Fruquintinib N (%)	2 (10.5%)	2 (10.5%)
Dose modification with Paclitaxel N (%)	5 (26.3%)	1 (5.3%)

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%)

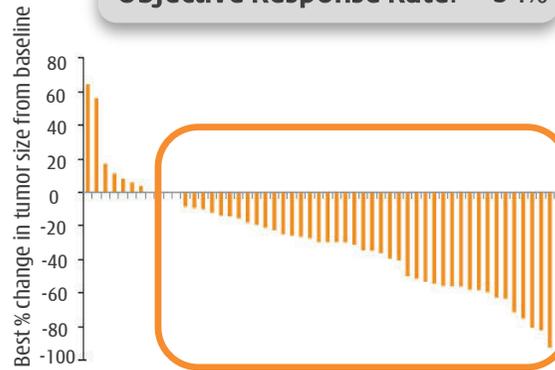
# VEGFR / immunotherapy (PD-1s) combinations

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



**Axitinib (VEGFR) monotherapy in 1L ccRCC**

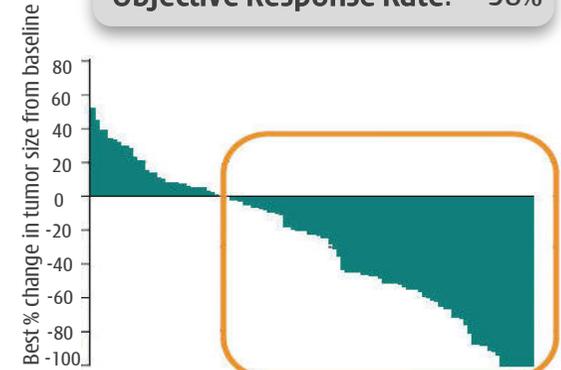
Complete Response: 0%  
Objective Response Rate: 34%



75% patients (n=56) experienced a reduction in tumor burden

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

Complete Response: 3%  
Objective Response Rate: 38%



67% patients (n=110) experienced a reduction in tumor burden

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

[1] BTD = Breakthrough Therapy Designation; Source: 1. B. Rini et al, Lancet Oncol 2013 14(12) 1233-42, Axitinib with or without dose titration for first-line metastatic renal-cell carcinoma: a randomised double-blind phase 2 trial; 2. 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; 3. 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.

# Fruquintinib & surufatinib both unique VEGFR TKIs

...ideal VEGFR combination 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	Sunitinib	Sorafenib	Anlotinib	Tivozanib	Lenvatinib	Axitinib	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>[1]</sup> production - amplifying PD-1 induced immune response

[1] Surufatinib = HMPL-012, formerly known as sulfatinib; Source: 1. D.D. Hu-Lowe et al, Clin Cancer Res 2008 14(22) 7272-83; 2. Q.L. Sun et al, Cancer Biol Ther 2014 15(12) 1635-45.

# Chi-Med immunotherapy collaborations

## Global Development

*Managed by AstraZeneca*

*Jointly managed by Chi-Med & partners*

**AstraZeneca**

**savolitinib + Imfinzi® (PD-L1)**

ccRCC/PRCC

**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**



5c

# Surufatinib

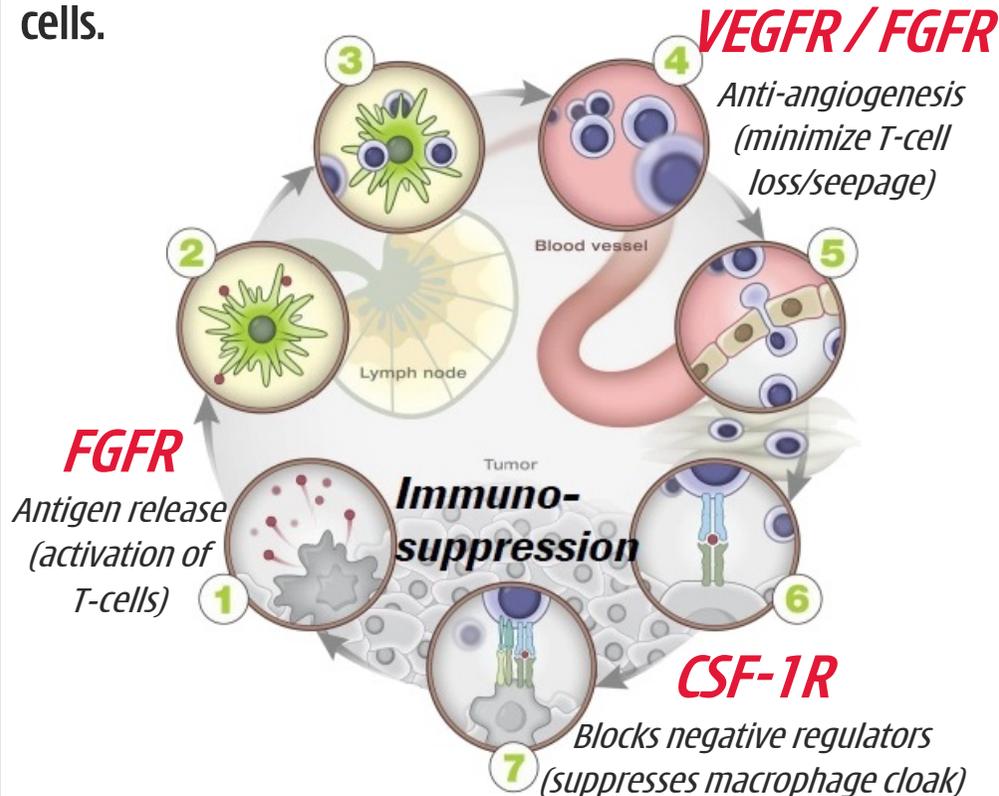
*Highly active TKI with unique angio-immuno activity*

# Surufatinib's unique angio-immuno kinase profile



Multi-indication global development program, initially for NETs<sup>[1]</sup>

Surufatinib's unique **angio-immuno kinase profile & MoA<sup>[1]</sup>** activates & enhances the body's immune system, namely T-cells, via VEGFR/FGFR while inhibiting the production of macrophages (CSF-1R) which cloak cancer cells.



**Activity 1: Aiming for fast/first approval in China for all NET<sup>[2]</sup> patients - 2x pivotal Phase III trials in progress**

	Pancreatic NET Phase III	Non-Pancreatic NET Phase III
Primary site	Pancreas	GI, lung, other or unknown
Population	Unresectable or metastatic disease; well differentiated (G1/G2); ≤2 prior systemic drugs.	
# of Sites	20-30 (China)	
# of Patients	~195	~270
Study design	Double-blind. Randomized 2:1 to surufatinib or placebo, until PD. Predefined interim analysis.	
Dosage	Surufatinib 300mg QD, 28 days per cycle (vs. placebo)	
Primary Endpoint	Progression-Free Survival (PFS) by BICR evaluation	
Secondary Endpoints	Overall Survival (OS), ORR, safety, etc.	
First Patient In / Readout	March 2016 / 2019 (IA)	December 2015 / 2019 (IA)

**Activity 2: Global development**

- U.S. Phase I (dose escalation) in solid tumors completed
- U.S. Phase Ib/II initiated in July 2018, focusing on pancreatic NET and biliary tract cancer
- PD-1 combination collaborations

**Activity 3: Exploratory PoC<sup>[3]</sup> in other indications**

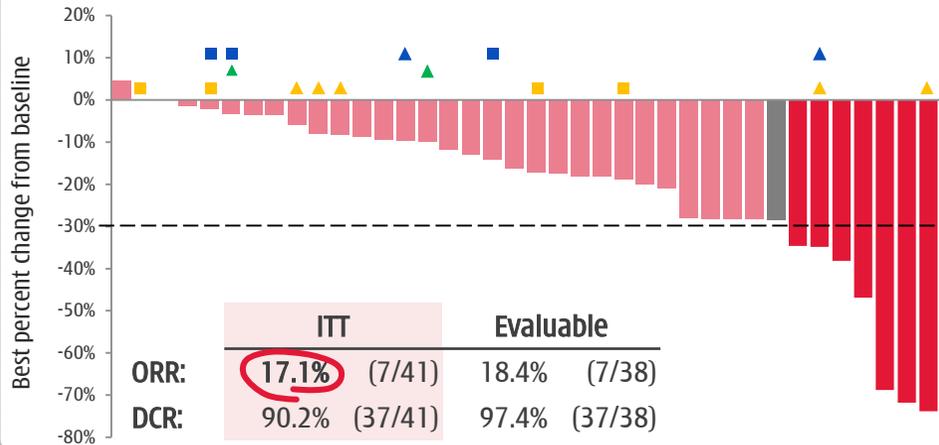
- China Ph.II studies underway in: (a) medullary thyroid cancer; (b) differentiated thyroid cancer; and (c) biliary tract cancer.

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

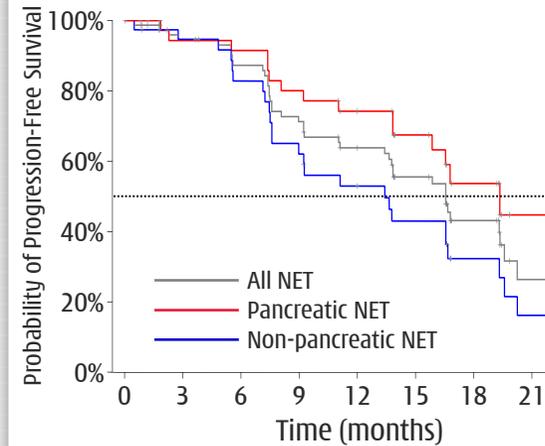
## Efficacy in all NET & patients who failed on Sutent®/Afinitor®



### Phase II: Pancreatic NET - Highest ORR seen to date in pNET.



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

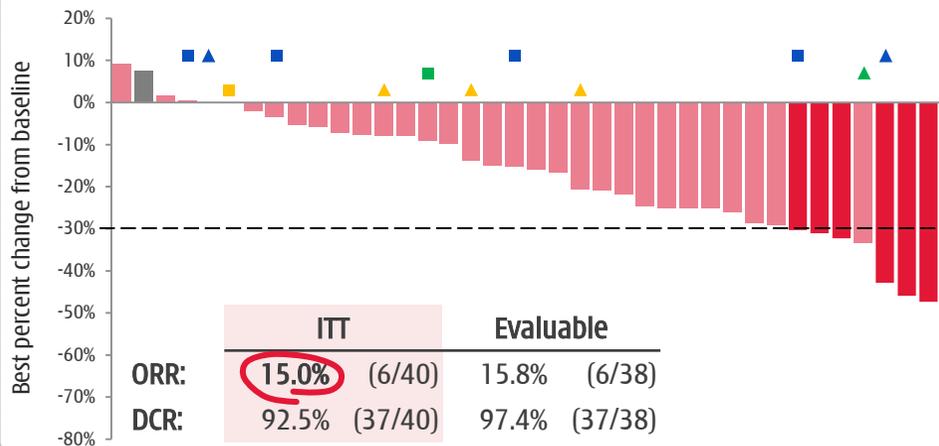


	Median PFS (months)	PDs or Deaths (% pts)
All NET (n=81)	16.6m (13.4, 19.4)	51.9% (42/81)
P-NET (n=41)	19.4m (13.8, 22.1)	39.0% (16/41)
Non-P NET (n=40)	13.4m (7.6, 16.7)	65.0% (26/40)

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

■ Partial Response   
 ■ Stable Disease   
 ■ Progressive disease   
 ■ Prior Sutent®   
 ■ Prior Famininib (VEGFR)   
 ■ Prior Afinitor®   
 ▲ Progressive Disease on Prior TKI

### Phase II: Non-Pancreatic NET - High ORR in non-pNET also.



### 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)	<b>Drug related AE leading to:</b>	
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 - global development

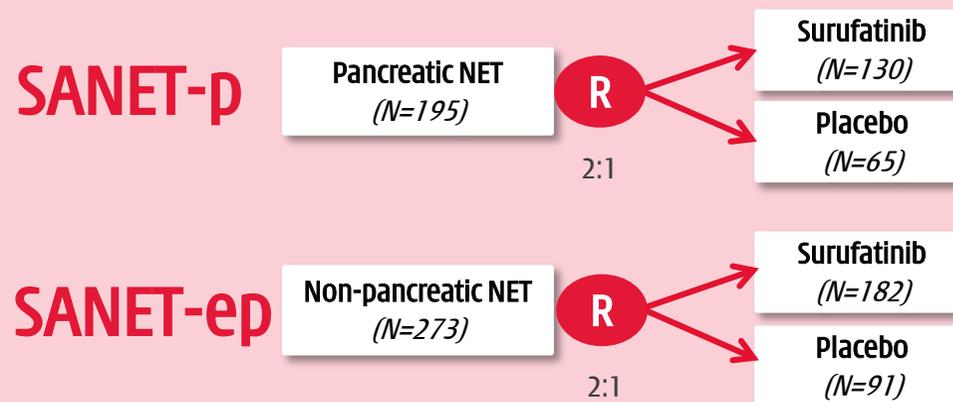
First un-partnered asset through China PoC & started US study



## Pancreatic NET ("P-NET") & Non-Pancreatic NET ("EP-NET")

- SANET-p & SANET-ep active in **25 China sites**;
- Primary endpoint - **median PFS**;
- Target to conduct **Interim Analysis in 2019** on SANET-ep in H1 2019 & SANET-p in H2 2019;
- Enrolment expected for both Phase III studies to **complete late 2019 / early 2020**;
- Potential **launch in China in late 2020 / 2021** - first un-partnered oncology asset for Chi-Med.

### China Phase III study design:



## Biliary Tract Cancer ("BTC")

- **Clear unmet medical need** - a few agents being tested in 2L BTC but standard of care not yet established;
- Phase II PoC initiated in early 2017;
- **Planning for Phase II/III pivotal study in BTC in China is underway aiming to initiate H1 2019.**

## U.S. Development Expanding

- Phase I dose escalation study in the U.S. completed (N=29), 5 dose cohorts (50-400mg QD), established **300mg. QD as RP2D** (same as China);
- U.S. Phase Ib/II study in **P-NET & BTC initiated July 2018**;
- Chi-Med C&R Team now in place in U.S. to manage.

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



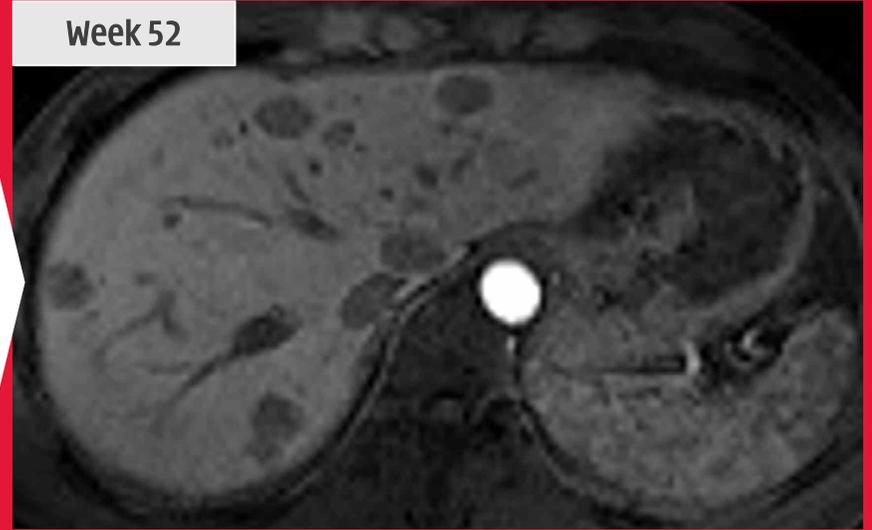
## Tumor devascularization & central necrosis

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

Baseline

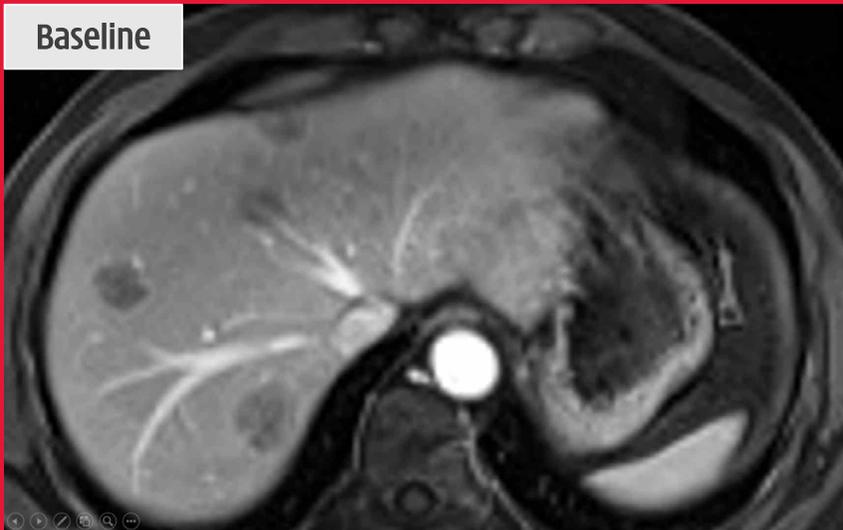


Week 52

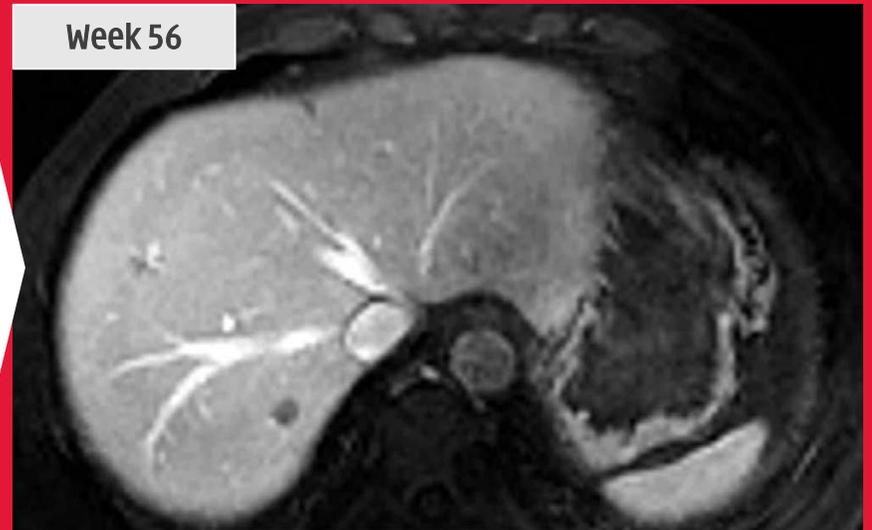


**Patient 2**  
**Rectum NET G2**  
w/ multiple liver metastases

Baseline



Week 56





5d

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

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

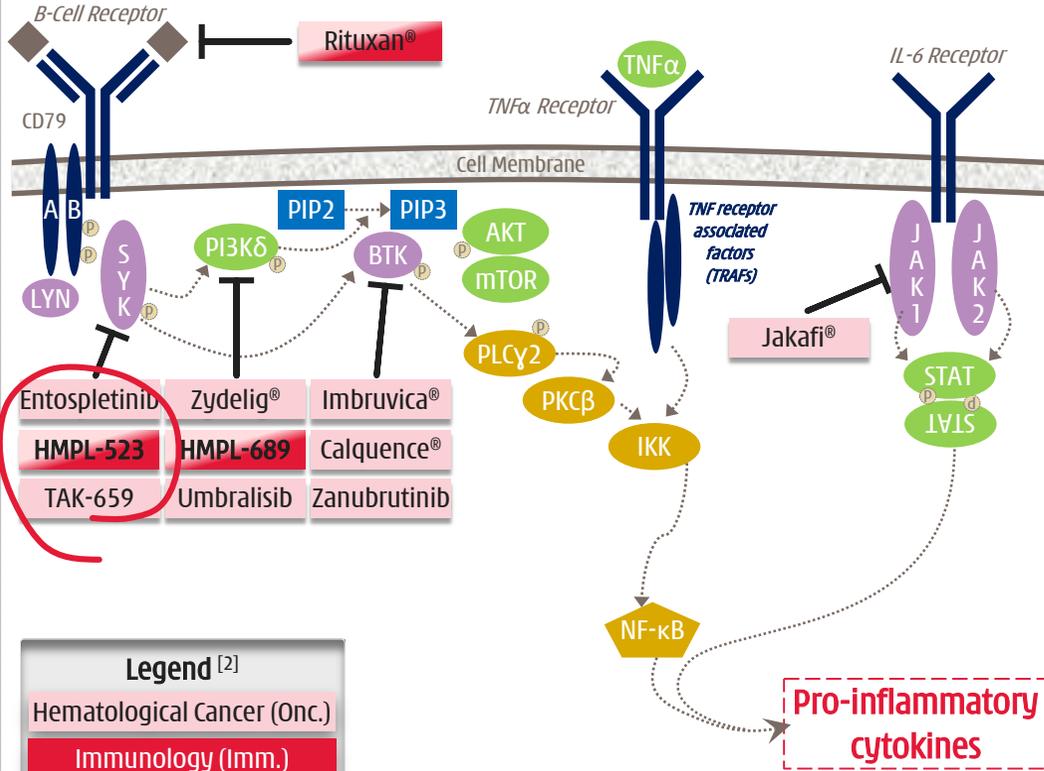
# HMPL-523 - hematological malignancies

## Syk exciting target emerging - Lymphoma PoC ongoing

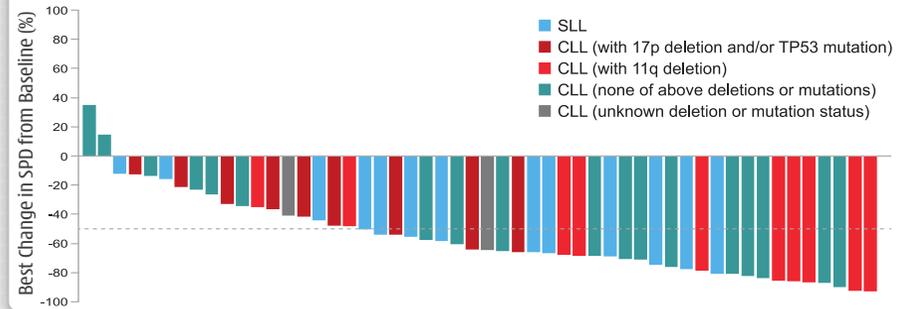


1. The B-cell signaling is **critical in hematological cancer** with three **breakthrough therapies** recently approved.

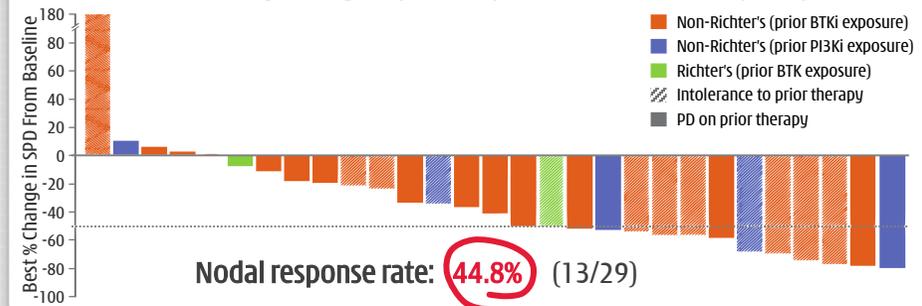
- 2018 sales: Imbruvica® \$6.2bn; Zydelig® \$0.1bn; Jakafi® \$2.4bn; & Rituxan® \$5.3bn [1].



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.

[1] Rituxan® 2017 sales in oncology only; [2] Approved Drug = ®; All others are clinical candidates; [3] ASH = American Society of Hematology; [4] Chronic lymphocytic leukemia ("CLL") & small lymphocytic lymphoma ("SLL"); [5] Sharman et al, ASH Meetings 2015 & 2016; [6] CYP3A4, CYP2D6 and CYP 1A2.

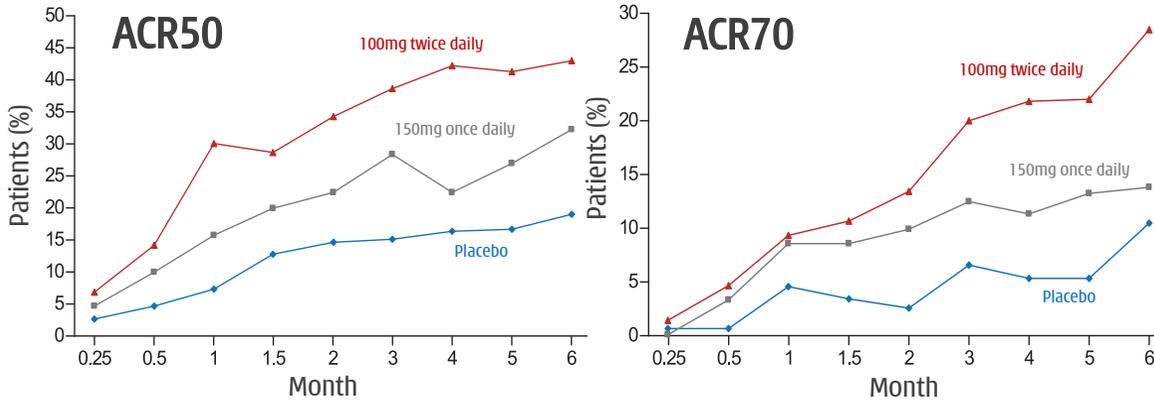
# HMPL-523 - immunology potential

Superior selectivity, better target coverage & efficacy vs. fosta.



1. Fostamatinib good Phase II<sup>[1]</sup> RA<sup>[2]</sup> dose response...

...but GI toxicity, infection & 23% put on antihypertensives.



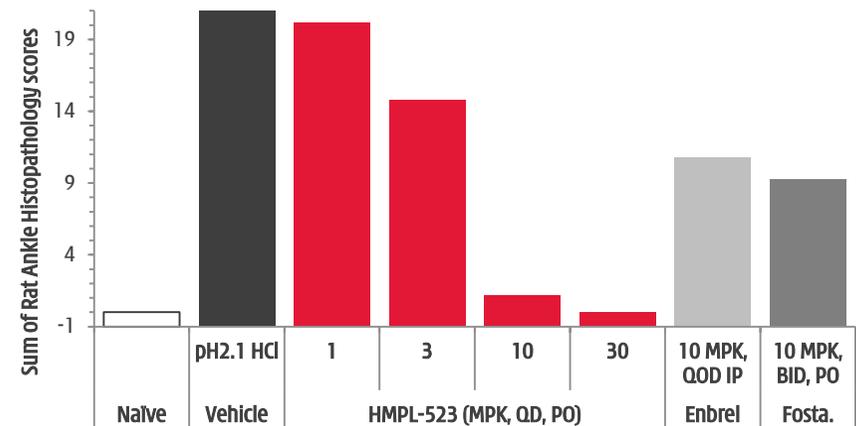
Percent of patients	Placebo (n = 153)	150mg QD (n = 152)	100mg BID (n = 152)
Diarrhea	3.0%	11.8% †	19.1% †
Upper respiratory infection	7.1	7.2	14.5 †
Urinary tract infection	4.6	3.3	5.9
Nausea	4.6	5.9	4.6
Neutropenia	0.7	6.6 †	5.9 †
Headache	5.2	6.6	5.9
Abdominal pain	2.6	6.6 †	5.9 †
ALT >3X ULN	2.0	3.9	3.9
Dizziness	2.0	2.6	4.6
Hypothyroidism	2.6	2.6	3.3
Cough	2.6	2.0	3.3

† P < 0.05 for comparison with placebo group; ALT = alanine aminotransferase.

2. HMPL-523 - far superior selectivity to fostamatinib...

...and very strong efficacy in preclinical RA models.

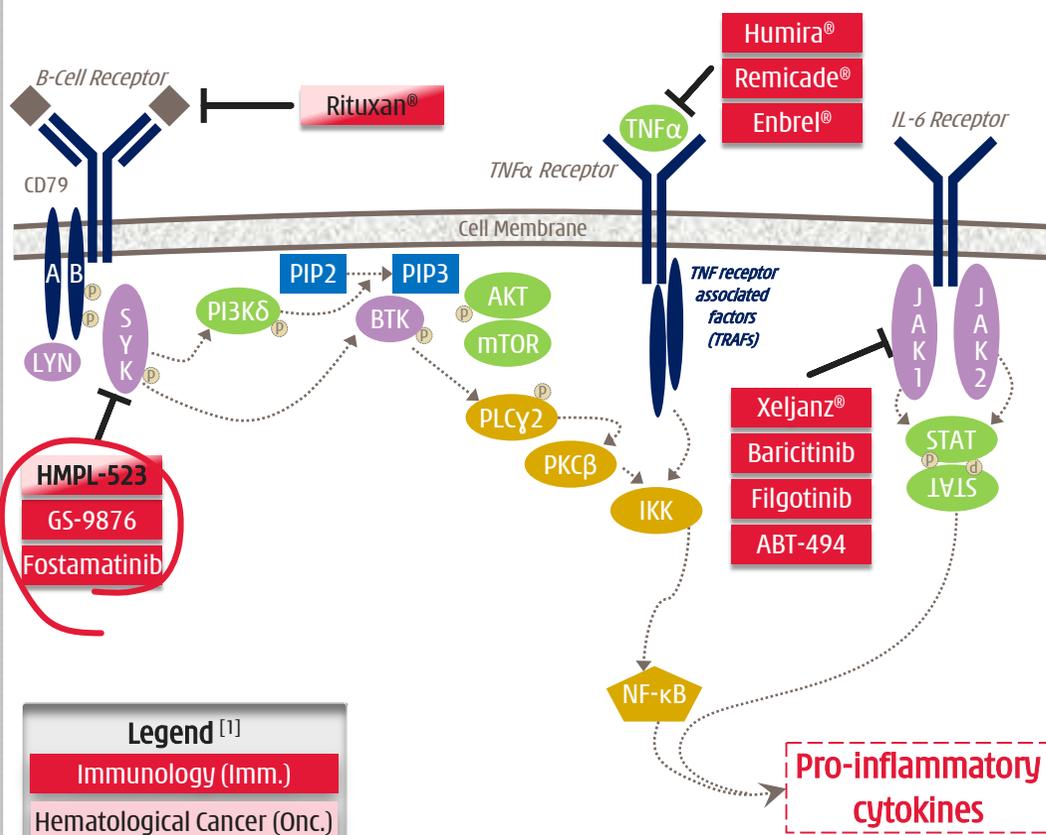
Selectivity	HMPL-523 IC <sub>50</sub> (nM)	fostamatinib IC <sub>50</sub> (nM)
Syk enzyme	25 ± 5 (n=10)*	54 ± 16 (n=10)*
JAK 1,2,3 enzyme	>300, >300, >300*	120, 30, 480*
FGFR 1,2,3	>3,000, >3,000, >3,000	89, 22, 32*
FLT3 enzyme	63*	9*
LYN enzyme	921*	160*
Ret enzyme	>3,000*	5**
KDR enzyme	390 ± 38 (n=3)*	61 ± 2 (n=3)*
KDR cell	5,501 ± 1,607 (n=3)*	422 ± 126 (n=3)*



[1] Fostamatinib is a prodrug of the SYK inhibitor R406 - Phase II study data per N ENGL J MED 363;14; \*: HMPL data and Eun-ho Lee, 2011; \*\*: Birth Defects Research (Part A) 2009, 85: 130-6; [2] RA = Rheumatoid Arthritis; GI = Gastrointestinal; QD = one dose per day; BID = two doses per day; QOD = one dose every other day; PO = by mouth (i.e. orally); IP = by Intraperitoneal injection; Naive = model score without induced arthritis.

# HMPL-523 - immunology potential

1. Syk, the **most upstream B-cell pathway kinase target** is **clinically validated in rheumatoid arthritis ("RA")**, but we believe currently Chi-Med & Gilead are the only companies pursuing.



2. RA expected to be a **\$45 billion<sup>[2]</sup> market in 2020** with B-cell pathway; anti-TNF; & JAK the main focus.

(Methotrexate-IR: placebo adjusted)	ACR20	ACR50	ACR70	2018 Sales (\$ billion) <sup>[3]</sup>
<b>B-Cell receptor -- mAbs</b>				
Rituxan® (24-Week)	33%	21%	11%	1.6
<b>Anti-TNFα/NF-κB -- mAbs</b>				
Humira® (24-Week)	33%	29%	18%	19.9
Remicade® (24-Week)	30%	22%	8%	5.3
Enbrel® (24-Week)	44%	36%	15%	6.9
<b>JAK Inhibitors -- Small molecules</b>				
Xeljanz® (24-Week)	25%	23%	13%	1.8
Xeljanz® (12-Week)	28%	21%	8%	
baricitinib 4mg QD (12-Week)	30%	28%	14%	n/a
filgotinib 100mg BID (12-Week)	35%	40%	23%	n/a
ABT-494 24mg QD (12-Week)	32%	24%	18%	n/a
<b>Syk Inhibitor -- Small molecule</b>				
fostamatinib 100mg BID (24-Week)	32%	24%	18%	n/a

3. Substantial market potential remains in RA.
- mAbs intravenous administration and shut down immune system for 4-6 weeks - **high infection / lymphoma risks.**
  - First-in-class JAKs in RA limited by **compound-related tox.**
  - Syk inhibition shown to benefit patients - but **fostamatinib failed due to major off-target toxicity.**

[1] Approved drug = ®; All other clinical candidates: mAb = antibody (extracellular); small molecule (intracellular); [2] Frost & Sullivan; [3] 2017 sales in immunology only.

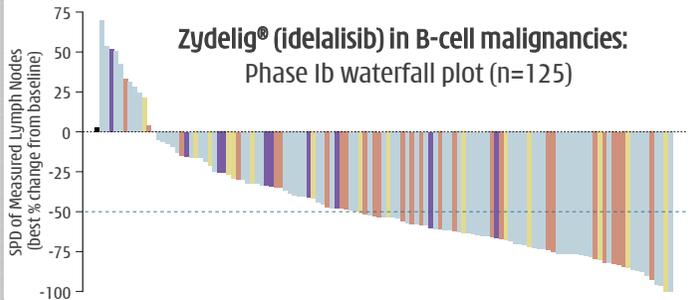
# HMPL-689 - Phase I Australia & China ongoing

## Designed to be a best-in-class inhibitor of PI3K $\delta$



### 1. PI3K $\delta$ now a proven target.

- PI3K $\delta$  activation associated with allergy, inflammation & oncology.
- Evidence that PI3K $\delta$  inhibitors effective in ibrutinib-resistant mutant population.



### 2. PI3K $\delta$ inhibitors being developed in a very broad range of indications.

Compound		Indication	Status	Issue
Zydelig® (idelalisib) PI3K $\delta$	Gilead	Chronic lymphocytic leukaemia, non-Hodgkin's lymphoma	Marketed	High incidence of liver toxicity seen with idelalisib (150mg bid)
AMG-319 PI3K $\delta$	Amgen	B-cell lymphoma, non-Hodgkin's lymphoma, T-cell lymphoma, chronic lymphocytic leukaemia	Phase I Trial	
Copiktra® (duvelisib) PI3K $\gamma/\delta$	Verastem/Infinity [1]	Relapsed or refractory chronic lymphocytic leukaemia / small lymphocytic lymphoma	Approved	Need to spare PI3K $\gamma$ -- serious infection seen & associated with a boxed warning for 4 fatal and/or serious toxicities
		Relapsed or refractory follicular lymphoma	Approved [2]	
Aliqopa® (copanlisib) PI3K $\alpha/\delta$	Bayer	Relapsed follicular B-cell non-Hodgkin lymphoma	Approved [2]	Serious and fatal infections and AEs

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

Designed to improve on existing PI3K $\delta$  inhibitors:

- Improved isoform selectivity (sparing PI3K $\gamma$ ).
- 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®
PI3K $\delta$	0.8 (n = 3)	2	1	0.7
PI3K $\gamma$ (fold vs. PI3K $\delta$ )	114 (142X)	104 (52X)	2 (2X)	6.4 (9X)
PI3K $\alpha$ (fold vs. PI3K $\delta$ )	>1,000 (>1,250X)	866 (433X)	143 (143X)	0.5 (1X)
PI3K $\delta$ human whole blood CD63+	3	14	15	n/a
PI3K $\beta$ (fold vs. PI3K $\delta$ )	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.



5e

## Epitinib

*EGFR inhibitor with blood-brain-barrier penetration*

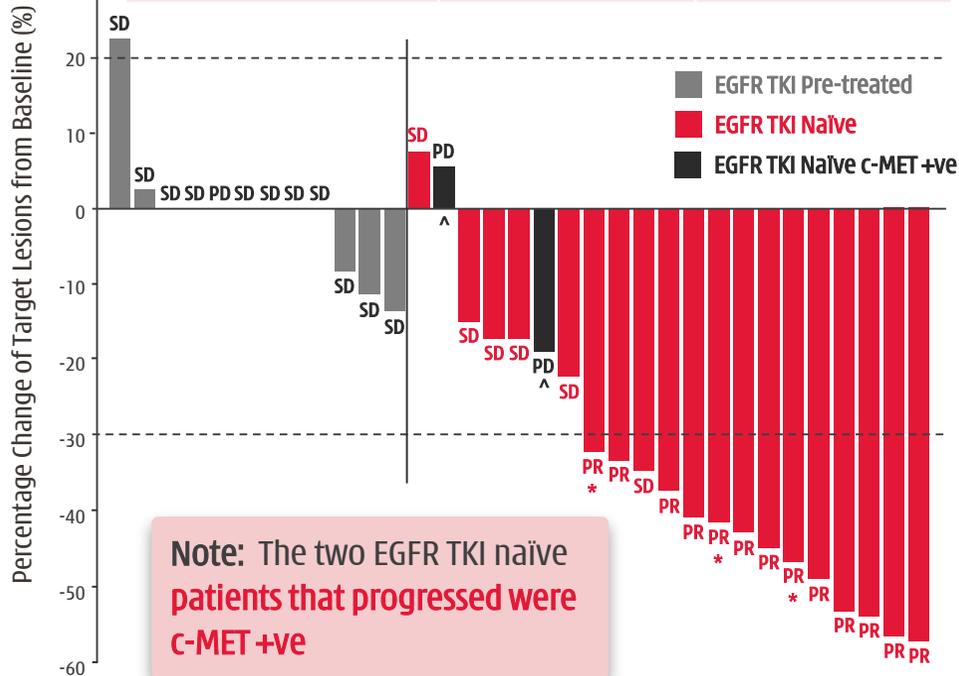
# Epitinib - 70% response in NSCLC w/ brain mets<sup>[1]</sup>



Unmet medical need. Investment case under review.

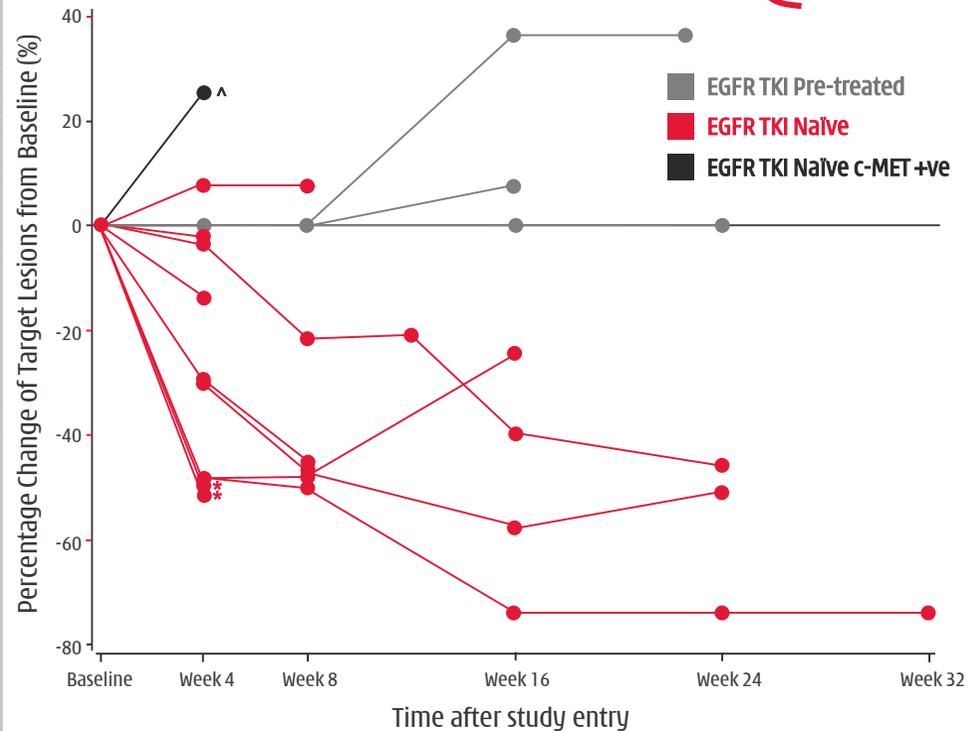
## 1. Phase Ib<sup>[1]</sup> - epitinib monotherapy in EGFRm+ NSCLC patients - efficacy in lung in-line with Iressa®/Tarceva®.

160mg once daily dose ("QD")	EGFR TKI naïve (N=21)	EGFR TKI naïve excl. c-MET +ve (N=19)
Objective Response Rate ("ORR")	61.9% (13/21) #	68.4% (13/19) #
Disease Control Rate ("DCR")	90.5% (19/21) #	100.0% (19/19) #



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

160mg QD dose	EGFR TKI naïve (N=11)	EGFR TKI naïve excl. c-MET +ve (N=10)
Intracranial ORR	63.6% (7/11) #	70.0% (7/10) #
Intracranial DCR	90.9% (10/11) #	100.0% (10/10) #

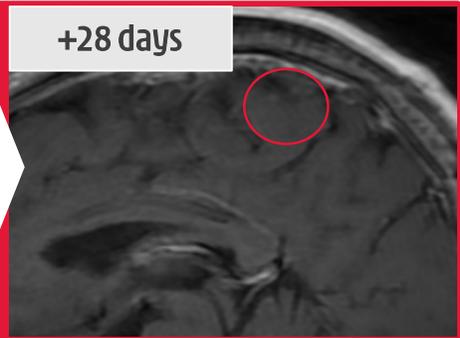
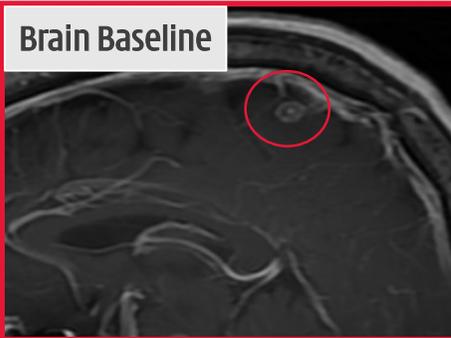
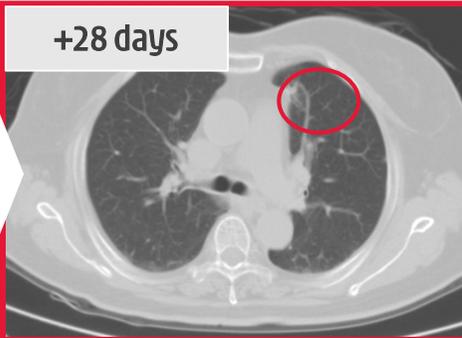
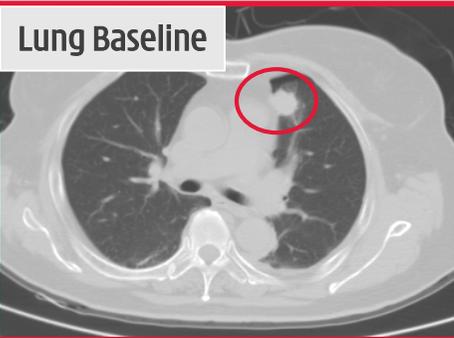


[1] Dose expansion stage - data cut-off September 20, 2016; [2] Li B, Bao YC, Chen B, *et al.* Therapy for non-small cell lung cancer patients with brain metastasis. Chinese-German J Clin Oncol, 2014, 13: 483-488;

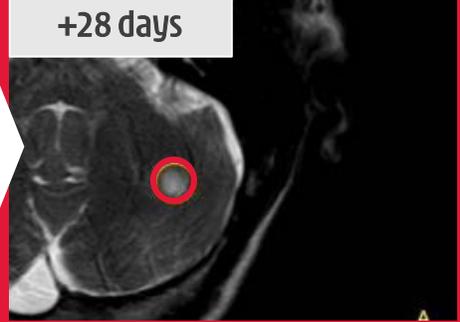
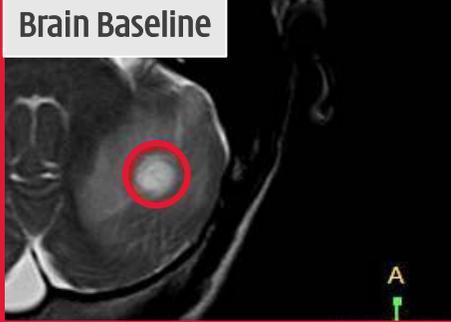
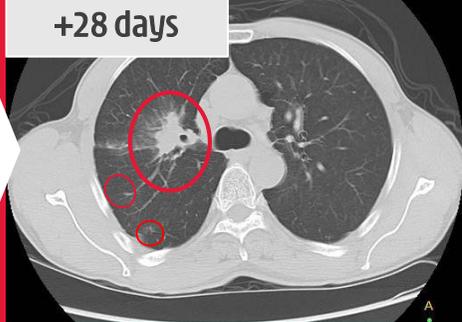
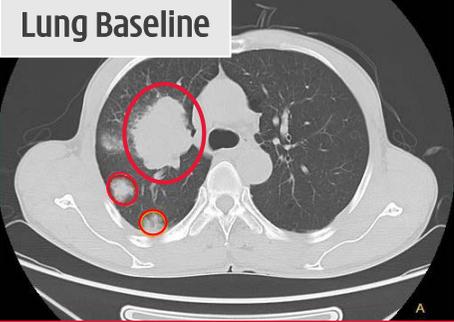
\* Unconfirmed PR, due to no further assessment at cut-off date; # Includes both confirmed and unconfirmed PRs; ^ c-MET amplification/high expression identified.

# Epitinib - Strong PoC efficacy - 160mg QD dose

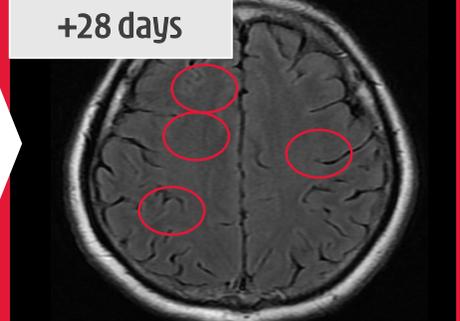
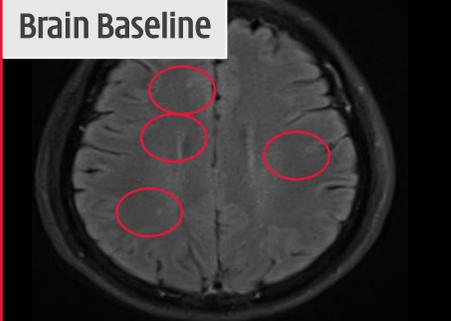
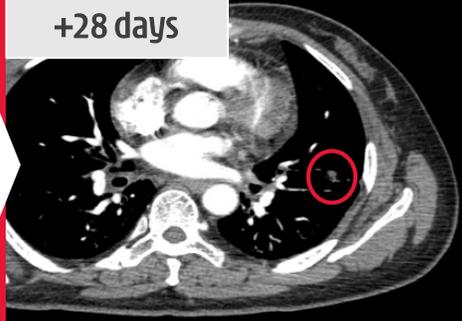
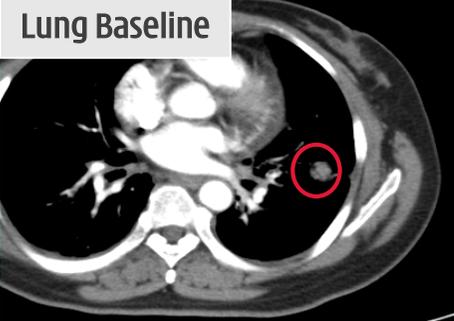
62-year-old female



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®).

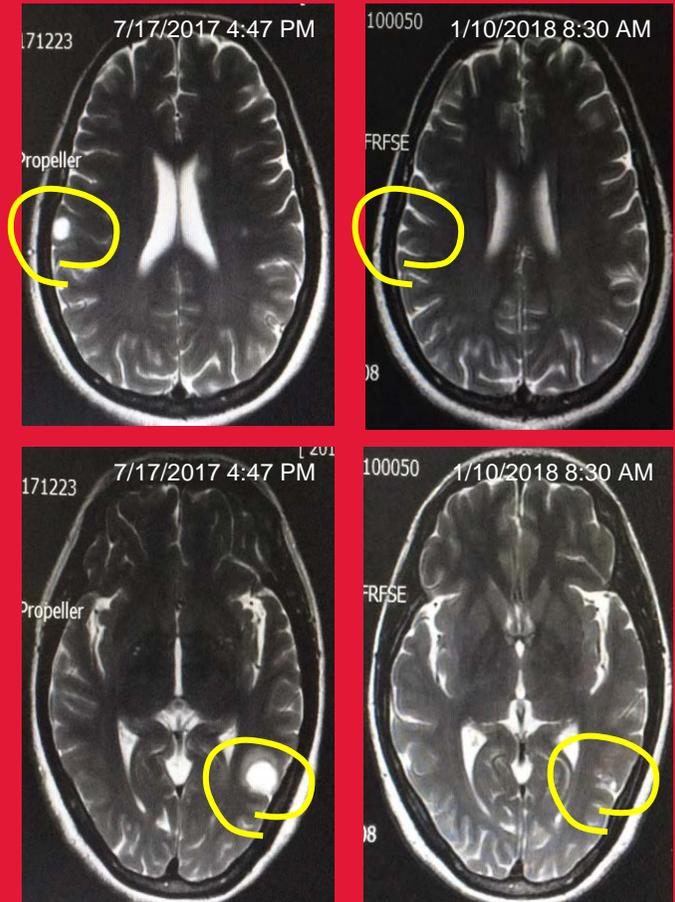
Dose Escalation Stage (n=35*) (Drug related AEs reported >10%)			Dose Expansion Stage (n=37) (Drug related AEs reported >10%)		
160mg QD dose	All Grades n (%)	Grade 3/4 n (%)	160mg QD dose	All Grades n (%)	Grade 3/4 n (%)
Skin rash	21 (60.0%)	1 (2.9%)	Skin rash	31 (83.8%)	2 (5.4%)
Diarrhea	12 (34.3%)	-	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.



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

*Potential best-in-class (EGFRwt) & first-in-class (FGFR1/2/3) assets*

# Theletinib

Potent & highly selective TKI - strong affinity to EGFRwt kinase

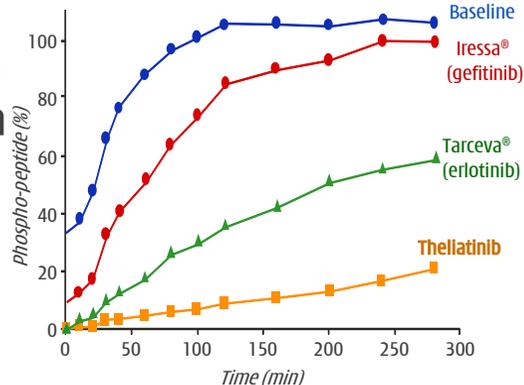
## 1. Major unmet medical need for wild-type EGFR activation tumors.

- 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.



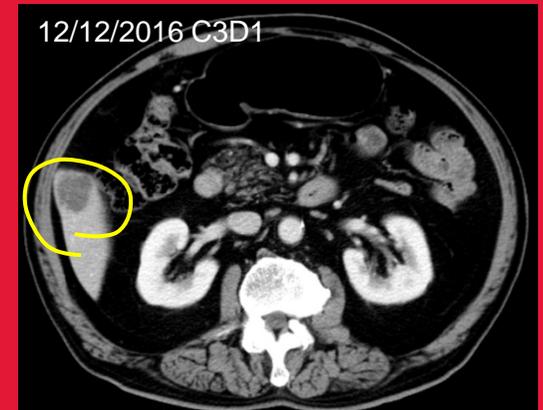
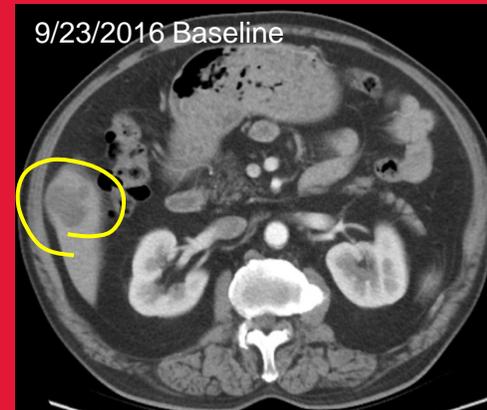
## 3. Esophageal cancer (EC): No effective treatment options.

- Major issue in Asia with poor prognosis: 5-year survival 10-20%

	new cases/year	deaths/year
U.S.	16,940 <sup>[1]</sup>	15,690 <sup>[1]</sup>
China	477,900 <sup>[1]</sup>	375,000 <sup>[1]</sup>

## 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).



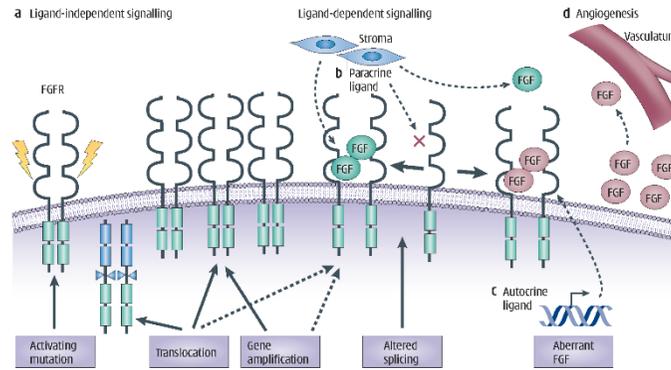
# HMPL-453 - Phase I in China ongoing

## Designed as first-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.

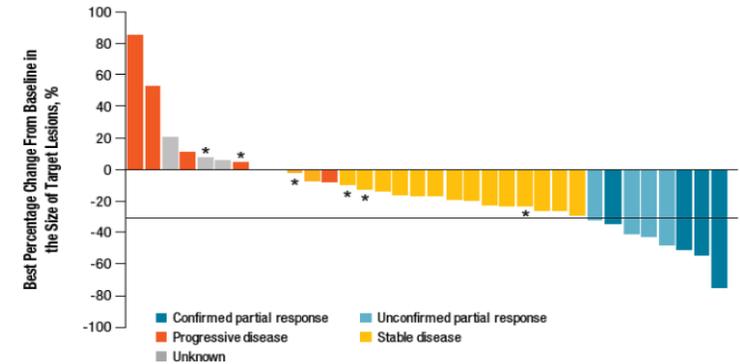


### 2. FGFR - diverse & complicated genetic changes with multiple tumor types harboring low incidence.

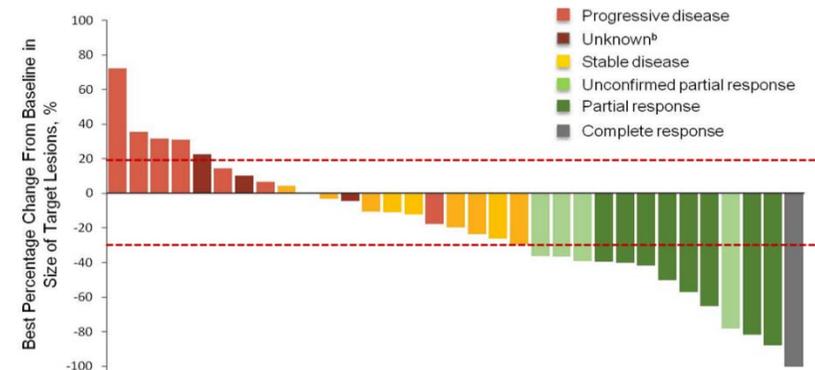
	Gene amplification	Gene translocation	Gene mutation
FGFR1	Lung squamous (7~15%) H&N squamous (10~17%) Esophageal squamous (9%) Breast (10~15%)	Lung squamous (n/a) Glioblastoma (n/a) Myeloproliferative syndrome (n/a) Breast (n/a)	Gastric (4%) Pilocytic astrocytoma (5~8%)
FGFR2	Gastric (5~10%) Breast (4%)	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%)

### 3. Biliary Tract Cancer (cholangiocarcinoma) and bladder cancer have made much progress in clinic to date.

- BJJ398 Phase II PoC in biliary tract cancer (2016 ASCO GI).



- BJJ398 Phase II PoC in bladder cancer (2016 ASCO).



CHI-

MED



6

## Appendix 3

*Further Chi-Med corporate information*

# Important milestones in Chi-Med's evolution

Innovation  
Start-up & M&A

Discovery  
Platform

China Registr. &  
Global Early Dev.

China Launches &  
Expanding Global Registration

2000 -2005

2006 -2010

2011 -2016

2017

Today



Global  
Innovation

Established  
Hutchison  
MediPharma



Lilly MERCK SERONO Janssen  
Research collaborations

AstraZeneca  
Global license deal  
savolitinib (c-MET)

Savo  
US IND

Suru  
US IND

Fruq  
US IND

523 (Syk)  
US IND

689 (PI3Kδ)  
US IND

2017  
WCLC  
savo. + Tagrisso® Ph Ib  
& II oral presentation

Innovent  
Innovent Biologics  
Global PD-1  
co-development deals



China  
Oncology

Lilly  
China license deal  
fruquintinib (VEGFR)

2017  
ASCO  
ANNUAL MEETING  
Fruquintinib FRESCO  
oral presentation

Fruquintinib FRESCO  
JAMA publication



ELUNATE®  
Fruquintinib Capsules  
Approval & Launch

China PD-1 co-  
dev. deals

Suru  
PRC IND

Fruq/ savo  
PRC IND

Epit/ Thel  
PRC INDS

523 (Syk)  
PRC IND

689 (PI3Kδ)  
PRC IND

453 (FGFR)  
PRC IND



Existing China  
Business

Shanghai Hutchison  
Pharmaceuticals  
上海和黄药业  
Shanghai Pharma  
Joint Venture (Rx)

<100 Med.  
Sales Reps.

白云山和黄中药  
Guangzhou Pharma  
Joint Venture (OTC)

Hutchison  
Sinopharm Pharmaceuticals  
国药和黄医药  
Sinopharm  
Joint Venture (Rx)

~1,300 Med.  
Sales Reps.

AstraZeneca  
Seroquel® & Concor®  
China promotion deals

>2,400 Med.  
Sales Reps.

# Chi-Med Group Structure - Major Entities

## Chi-Med Group Level

Revenues - 2018 \$214.1m (2017: \$241.2m)  
 Net Loss Attributable to Chi-Med - 2018: -\$74.8m (2017 net loss: -\$26.7m)

Non-Consolidated Joint Ventures  
 Chi-Med Subsidiaries

## Innovation Platform

Revenue - **2018: \$41.2m** (2017: \$36.0m)  
 Net Loss Attributable to Chi-Med - **2018: -\$102.4m** (2017: -\$51.9m)



## Commercial Platform

Sales of Subs & JVs - **2018: \$664.4m** (2017: \$638.6m<sup>[1]</sup>)  
 Net Income Attributable to Chi-Med - **2018: \$41.4m** (2017: \$37.5m<sup>[2]</sup>)



99.8%

## Prescription Drugs

50%

51%

**Hutchison MediPharma ("HMP")**  
*Oncology/Immunology Drug R&D*

Revenue:  
**2018: \$41.2m** (2017: \$36.0m)

**Shanghai Hutchison Pharma ("SHPL")**  
*Prescription Drugs*  
 Partner: Shanghai Pharma Group  
 Revenue:  
**2018: \$275.7m** (2017: \$244.6m)

**Hutchison Sinopharm ("HSP")<sup>[3]</sup>**  
*Rx Drug Commercial Co.*  
 Partner: Sinopharm Group  
 Revenue:  
**2018: \$132.8m** (2017: \$166.4m)

50%

## Consumer Health

50%<sup>[4]</sup>

50%

**Nutrition Science Partners ("NSP")**  
*Botanical Drug /GI Disease R&D*  
 Partner: Nestlé Health Science  
 Revenue:  
**2018: nil** (2017: nil)

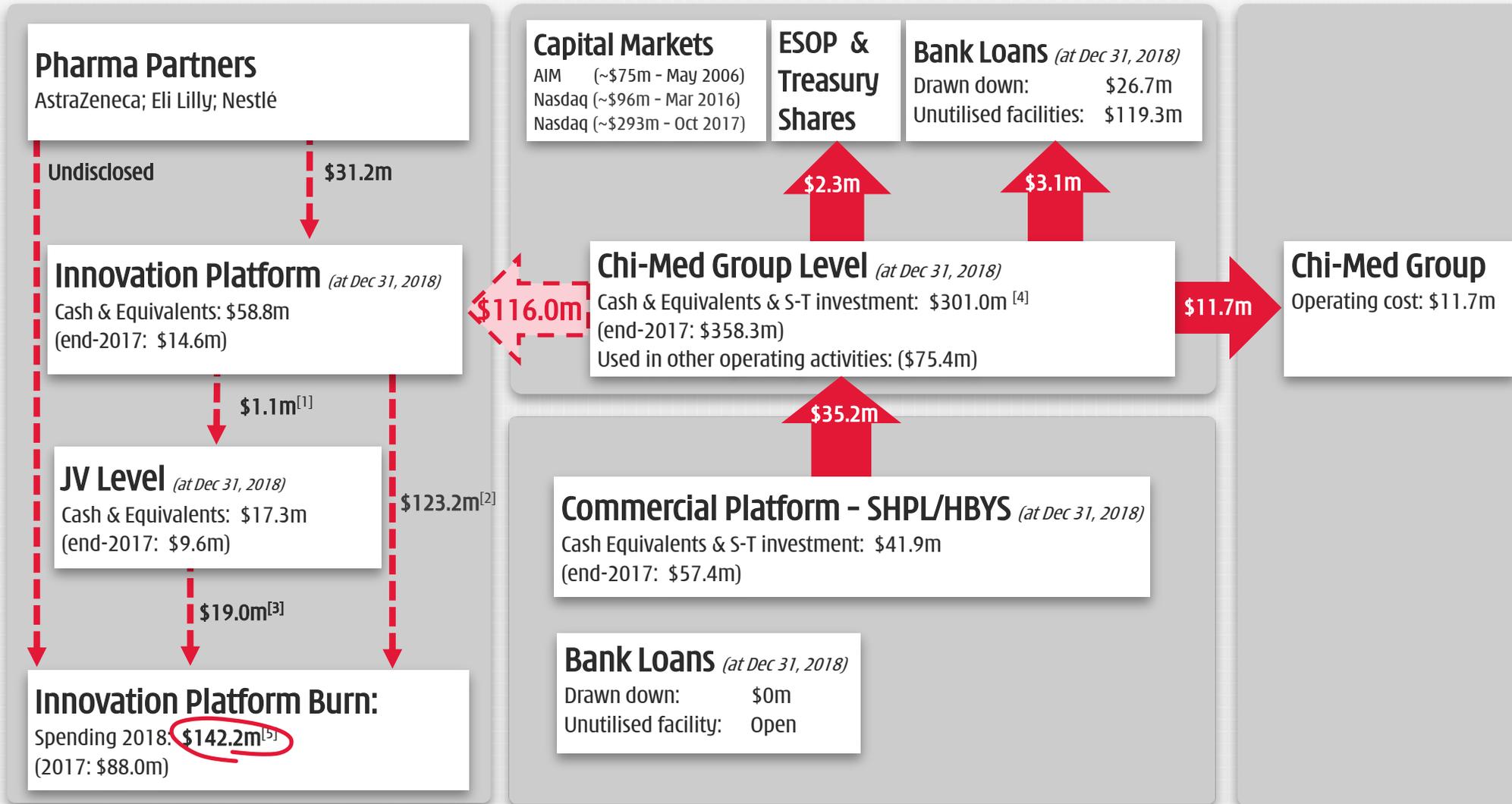
**Hutchison BYS Chinese Med. ("HBYS")**  
*Over-the-counter Drugs ("OTC")*  
 Partner: Guangzhou Pharma Holdings  
 Revenue:  
**2018: \$215.8m** (2017: \$188.8m<sup>[1]</sup>)

**Hutchison Hain Organic ("HHO")**  
*Health Related Consumer Prods.*  
 Partner: Hain Celestial Group  
 Revenue:  
**2018: \$26.7m** (2017: \$28.9m)

[1] Excluding Guanbao (divested in Sep 2017); [2] Non-GAAP: excludes the share of government subsidies from SHPL of \$2.5million in 2017; [3] Excluded HSP's Zhi Ling Tong infant nutrition business, revenue from prescription drug business has decreased by 20% as a result of the Chinese government's implementation of the new Two-Invoice System ("TIS"), pursuant to which we had converted to earning service fees from the commercialization of certain third-party products instead of recognizing the gross sales from these products in our revenue as we had done prior to implementation of TIS in October 2017; despite the TIS change, service fees (non-GAAP) earned from the key third-party product, anti-psychotic Seroquel®, grew rapidly, up 51% to \$17.2 million (2017: \$11.4m); [4] Held through an 80% owned subsidiary.

# FY2018 Inter-group cash flow

\$301.0m cash (Dec 31, 2018); \$119.3m in undrawn bank facilities



[1] \$8.0m capital injection to NSP offset by \$6.9m service income received from NSP; [2] Including research & development cost and general & admin. expenses; [3] Share of NSP operating loss; [4] Including \$214.9m short-term investment (deposits over 3 months) as at end of 2018; [5] Please see appendix "Non-GAAP Financial Measures and Reconciliation" for a Reconciliation of GAAP to adjusted research and development expenses.

# 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 \$1.7 - 1.8 billion.<sup>[1]</sup>  
Given our share in the JVs, Chi-Med's share of this value is approximately \$0.8 - 0.9 billion.

	Code	NET SALES			NET INCOME				VALUATION <sup>[4]</sup>	
		2017 Jan-Jun	2018 Jan-Jun	17-18 1H Growth	2017 Jan-Jun	2018 Jan-Jun	17-18 1H Growth	2018 1H Margin	Market Cap.	P/E
<b>CHI-MED Commercial Platform -- Subsidiaries/JVs<sup>[2]</sup></b>		<b>328.0<sup>[3]</sup></b>	<b>360.3</b>	<b>10%</b>	<b>51.9</b>	<b>55.1</b>	<b>6%</b>	<b>15%</b>	<b>n/a</b>	<b>n/a</b>
Tianjin Zhong Xin Pharma	600329	451.3	470.2	4%	41.6	47.6	14%	10%	1,699	22
Li Zhu Pharma	000513	645.8	689.6	7%	83.2	102.1	23%	15%	3,619	21
Shandong Dong E E Jiao	000423	443.3	451.1	2%	136.4	130.5	-4%	29%	4,519	15
Zhejiang Kang En Bai Pharma	600572	353.6	540.3	53%	58.6	83.1	42%	15%	3,201	24
Kunming Pharma	600422	412.4	511.4	24%	32.7	27.7	-15%	5%	831	18
Guizhou Yi Bai Pharma	600594	294.9	285.9	-3%	30.0	26.2	-13%	9%	723	18
Jin Ling Pharma	000919	258.5	236.4	-9%	18.6	17.4	-6%	7%	533	31
Jiangsu Kang Yuan	600557	251.3	278.7	11%	29.3	30.8	5%	11%	1,137	19
Zhuzhou Qian Jin Pharma	600479	228.5	225.0	-2%	8.1	12.1	49%	5%	572	13
ZhangZhou Pian Zai Huang	600436	264.8	363.2	37%	63.9	91.7	44%	25%	9,681	62
<b>Peer Group -- Median (10 Comps. excl. Chi-Med)</b>		<b>324.2</b>	<b>407.1</b>	<b>26%</b>	<b>37.2</b>	<b>39.2</b>	<b>6%</b>	<b>10%</b>	<b>1,418</b>	<b>20</b>
<b>All 61 Listed China Pharma. Companies -- Median</b>		<b>258.5</b>	<b>278.7</b>	<b>8%</b>	<b>29.3</b>	<b>31.6</b>	<b>8%</b>	<b>11%</b>	<b>1,137</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 2018E Net Sales in the ~\$400-1,400 million range.

Source: Company data, Deutsche Bank, FactSet

[1] Peer group/China Pharma multiple of 20x-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 March 1<sup>st</sup>, 2019; Trailing Twelve Month PE weighted averaged based on market capitalization.

# Deep portfolio of household name drugs



Top 7 products represent 69% of sales<sup>[1]</sup> and 89% of gross profit<sup>[1]</sup>

Main Products <sup>[2]</sup> - SALES (Non-GAAP)	2012	2013	2014	2015	2016	2017	2018
 <p><b>SXBX pill</b> Coronary artery disease (Rx) 17% National market share Patent expiry 2029</p>	102,215 +29%	123,587 +21%	138,848 +12%	159,326 +15%	195,371 +23%	209,246 +7%	233,096 +11%
 <p><b>Banlangen granules</b> Anti-viral/flu (OTC) 54% National market share</p>	65,381 +14%	72,300 +11%	55,573 -23%	54,793 -1%	56,664 +3%	59,898 +6%	62,585 +4%
 <p><b>FFDS tablet</b> Angina (OTC) 38% National market share</p>	60,181 +6%	69,996 +16%	76,297 +9%	60,154 -21%	59,906 0%	58,936 -2%	56,342 -4%
 <p><b>NXQ tablet</b> Cerebrovascular disease (OTC) Proprietary formulation</p>	6,933 +85%	10,142 +46%	14,681 +45%	17,581 +20%	21,000 +19%	20,408 -3%	37,250 +83%
 <p><b>Seroquel tablets</b> Bi-polar/Schizophrenia (Rx) 6% National market share</p>	n/a	n/a	n/a	21,131	34,380 +63%	35,359 +3%	29,211 <sup>[3]</sup> -17%
 <p><b>KYQ granules</b> Periodontitis (OTC) &gt;90% National market share</p>	16,351 +6%	16,318 0%	18,370 +13%	17,051 -7%	17,210 +1%	17,620 +2%	19,329 +10%
 <p><b>Danning tablet</b> Gallbladder/stone (Rx) Patent expiry 2027</p>	11,648 +17%	12,364 +6%	13,822 +12%	13,526 -2%	9,041 -33%	16,089 +78%	17,378 +8%

[1] Based on aggregate Non-GAAP sales and gross profit of consolidated subsidiaries and non-consolidated joint ventures of Commercial Platform, please see appendix "Non-GAAP Financial Measures and Reconciliation"; [2] Rx = prescription drug; OTC = over-the-counter drug; SXBX pill = She Xiang Bao Xin pill; FFDS tablet = Fu Fang Dan Shen tablet; NXQ tablet = Nao Xin Qing tablet; KYQ granules = Kou Yan Qing granules; Market shares according to Frost & Sullivan or QuintilesIMS; [3] From October 2017, the majority of sales changed to a fee-for-service model due to the Two-invoice policy. Net service fee increased by 51% to \$17.2m in 2018 (2017: \$11.4m).

(US\$'000)  
(Growth % vs. Year Ago)

# Non-GAAP Financial Measures and Reconciliation (1/2)



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

	2018	2019 Guidance
Cash and cash equivalents and short-term investments at end of year	301.0	150-180 <sup>[1]</sup>
Less: cash and cash equivalents and short-term investments at beginning of year	(358.3)	(300)
<b>Adjusted Group net cash flows</b>	<b>(57.3)</b>	<b>(120) - (150)</b>
Add: Net cash used in financing activities for the year	8.2	---- <sup>[1]</sup>
<b>Adjusted Group net cash flows excluding financing activities</b>	<b>(49.1)</b>	<b>(120) - (150)</b>

## Reconciliation of Adjusted Service Fees for Seroquel:

	2018	2017
Revenue - Seroquel	29.2	35.4
Less: Cost of goods - Seroquel	(12.0)	(24.0)
<b>Adjusted services fees for Seroquel</b>	<b>17.2</b>	<b>11.4</b>

## Reconciliation of Top 7 products' Gross Profit as Percentage of Aggregated Gross Profit for Commercial Platform:

	2018
Revenue from external customers - commercial platform	172.9
Less: Costs of goods and services	(142.4)
<b>Gross profit - commercial platform</b>	<b>30.5</b>
Add: Gross profit - HBYS and SHPL	306.1
<b>Adjusted gross profit</b>	<b>336.6</b>
<b>Top 7 products gross profit</b>	<b>298.1</b>
% of Top 7 products to adjusted gross profit	89%

## Reconciliation of Adjusted Research and Development Expenses:

	2018	2017
Segment operating loss - Innovation Platform	(102.6)	(52.0)
Less: Segment revenue from external customers - Innovation Platform	(41.2)	(36.0)
Add: Costs of goods - third parties	1.6	-
<b>Adjusted R&amp;D expenses</b>	<b>(142.2)</b>	<b>(88.0)</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.

(US\$ millions unless otherwise stated)

# Non-GAAP Financial Measures and Reconciliation (2/2)



## 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).

(US\$ millions)	IFRS											US GAAP						17-18 Growth
	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18		
<b>Sales (Non-GAAP)</b>	<b>21.9</b>	<b>27.9</b>	<b>65.1</b>	<b>101.4</b>	<b>119.0</b>	<b>155.8</b>	<b>197.0</b>	<b>236.4</b>	<b>278.6</b>	<b>360.7</b>	<b>402.3</b>	<b>465.4</b>	<b>518.9</b>	<b>627.4</b>	<b>677.2</b>	<b>664.4</b>	<b>-2%</b>	
<b>Prescription Drugs</b>	<b>17.2</b>	<b>21.8</b>	<b>23.3</b>	<b>23.2</b>	<b>28.1</b>	<b>39.5</b>	<b>54.4</b>	<b>71.2</b>	<b>92.4</b>	<b>116.5</b>	<b>138.2</b>	<b>204.9</b>	<b>286.6</b>	<b>372.3</b>	<b>411.0</b>	<b>408.5</b>	<b>-1%</b>	
- Consolidated subsidiary	-	-	-	-	-	-	-	-	-	-	-	50.2	105.5	149.9	166.4	132.8	-20%	
- 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	13%	
<b>Consumer Health</b>	<b>4.7</b>	<b>6.1</b>	<b>41.8</b>	<b>78.2</b>	<b>90.9</b>	<b>116.3</b>	<b>142.6</b>	<b>165.2</b>	<b>186.2</b>	<b>244.2</b>	<b>264.1</b>	<b>260.5</b>	<b>232.3</b>	<b>255.1</b>	<b>266.2</b>	<b>255.9</b>	<b>-4%</b>	
- 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	3%	
- 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	-5%	
<b>Total Sales Growth</b>	<b>n/a</b>	<b>27%</b>	<b>133%</b>	<b>56%</b>	<b>17%</b>	<b>31%</b>	<b>26%</b>	<b>20%</b>	<b>18%</b>	<b>29%</b>	<b>n/a</b>	<b>16%</b>	<b>11%</b>	<b>21%</b>	<b>8%</b>	<b>-2%</b>		
- GuanBao divested in Sept'2017	-	-	-	-	-	-	-	-	(11.4)	(50.5)	(51.6)	(49.7)	(40.7)	(45.0)	(38.6)	0.0	n/a	
<b>Adjusted Consumer Health</b>	<b>4.7</b>	<b>6.1</b>	<b>41.8</b>	<b>78.2</b>	<b>90.9</b>	<b>116.3</b>	<b>142.6</b>	<b>165.2</b>	<b>174.8</b>	<b>193.7</b>	<b>212.5</b>	<b>210.8</b>	<b>191.6</b>	<b>210.1</b>	<b>227.6</b>	<b>255.9</b>	<b>12%</b>	
- 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	14%	
<b>Adjusted Sales (Non-GAAP)</b>	<b>21.9</b>	<b>27.9</b>	<b>65.1</b>	<b>101.4</b>	<b>119.0</b>	<b>155.8</b>	<b>197.0</b>	<b>236.4</b>	<b>267.2</b>	<b>310.2</b>	<b>350.7</b>	<b>415.7</b>	<b>478.2</b>	<b>582.4</b>	<b>638.6</b>	<b>664.4</b>	<b>4%</b>	
<b>Total Adjusted Sales Growth</b>	<b>n/a</b>	<b>27%</b>	<b>133%</b>	<b>56%</b>	<b>17%</b>	<b>31%</b>	<b>26%</b>	<b>20%</b>	<b>13%</b>	<b>16%</b>	<b>13%</b>	<b>19%</b>	<b>15%</b>	<b>22%</b>	<b>10%</b>	<b>4%</b>		
<b>Net (loss)/Income after tax (Non-GAAP)</b>	<b>(10.7)</b>	<b>(3.6)</b>	<b>2.2</b>	<b>6.7</b>	<b>11.2</b>	<b>14.7</b>	<b>21.5</b>	<b>27.9</b>	<b>30.1</b>	<b>33.1</b>	<b>39.7</b>	<b>48.8</b>	<b>54.1</b>	<b>63.3</b> <sup>[3]</sup>	<b>77.3</b> <sup>[4]</sup>	<b>83.6</b>	<b>8%</b>	
<b>Prescription Drugs</b>	<b>(0.4)</b>	<b>1.3</b>	<b>1.9</b>	<b>1.3</b>	<b>1.9</b>	<b>2.8</b>	<b>6.0</b>	<b>11.9</b>	<b>14.2</b>	<b>17.7</b>	<b>22.4</b>	<b>26.5</b>	<b>31.9</b>	<b>41.4</b>	<b>53.0</b>	<b>63.9</b>	<b>21%</b>	
- Consolidated subsidiary	-	-	-	-	-	-	-	-	-	-	-	0.1	0.6	1.6	2.4	4.1	74%	
- 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	18%	
<b>Consumer Health</b>	<b>(10.3)</b>	<b>(4.9)</b>	<b>0.3</b>	<b>5.4</b>	<b>9.3</b>	<b>11.9</b>	<b>15.5</b>	<b>16.0</b>	<b>15.9</b>	<b>15.4</b>	<b>17.3</b>	<b>22.3</b>	<b>22.2</b>	<b>21.9</b>	<b>24.3</b>	<b>19.7</b>	<b>-19%</b>	
- 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	-20%	
- 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	-19%	
<b>% Margin</b>	<b>-48.9%</b>	<b>-12.9%</b>	<b>3.4%</b>	<b>6.6%</b>	<b>9.4%</b>	<b>9.4%</b>	<b>10.9%</b>	<b>11.8%</b>	<b>10.8%</b>	<b>9.2%</b>	<b>9.9%</b>	<b>10.5%</b>	<b>10.4%</b>	<b>10.1%</b>	<b>11.4%</b>	<b>12.6%</b>		
<b>Net (loss)/income attrib. to Chi-Med</b>	<b>(5.7)</b>	<b>(3.7)</b>	<b>(0.5)</b>	<b>1.2</b>	<b>4.5</b> <sup>[2]</sup>	<b>5.9</b> <sup>[2]</sup>	<b>9.3</b> <sup>[2]</sup>	<b>12.6</b> <sup>[2]</sup>	<b>13.6</b> <sup>[2]</sup>	<b>14.6</b> <sup>[2]</sup>	<b>18.2</b> <sup>[2]</sup>	<b>22.8</b> <sup>[2]</sup>	<b>25.2</b> <sup>[2]</sup>	<b>29.9</b> <sup>[3]</sup>	<b>37.5</b> <sup>[4]</sup>	<b>41.4</b>	<b>10%</b>	
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	21%	
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	-16%	
<b>Net (loss)/income attrib. to Chi-Med growth</b>	<b>n/a</b>	<b>-35%</b>	<b>-86%</b>	<b>340%</b>	<b>275%</b>	<b>31%</b>	<b>58%</b>	<b>35%</b>	<b>8%</b>	<b>7%</b>	<b>n/a</b>	<b>26%</b>	<b>10%</b>	<b>19%</b>	<b>25%</b>	<b>10%</b>		

[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.

# National Drug Reimbursement List Pricing ("NDRL")

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



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 Drug Reimbursement List Pricing ("NDRL")

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



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	\$6,216	\$3,384	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	\$3,868	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.



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Thank you

