### **INVESTOR UPDATE**

R&D, COMMERCIAL AND ASCO UPDATE WEBCAST

May 26, 2021

Nasdaq / AIM: HCM





### Safe Harbor Statement & Disclaimer



The performance and results of operations of the HUTCHMED Group contained within this presentation are historical in nature, and past performance is no guarantee of future results.

This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the U.S. Private Securities Litigation Reform Act of 1995. These forward-looking statements can be identified by words like "will," "expects," "anticipates," "future," "intends," "plans," "believes," "estimates," "pipeline," "could," "potential," "first-in-class," "best-in-class," "designed to," "objective," "guidance," "pursue," or similar terms, or by express or implied discussions regarding potential drug candidates, potential indications for drug candidates or by discussions of strategy, plans, expectations or intentions. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that any of our drug candidates will be approved for sale in any market, or that any approvals which are obtained will be obtained at any particular time, or that any such drug candidates will achieve any particular revenue or net income levels. In particular, management's expectations could be affected by, among other things: unexpected regulatory actions or delays or government regulation generally; the uncertainties inherent in research and development, including the inability to meet our key study assumptions regarding enrollment rates, timing and availability of subjects meeting a study's inclusion and exclusion criteria and funding requirements, changes to clinical protocols, unexpected adverse events or safety, quality or manufacturing issues; the inability of a drug candidate to meet the primary or secondary endpoint of a study; the impact of the COVID-19 pandemic or other health crises in China or globally; the inability of a drug candidate to obtain regulatory approval in different jurisdictions or gain commercial acceptance after obtaining regulatory approval; global trends toward health care cost containment, including ongoing pricing pressures; uncertainties regarding actual or potential legal proceedings, including, among others, actual or potential product liability litigation, litigation and investigations regarding sales and marketing practices, intellectual property disputes, and government investigations generally; and general economic and industry conditions, including uncertainties regarding the effects of the persistently weak economic and financial environment in many countries and uncertainties regarding future global exchange rates. For further discussion of these and other risks, see HUTCHMED's filings with the U.S. Securities and Exchange Commission and on AIM. HUTCHMED is providing the information in this presentation as of this date and does not undertake any obligation to update any forward-looking statements as a result of new information, future events or otherwise.

In addition, this presentation contains statistical data, third-party clinical data and estimates that HUTCHMED obtained from industry publications and reports generated by third-party market research

firms, including Frost & Sullivan, IQVIA, independent market research firms, clinical data of competitors, and other publicly available data. All patient population, market size and market share estimates are based on Frost & Sullivan or QuintilesIMS/IQVIA research, unless otherwise noted. Although HUTCHMED believes that the publications, reports, surveys and third-party clinical data are reliable, HUTCHMED has not independently verified the data and cannot guarantee the accuracy or completeness of such data. You are cautioned not to give undue weight to this data. Such data involves risks and uncertainties and are subject to change based on various factors, including those discussed above.

Nothing in this presentation or in any accompanying management discussion of this presentation constitutes, nor is it intended to constitute or form any part of: (i) an invitation or inducement to engage in any investment activity, whether in the United States, the United Kingdom or in any other jurisdiction; (ii) any recommendation or advice in respect of any securities of HUTCHMED; or (iii) any offer for the sale, purchase or subscription of any securities of HUTCHMED.

No representation or warranty, express or implied, is made as to, and no reliance should be placed on, the fairness, accuracy, completeness or correctness of the information, or opinions contained herein. Neither HUTCHMED, nor any of HUTCHMED's advisors or representatives shall have any responsibility or liability whatsoever (for negligence or otherwise) for any loss howsoever arising from any use of this presentation or its contents or otherwise arising in connection with this presentation. The information set out herein may be subject to updating, completion, revision, verification and amendment and such information may change materially.

All references to "HUTCHMED" as used throughout this presentation refer to HUTCHMED (China) Limited and its consolidated subsidiaries and joint ventures unless otherwise stated or indicated by context. This presentation should be read in conjunction with HUTCHMED's results for the year ended December 31, 2020 and HUTCHMED's other SEC filings, copies of which are available on HUTCHMED's website (www.hutch-med.com).

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

# **Agenda**



8:00	Overview	Christian Hogg
8:05	Clinical Development Updates	Weiguo Su & Marek Kania
	Savolitinib	
	Surufatinib	
	Fruquintinib	
	HMPL-689	
	HMPL-523	
	Early Programs & Discovery Strategy	
8:50	Market Potential & Introduction to Commercial	Christian Hogg
	China Commercial	Hong Chen
	US Commercial	Tom Held
9:10	Introduction to CMC	Christian Hogg
	CMC	Zhenping Wu
9:30	Conclusion & Q&A	Christian Hogg

### **Speakers**

# HUTCHMED

#### **HUTCHMED Management Team**



Christian Hogg Chief Executive Officer

P&G

32/**21** 



Weiguo Su Chief Scientific Officer



31/16



25/11

Hong Chen Chief Commercial Officer, China

Bristol Myers Squibb

**U** NOVARTIS



30/1

Tom Held Head of Commercial, U.S.

O Daiichi-Sankyo

**U** NOVARTIS



27/3

Marek Kania Managing Director & Chief Medical Officer, International





27/13

Zhenping Wu Pharmaceutical Sciences



**P**fizer



32/13

Johnny Cheng Chief Financial Officer

Nestle Nestle

KPING



30/20

Junjie Zhou General Manager, SHPL





May Wang Business Dev. & Strategic Alliances





Mark Lee Corporate Finance & Development

CREDIT SUISSE 22/12



Charles Nixon General Counsel





Andrew Shih HR – Organization & Leadership Dev.



25/**2** 



Thomas Fu Global Quality



22/**1** 



Yiling Cui Government Affairs



hh



Enrico Magnanelli

International

22/3



# **OVERVIEW**

Christian Hogg, CEO

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



Realizing the global potential of HUTCHMED's novel oncology assets



Building a fully integrated oncology business in China

## What we will see today



Integrated China & International Development

Expanding international team supporting global development

7 global programs in 2021: activities in China, US, EU, Japan & Australia

**Savolitinib** 

**Starting multiple global & China registration studies in 2021** – NSCLC, PRCC, GC Potential 1<sup>st</sup> approval in China mid-year

Surufatinib & Fruquintinib

Filing 1st US FDA NDA and EU MAA
Multiple PD-1 combos entering registration studies

Transitioning
Pipeline in Hematology

HMPL-689 (PI3K $\delta$ ) entering China & US registration studies HMPL-523 (Syk) Ph. III planning; HMPL-306 (IDH1/2) & HMPL-295 (ERK) US & China Ph. Is

Early-stage Pipeline & Discovery Research

**HMPL-453** (FGFR) and **HMPL-760** (BTK) progressing; **3 more INDs** in H1 2021 Rich research pipeline

Oncology Commercial & Supply Chain

**Leveraging powerful China commercial expertise,** growing oncology sales rapidly **US** org. preparing for **1**<sup>st</sup> **US launches** – potentially **suru early 2022** & fruq 2023 Long term production and supply chain strategy



# CLINICAL DEVELOPMENT UPDATES

Weiguo Su, Chief Scientific Officer

Marek Kania, Managing Director & Chief Medical Officer – International

HUTCHMED

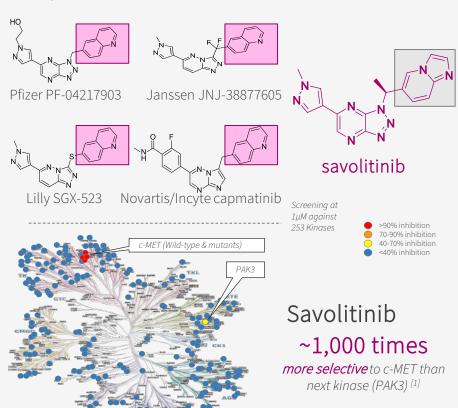
# **SAVOLITINIB**

# Savolitinib recap: MoA and data summary



#### Designed to avoid known renal toxicity while retaining potency

Quinolinone metabolite in 1<sup>st</sup>-gen MET compounds has low solubility in humans and when metabolized by the kidneys, appeared to crystallize, resulting in obstructive toxicity.



#### **Evidence of clinical differentiation**

- >1,100 patients in clinical trials to date
- Competitive anti-tumor effect across multiple
   MET aberrations in multiple tumor types
- Single agent and combination settings
- Potential first-in-class in China
- Currently testing in multiple tumor types:
  - NSCLC with Exon14 skipping
  - EGFRm + NSCLC
  - MET-driven PRCC
  - MET amplified GC

# Savolitinib: MET Exon14 skipping alterations



Encouraging anti-tumor activity across multiple settings in NSCLC

#### **NSCLC with MET Exon14 skipping alterations**

- 3% of NSCLC, up to 22% in PSC
- Most common in elderly patients
- No effective treatments with poor prognosis

#### **Savolitinib registration in China**

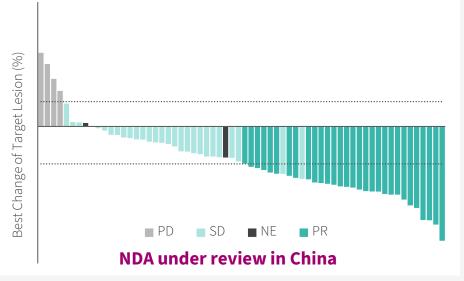
- NDA under review
- On track for mid-2021 approval

# MET Exon14 skipping alterations in other tumor types

- Secondary GBM
- Gl tumors
- Histiocytic sarcoma

# Phase II in NSCLC harboring MET Exon 14 skipping alterations (data by IRC)

China Phase II registration [1]	Efficacy Evaluable (N=61)	Full Analysis (N=70)
ORR, % [95% CI]	49.2% [36.1–62.3]	42.9% [31.1–55.3]
DCR, % [95% CI]	93.4% [84.1–98.2]	82.9% [72.0–90.8]
mDoR, mo <sup>[2]</sup>	8.3 [5.3–16.6]	8.3 [5.3–16.6]



# EGFR TKI refract. NSCLC w/ MET amplification



Phase III registration studies are being planned in combinations with TAGRISSO® (osimertinib)

	TATTON B Savo 600mg [1] + TAGRISSO®			TATTON D Savo 300mg + TAGRISSO®	SAVANN populati
	<b>B1</b> Prior 3 <sup>rd</sup> -gen EGFR-TKI	B2 No prior 3 <sup>rd</sup> – gen EGFR-TKI (T790M neg.)	<b>B3</b> No prior 3 <sup>rd</sup> -gen EGFR-TKI (T790M pos.)	<b>D</b> No prior 3 <sup>rd</sup> -gen EGFR-TKI (T790M neg.)	<ul> <li>2L/3L EGFRm+</li> <li>After 1L or 2L TAG</li> <li>MET amp. / over-</li> <li>No MET inhibitor</li> <li>No prior chemo of</li> </ul>
ORR*, % [95% CI]	<b>33%</b> [22-46]	<b>65%</b> [50–78]	<b>67%</b> [41–87]	<b>62%</b> [46–76]	PRIMARY END  • 300mg QD ORF
<b>DCR</b> *,% [95% CI]	<b>75%</b> [64–85]	<b>88%</b> [76–96]	<b>100%</b> [81–100]	<b>93%</b> [81–99]	
Median DoR, mo. [95% CI]	<b>9.5</b> [4.2–14.7]	<b>10.7</b> [6.1–14.8]	<b>11.0</b> [2.8-NR]	<b>9.7</b> [4.5–14.3]	Data will info
Median PFS, mo. [95% CI]	<b>5.5</b> [4.1–7.7]	<b>9.1</b> [5.5–12.8]	<b>11.1</b> [4.1–22.1]	<b>9.0</b> [5.6–12.7]	Plan to subm

#### NAH: Broadest TAGRISSO® refractory ion - FISH+ and/or IHC+ line agnostic

#### **NSCLC**

- GRISSO®
- -express.
- r therapy
- or I-O

#### Savo 300mg QD + TAGRISSO® Enrolled v

#### Savo 300mg BID<sup>[2]</sup> + TAGRISSO® Enrolling

Savo 600mg QD + TAGRISSO® Enrolling

#### DPOINT

#### SECONDARY ENDPOINTS

- 300mg OD
  - ORR by MET FISH+ / IHC+; PFS; DoR: OS: safety
- 300mg BID & 600mg QD
  - Efficacy (ORR; PFS; DoR; OS); safety / tolerability

orm Phase III design, to initiate late 2021

nit data for presentation in H1 2022

<sup>[1]</sup> Most pts enrolled to Part B1, B2, B3 on 600 mg savolitinib; final 21 patients enrolled in Part B were dosed with savolitinib by body weight following a protocol amendment, as follows: pts <55 kg (n=8) 300mg daily, pts >55 kg (n=13) 600mg daily. Best response data are for patients who had an opportunity to have two follow-up scans; \* Complete or partial response confirmed at ≥4 weeks. # Disease control rate = confirmed complete response + confirmed partial response + stable disease at ≥5 wks; CI, confidence interval; NR, not reached. Han JY, et al. Osimertinib + savolitinib in patients with EGFRm MET-amplified/overexpressed NSCLC: Phase Ib TATTON Parts B and D final analysis. WCLC January 2021 #FP14.03.

### **Savolitinib: Promising in MET-driven PRCC**



Global Phase III trial in planning in combination with IMFINZI® (durvalumab)

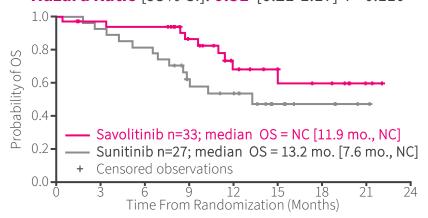


#### SAVOIR: Single agent anti-tumor activity in MET-driven PRCC

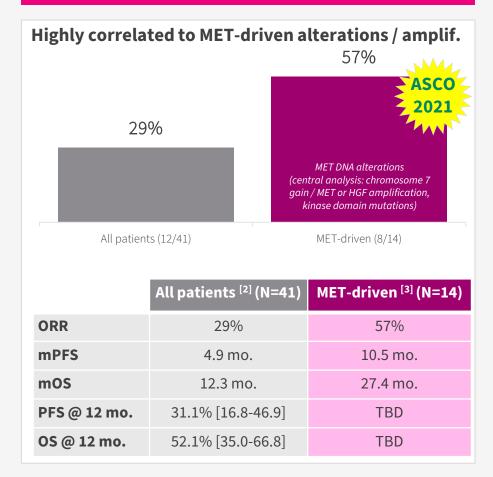
All 9 savo responders remained in response at data cut-off

SAVOIR [1]	Savolitinib (N=33)	Sunitinib (N=27)	
<b>ORR*</b> [95% CI]	27% [13.3-45.5]	7% [0.9-24.3]	
PFS [95% CI]	7.0 mo. [2.8–NC]	5.6 mo. [4.1–6.9]	
	Hazard Ratio: 0.71 [0.37-1.36]		

# **Strong signal of potential overall survival benefit Hazard Ratio** [95% CI]: **0.51** [0.21-1.17] *P=0.110*



#### CALYPSO: IMFINZI® (PD-L1i) combination activity<sup>[2][3]</sup>

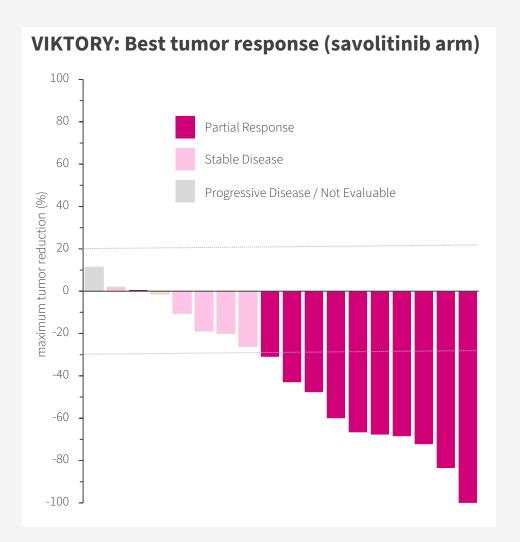


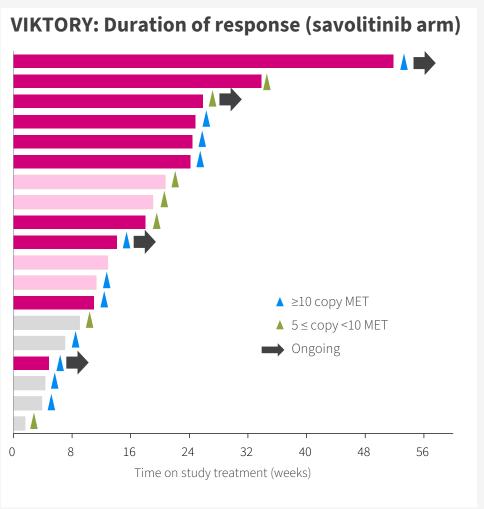
<sup>\*1</sup> of 2 sunitinib responders remained in response at data cut-off. NC = not calculated.
[1] Choueiri TK, et al. Efficacy of Savolitinib vs Sunitinib in Patients With MET-Driven Papillary Renal Cell Carcinoma: The SAVOIR Phase 3 Randomized Clinical Trial. JAMA Oncol. Published online May 29, 2020. doi:10.1001/jamaoncol.2020.2218; [2] ASCO-GU 2020 Suárez C et al. J Clin Oncol 38, 2020 (suppl 6; abstr 619); [3] ASCO 2021 Suárez C et al. J Clin Oncol 39, 2021 (suppl 15; abstr 4511).

# Savolitinib recap: MET ampl. in gastric cancer



#### Initiating Phase II trial in China





# **Savolitinib development summary**



#### **CHINA**

#### MET Exon14 alteration NSCLC

- NDA under review
- On track for mid-2021 approval

#### 2L EGFR TKI refractory NSCLC with MET amplification

- Savolitinib + TAGRISSO® Phase III registration study
- FPI expected late Q3 2021 **SACHI Study**

#### 1L EGFRm+ NSCLC with MET overexpression

- Savolitinib + TAGRISSO® Phase III registration study
- FPI expected late Q3 2021 SANOVO Study

#### Gastric cancer with MET amplification

- Single arm study with potential for registration
- FPI expected in mid-2021

#### **GLOBAL**

#### **MET-driven PRCC**

- Phase III registration study
- Savolitinib + IMFINZI® vs. sunitinib in MET-driven PRCC
- Expected study initiation Q3 2021
  - SAMETA Study

# 2L TAGRISSO® refractory NSCLC with MET amplification

- Savolitinib + TAGRISSO® Phase III registration study
- FPI expected late YE 2021



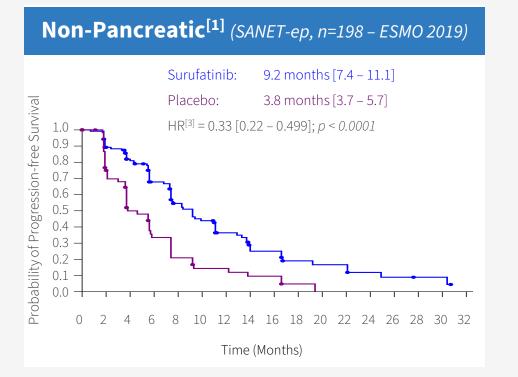
# **SURUFATINIB**

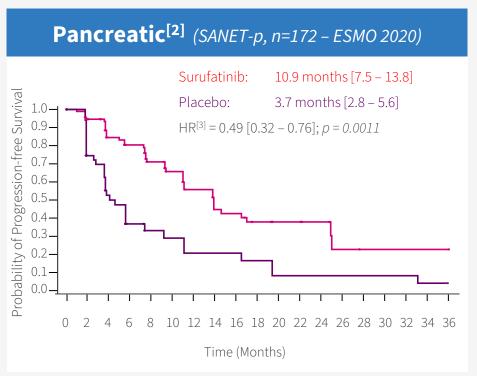
(SULANDA® in China)

# **Surufatinib recap: efficacy across NETs**



- >800 patients in clinical trials to date
- Proven single-agent efficacy: SANET-ep & SANET-p Phase IIIs met endpoints at interim
- China approved for non-pancreatic NET; NDA in review for pancreatic NET
- US NDA submitted





# **Surufatinib: NET registration update**



#### **CHINA**

#### Extra-pancreatic (non-pancreatic) NET

- NDA approved Dec 2020
- Launched Jan 2021
- Preparing for NRDL discussion

#### Pancreatic NET NDA under review

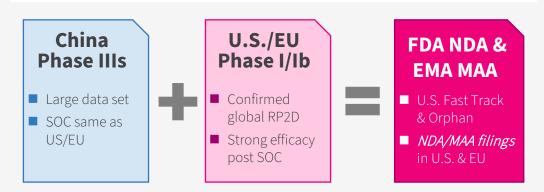
On track for potential H2 2021 approval

#### **GLOBAL**

#### US FDA NDA submitted April 2021

- Fast Track Designations for both pNET & non-pNET
- Orphan Drug designation granted for pNET
- FDA decision on acceptance of NDA at end of June

EMA MAA submission mid-2021 Japan registration path agreed with PMDA Additional data published ASCO 2021



# Surufatinib: US Phase I/Ib monotherapy update HUTCHMED



2021 ASCO ANNUAL MEETING

**ASCO** 2021

# Dose escalation completed

RP2D determined to be 300mg QD Similar PK & tox profile btw China & US patients



#### **Dose Expansion**

NETs data provides signal of efficacy

Advanced or metastatic pNET

Advanced or metastatic epNET

Advanced or metastatic BTC

Advanced or metastatic STS

Treatment until unacceptable tox, disease progression or withdrawal of consent

Primary: PFS rate @ 11 mths Secondary: ORR, DCR, TTR, DoR, PK, safety

	epNET	PNET
Median lines of therapy	2 (2–5)	4 (1-8)
All patients previously	received everolimus a	nd/or sunitinib
mPFS [95% CI], mo.	11.5 [6.5–11.5]	15.2 [5.2-NR]
ORR [95% CI]	6.3% [0.2–30.2]	18.8% [4.0–45.6]
DCR [95% CI]	93.8% [69.8–99.8]	87.5% [61.7–98.4]

#### Safety data highlights

Most common AEs of any grade:

Fatigue: 46.9%
Hypertension: 43.8%
Proteinuria: 37.5%
Diarrhea: 34.4%
Vomiting: 28.1%

Nausea:

Most common AEs ≥ grade 3:

Hypertension: 37.5%
Diarrhea: 9.4%
Proteinuria: 6.3%
Dysphagia: 6.3%
Anemia: 6.3%

AEs leading to discontinuation: 21.9%

25.0%

# **Surufatinib: US Phase I/Ib patient cases**



# 74 y.o. male with pancreatic NET metastatic to the liver

Previously progressed on multiple lines of therapy



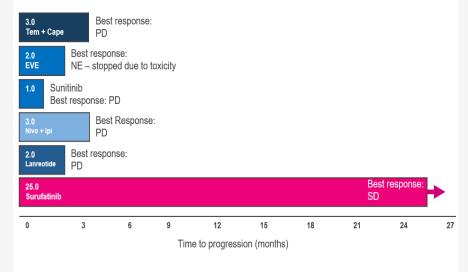
- Cytotoxic chemo: multiple dose reductions due to side effects
- Everolimus: severe side effects discontinued within a few weeks
- Surufatinib: ~15 months without dose reductions; overall improvement in QoL

#### "I like this treatment; this the best so far - I have no side effects"

 Patient clearly stated quality of life (QoL) important when considering future therapy options

# 57 y.o. male with pancreatic NET metastatic to the liver and mesentery

Previously progressed on multiple lines of therapy



#### In surufatinib trial since March 2019 (2+ years)

- Remains with stable disease
- Continues to have good tolerance

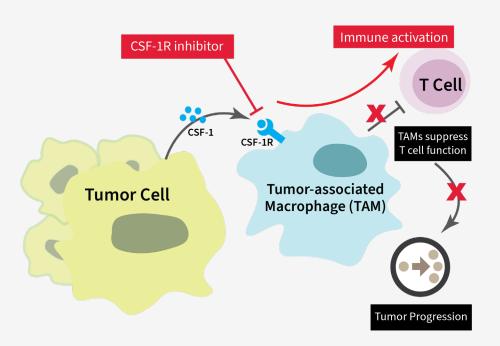
# Surufatinib recap: unique MOA differentiation



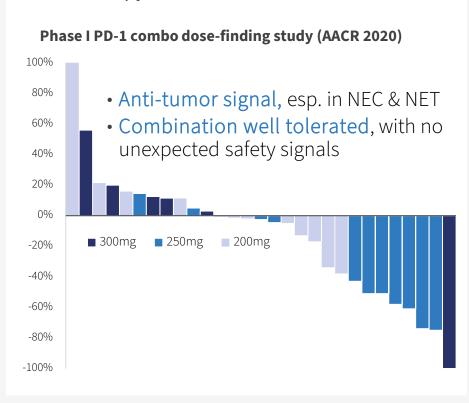
Potentially enhance immune-mediated anti-tumor effect in addition to anti-angiogenesis

Inhibits VEGFR1/2/3 & FGFR1 – blocking vascular cell growth and angiogenesis

Inhibits CSF-1R – limits production of TAMs which cloak the cancer cell from T-cell attack



# Synergistic effect with PD-1 inhibitors in NET/NEC, which had showed limited activity to date as a monotherapy or in combination with chemotherapy



# **Surufatinib: Promising PD-1 combos**



Planning first Phase III in China in ≥2L NEC with Junshi; additional registration studies under discussion



PD-1	Patient focus		Status/ plan
TUOYI	NENs ASCO	CN	
TUOYI	Biliary tract	CN	
TUOYI	Gastric ASCO 2021	CN	Phase II ongoing
TUOYI	Thyroid	CN	
TUOYI	Small cell lung	CN	Total N~250
TUOYI	Soft tissue sarcoma	CN	to select 1-3 for registration
TUOYI	Endometrial	CN	intent studies
TUOYI	Esophageal	CN	
TUOYI	NSCLC	CN	
TYVYT	Solid tumors	CN	Phase I dose escalation completed
Tisle- lizumab	Solid tumors	US EU	Phase I/Ib ongoing

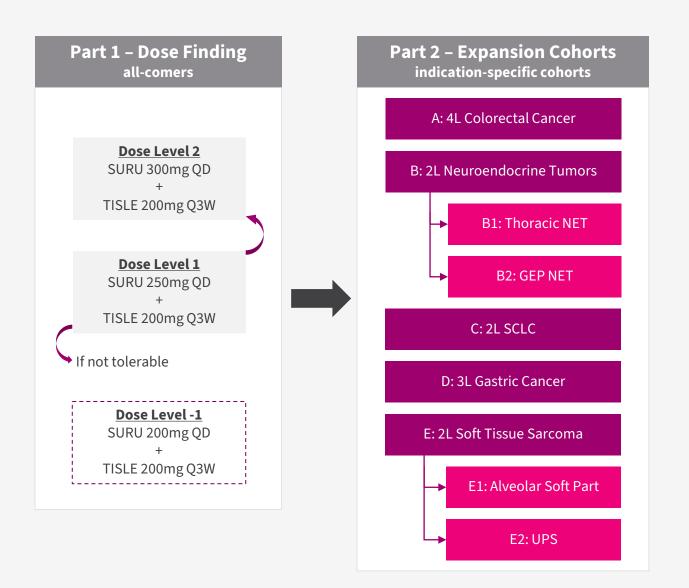
ABSTRACT (data cut off Dec 30, 2020)	Surufatinib + toripalimab [1]	Surufatinib + toripalimab [2]
Indication	Neuroendocrine Carcinoma (2L)	Gastric or GEJ (2L)
Efficacy evaluable	20	15
Duration of treatment, mo.	5	3
ORR	20.0% [5.7 – 43.7]	Confirmed: 13.3% [1.7 – 40.5] Unconfirmed: 33.3% [11.8 – 61.6]
DCR	70% [45.7 – 88.1]	73.3% (44.9 – 92.2]
mPFS, mo.	3.94 [1.3 - NR]	3.71 (1.41 – NR]
mOS, mo.	Not mature at DCO	Not mature at DCO

- Preparing to initiate Phase III in 2L or above NEC
- Registration design for GC under discussion
- Remaining cohorts continue to mature



## Surufatinib PD-1 combos global aspirations

Surufatinib + Tislelizumab (PD-1 mAb) first patient enrolled in March 2021



#### **Rationale**

- Global aspirations
- Global PD-1 partner
- May lead to accelerated opp given high unmet need

#### **Status**

- Part 1 enrolling rapidly
- Multiple US sites active
- EU site pending activation in Part 2



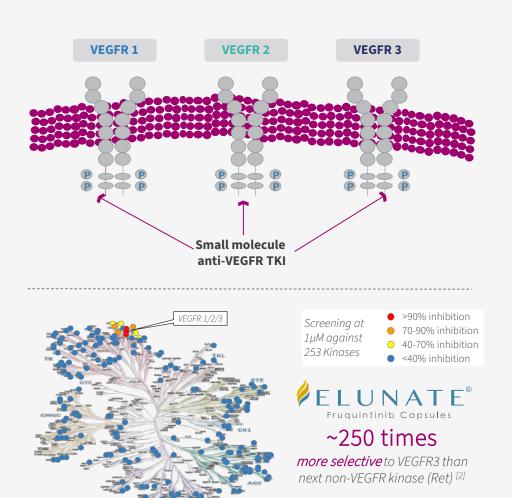
# **FRUQUINTINIB**

(ELUNATE® in China)





Efficacy with limit off-target toxicity



- Potent against VEGFR1,2,3, resulting in consistent clinical benefit for patients who failed bevacizumab
- Highly selective vs. other kinases with good safety profile with readily manageable AEs
- Combinable with chemo, targeted therapies and IO

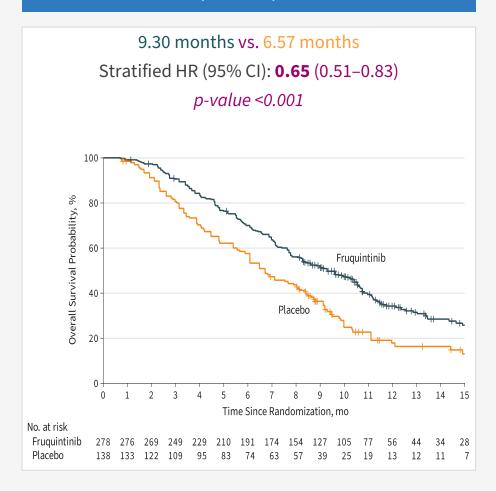
3 <sup>rd</sup> -Line Metastatic Colorectal Cancer	FRESCO	Phase III
Treatment arms	ELUNATE®	Placebo
≥G3 AE (Safety population)	61.1%	19.7%
VEGFR on-target related AEs ≥ G3:		
Hypertension	21.2%	2.2%
Hand-Foot Syndrome	10.8%	0.0%
Off-target (i.e. non-VEGFR) related AEs	≥ G3:	
Hypophosphatemia	0.0%	1.5%
Hypokalemia	0.7%	0.7%
Rash/desquamation	0.0%	0.0%
Lipase increase	0.0%	0.0%
Hepatic function (Liver function) AEs ≥	G3:	
ALT increased	0.7%	1.5%
AST increased	0.4%	0.7%
Blood bilirubin increased	1.4%	1.5%



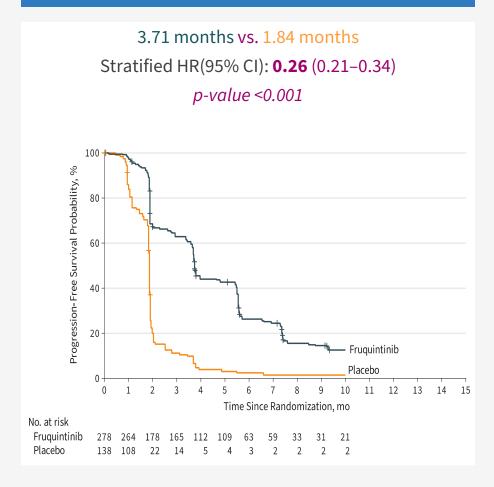


Approved and launched in China for late-stage CRC; anti-tumor effect in multiple settings

#### FRESCO PHASE III (≥3L CRC): OVERALL SURVIVAL



#### FRESCO PHASE III: PROGRESSION-FREE SURVIVAL

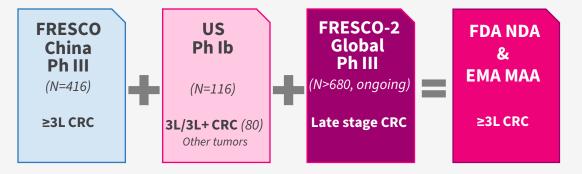


## FRESCO-2 to support 3L+ mCRC US/EU/JP NDA



Regulatory alignment on fruquintinib across all major markets

#### Basis for US, EU, Japan filings



- FRESCO + US CRC Ph Ib data + FRESCO-2, could support US NDA & EU MAA in third-line and above metastatic CRC
- Enrolling >150 sites across 14 countries
- Target fully enrolled end of 2021
- US Fast Track designation → potential rolling submission
- Extensive list of supportive studies

Target	t 1 <sup>st</sup> gen TKI 2nd gen TKI		en TKI	Next gen TKI	
	Suni- tinib	Rego- rafenib	Lenva- tinib	Axitinib	Fruq- uintinib
VEGFR1 (nM)	2	13	4.7	3	33
VEGFR2 (nM)	9	4.2	4	7	25
VEGFR3 (nM)	19	46	2.3	1	0.5
Phos-KDR (nM)	10	3	0.25	0.2	0.6
Other kinases (IC50 < 100nM)	PDGFRa PDGFRβ c-Kit Flt3 Ret Fms	BRAF cRAF RET PDGFRB FGFR1-2 DDR2 SAPK2 Lyn Tir2 AbI TrKA EphA2 KIT	PDGFRa PDGFRB FGFR1-4 c-Kit Ret	PDGFRa PDGFRB FGFR1 c-Kit CSF-1R	none





Fruquintinib/sintilimab (TYVYT®) combo basket China Phase II and status update

Patient focus	Status and plans
CRC	Strategy for CRC being discussed  ASCO 2021 2021
Hepatocellular carcinoma 2L	<ul> <li>Stage I fully enrolled with promising emerging results</li> <li>Registration strategy under discussion with PI</li> </ul>
Endometrial cancer 2L	<ul> <li>Stage I fully enrolled with promising results</li> <li>Registration study proposed and awaiting CDE feedback</li> </ul>
RCC 2L	<ul> <li>Stage I fully enrolled with encouraging results</li> <li>Registration strategy under discussion with PI</li> </ul>
GC 2L	Newly added, enrolling
Cervical cancer 2L	Newly added, enrolling
NSCLC 1L	Newly added, enrolling

# **Fruquintinib: PD-1 inhibitor combinations**



Durable benefit seen in advanced colorectal cancer



		ASCO	ASCO	
ABSTRACT	Fruq mono Ph. III (FRESCO)	Fruq + sintilimab <sup>[1]</sup>	Fruq + geptanolimab <sup>[2]</sup>	Lenvatinib + pembrolizumab <sup>[3]</sup>
Prior lines of tx	≥2	≥2	67% ≥2	94% ≥2
RP2D VEGFRi dose (n)	5mg QD 3w/1w (278)	5mg QD 2w/1w (22)	4mg QD 3w/1w (15) <sup>[4]</sup>	20mg QD <i>(30)</i>
Data cut-off	Jan 17, 2017	Jan 5, 2021	Dec 15, 2020	Apr 10, 2020
ORR	4.7% [2.1-7.2]	27.3% [10.7-50.2]	26.7%	21.9% [9.3-40.0]
DCR	62.2%	TBD	80%	46.9% [29.1-65.3]
mPFS, months	3.7 [3.7-4.6]	6.8 [5.6-NE]	7.3 [1.9-NE]	2.3 [2.0-5.2]
OS, months	9.3 [8.2–10.5]	TBD	Not mature at DCO	NA

## Fruquintinib: tislelizumab combinations



#### **Safety Lead-In**

n = 6-12

FRUQ 5mg QD 3wk/1wk

TISLE 300mg Q4W



If not tolerable

FRUQ 4mg QD 3wk/1wk

TISLE 300mg Q4W

#### Phase Ib/II Expansion

n = 20-30 for each cohort

A: 2L+ TNBC (IO-Treated)

B: 2L+ TNBC (IO-Naive)

Treatment until unacceptable toxicity or disease progression or withdrawal of consent

#### **Status**

Led by HUTCHMED

Part 1 in progress; potential patients identified

#### Safety Lead-In

n = 6-12

FRUQ 5mg QD 3wk/1wk

TISLE 300mg Q4W



If not tolerable

FRUQ 4mg QD 3wk/1wk

TISLE 300mg Q4W

#### Phase Ib/II Expansion

n = ~30 for each cohort

A:: 2L GC

B: 3L MSS CRC after chemo, and ≥1 anti-VEGF or EGFR mAb treatment

C: 1L PD-L1+ NSCLC

Treatment until unacceptable toxicity or disease progression or withdrawal of consent

#### **Status**

Led by BeiGene

Part 1 in progress; potential patients identified

# Fruquintinib: development summary



#### Current development status and next steps

#### **CHINA**

# FRUTIGA: Phase III in 2L gastric cancer ongoing

- Expect fully enrolled around YE 2021
- Top-line data expected H2 2022

#### PD-1

- CRC data promising, registration strategy being formulated
- EMC registration study under discussion with CDE, expect to initiate H2 2021
- Registration plans for HCC and RCC currently under discussion with PIs
- 3 new cohorts added and are enrolling

#### **GLOBAL**

#### **Colorectal cancer**

- FRESCO-2 Phase III initiated in U.S., EU & Japan
- U.S. Phase Ib/II completed
- Basis for US, EU Japan NDA clear
  - Support for US NDA in third-line and above mCRC

#### PD-1 combinations

 Ongoing proof-of-concept studies across multiple cohorts, led by both HUTCHMED and BeiGene

HUTCHMED

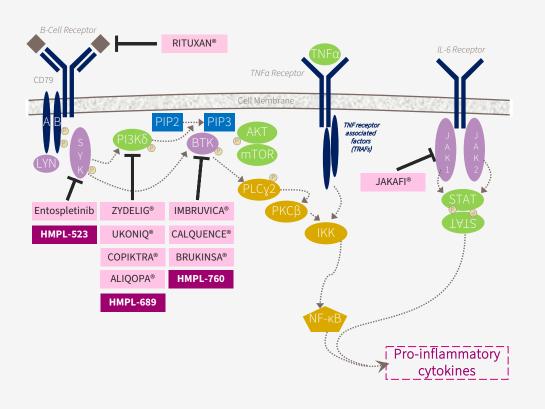
**HMPL-689** 

# HMPL-689 Recap: Highly selective PI3Kδ inhibitor



#### First in our next wave of innovation

#### B-cell signaling is critical in hematological cancer



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

- Improved isoform selectivity (sparing PI3Kγ)
- Improved potency at whole blood level (>5x more potent than Zydelig) to cut compound related toxicity
- Improved PK particularly efflux and drug/drug interaction due to CYP inhibition / induction, critical for combos

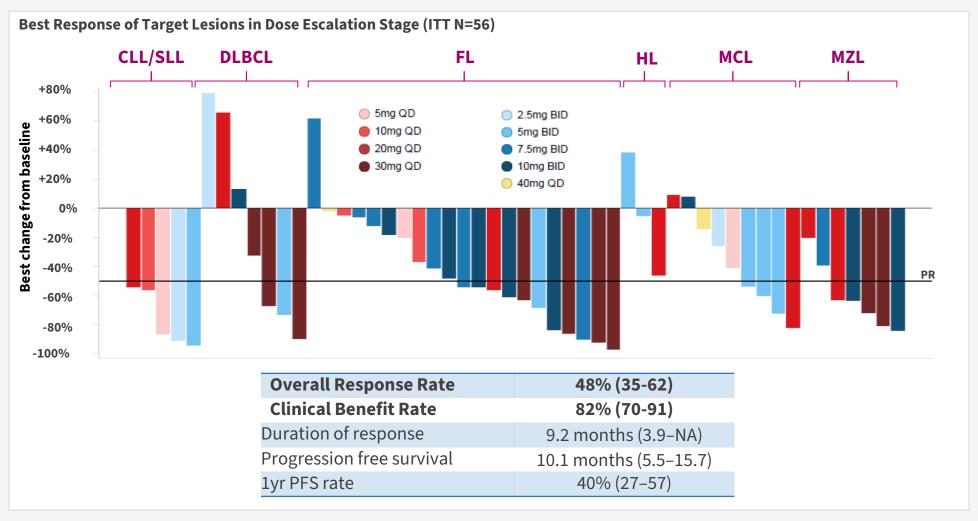
Enzyme IC <sub>50</sub> (nM)	HMPL-689	ZYDELIG®	COPIKTRA®	ALIQOPA®
ΡΙ3Κδ	0.8	2	1	0.7
PI3Kγ (fold vs. PI3Kδ)	114 <b>(142x)</b>	104 <b>(52x)</b>	2 <b>(2x)</b>	6.4 <b>(9x)</b>
PI3Kα (fold vs. PI3Kδ)	>1,000 <b>(&gt;1,250x)</b>	866 <b>(433x)</b>	143 <b>(143</b> x)	0.5 <b>(1x)</b>
PI3Kβ (fold vs. PI3Kδ)	87 <b>(109x)</b>	293 <b>(147x)</b>	8 <b>(8x)</b>	3.7 <b>(5x)</b>
PI3Kδ human <u>whole</u> <u>blood</u> CD63+	3	14	15	n/a

### ١١

HUTCHM

### HMPL-689 Recap: Dose escalation data (ASH)

Promising clinical activity in multiple tumor types



# **HMPL-689 Recap: Dose escalation data (ASH)**



#### Well tolerated with a favorable safety profile

	HMPL-689 <sup>[1]</sup>	<b>Zydelig®</b> (idelalisib) <sup>[2]</sup>	Aliqopa® (copanlisib) <sup>[2]</sup>	Copiktra® (duvelisib) <sup>[2]</sup>	<b>Ukoniq®</b> (umbralisib) <sup>[2]</sup>	Parsaclisib (Dose escalation) <sup>[3]</sup>	Parsaclisib (CITADEL-204/ MZL) <sup>[4]</sup>	<b>Zandelisib</b> (intermittent dosing) <sup>[5]</sup>	<b>Zandelisib</b> (Dose escalation) <sup>[6]</sup>
n	56	146	168	442	221	72	100	21	30
Neutropenia	43% / 11%	53% / <b>25%</b> *	32% / <b>25%</b>	34% / <b>30%</b>	33% / 16%*	44% / <b>20%</b> *	13% / 9%	na / 14%	45% / 13%*
Anemia	16% / 0%	28% / 2%*	na	20% / 11%	27% / 3%*	31% / 8%*	14% / 5%	na / 0%	13% / 0%*
Thrombocytopenia	11% / 0%	26% / 6%*	22% / 8%	17% / 10%	26 % / 4%*	35% / 10%*	na	na / 0%	22% / 0%*
Diarrhea or colitis	<5% / <5%	47% / 14%	36% / 5%	50% / 23%	58% / 10%	36% / 9%	44% / 11%	na / 4%	45% / 19%
Rash	11% / 5%	21% / 3%	15% / 2%	31% / 9%	18% / 3%	31% / 6%	17% / 2%	na / 2%	42% / 13%
ALT increased	27% / 2%	50% / <b>19%</b>	na	40% / <mark>8%</mark>	33% / 8%	28% / 1%	26% / 4%	na / 0%	39% / <b>6%</b>
AST increased	21% / 2%	41% / <b>12%</b>	na	37% / <b>6%</b>	32% / <b>7%</b>	29% / 1%	19% / 2%	na / 0%	25% / <b>6%</b>
Pyrexia	14% / 0%	28% / 2%	na	26% / 2%	na	18% / 1%	13% / 1%	na	na
Pneumonia	25% / 16%	25% / 16%	21% / 14%**	21%/15%	PJP prophylaxis recommended	na	7% with PJP prophylaxis	PJP prophylaxis	na
Hypertension	7% / 5%	na	35% / 27%	na	na	7% / 0%	na	na	na
Hyperglycemia	11% / 2%	na	54% / 39%	na	na	10% / 1%	na	na	na

# HMPL-689: Clinical profile being confirmed



China-based Phase Ib dose expansion cohorts enrolling to inform registration studies

#### Dose expansion

30~40 pts for each cohort

Λ.	$\sim$		N /	_	
$\Delta \cdot$		-	W		
$\neg$	_	_+	IV.	_	ш

B: 3L+ CLL/SLL

C: 3L+ FL (stage 1,2,3a)

D: MCL, DLBCL, FL(3b)

E: T-cell lymphoma

Treatment until unacceptable tox, disease progression or withdrawal of consent

- Expansion completed registration intent Phase II initiated
- Expansion continuing to enroll
- Expansion completed registration intent Phase II initiated
- Expansion continuing to enroll
- Expansion continuing to enroll

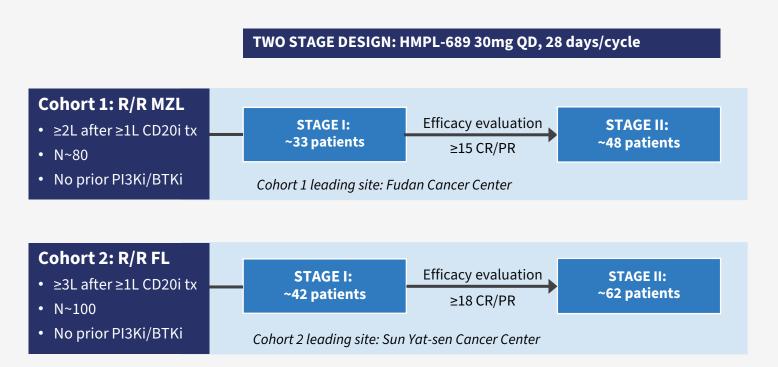
**Primary endpoint: ORR** 

**Secondary endpoints:** PFS, TTR, DoR, PK

## HUTCHMED

## **HMPL-689: China registration intent Phase II**

First patient enrolled April 2021



- Tumor evaluations (TE)
- every 8 weeks in the first 24 weeks
- every 12 weeks thereafter

- Primary efficacy endpoint IRC-assessed ORR
- Secondary efficacy endpoints
  IRC-assessed CRR, PFS, CBR, TTR, and DoR; Invassessed ORR, CRR, PFS, CBR, TTR, DoR, and OS
- Full enrollment targets
  - FL by H1 2022
  - MZL by H2 2022

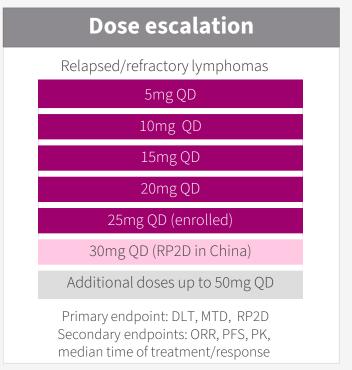
## HMPL-689: US/EU Lymphoma Phase Ib

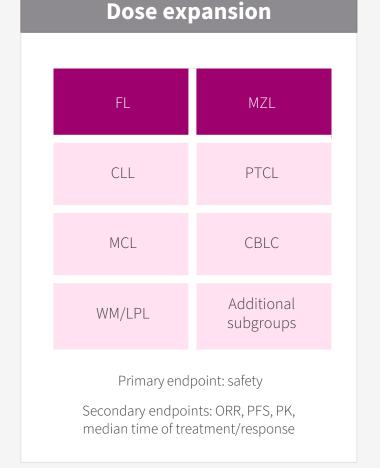


Intl to build on China data, and engage FDA in H2 2021

#### **Next step: Complete dose escalation in Q3 2021**

- Dose expansion to focus on FL and MZL
- End of Phase I meeting with US FDA H2 2021 to confirm registration path















**DENMARK** 





**FINLAND** 



**FRANCE** 

23 target sites in 7 countries

## HMPL-689 US Phase I - Dose escalation



#### Follicular lymphoma patient with sustained partial response

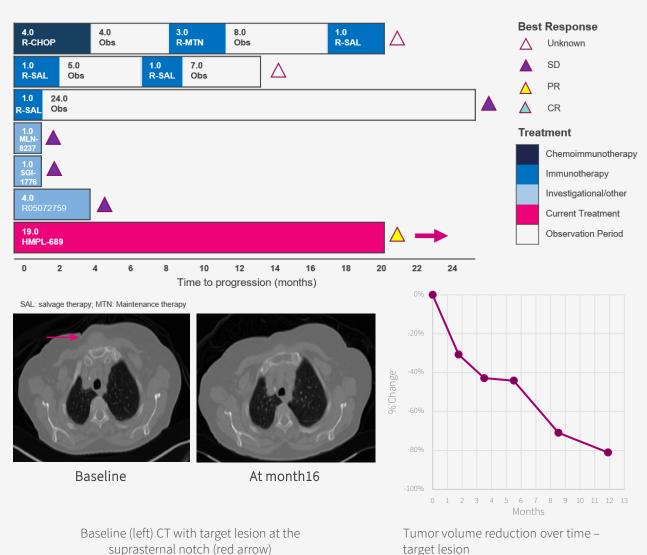
85 yo female, ECOG PS 1, with Stage II FL, initial diagnosis 2003

## Failed multiple lines of salvage therapy

- Several investigational therapies without tumor response:
  - SGI-1776 PIM kinase inhibitor
  - MLN-8237 Aurora A kinase inhibitor
  - R05072759 / obinutuzumab anti-CD20 monoclonal antibody

HMPL-689 started at 10mg, escalated to 20mg

- PR at 10 mg dose level
- Continues on Cycle 19; no reported AEs
- Duration of response 9 months and ongoing



## **HMPL-689 US Phase I - Dose escalation**

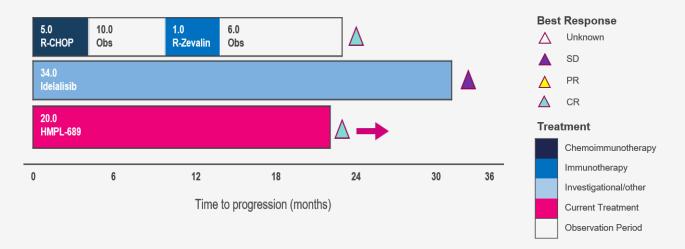


Follicular lymphoma patient with sustained complete response

59 yo female, ECOG PS 1, with Stage III FL, initial diagnosis 2013

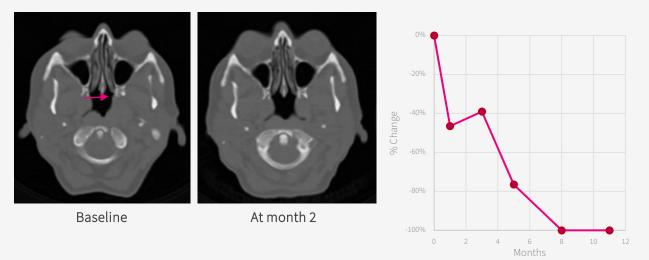
## Failed 3 lines of prior treatment including a PI3K regimen

- R-CHOP, R-Zevalin, *idelalisib*
- Best response of SD on idelalisib



HMPL-689 started at 10mg, escalated to 20 mg

- CR at 10 mg dose level in 1<sup>st</sup> follow-up scan
- Patient continues on Cycle
   20 with no reported AEs
- Duration of response 17 months and ongoing



Baseline CT with nasopharyngeal target lesion (red arrow)

Tumor volume reduction over time – target lesion

## HMPL-689: development summary and registration pathway



#### **CHINA**

#### **Monotherapy**

- FL / MZL registration study ongoing
  - NDA submission potentially late 2022 / early 2023
- Additional indications will be planned

#### **Combinations**

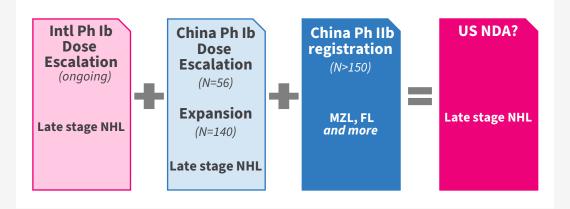
- Additional indications
- Earlier lines
- IND to be submitted H2 2021
  - Standard of care
  - PD-1 inhibitor
  - VEGFR inhibitor
  - Other targeted therapies (to be disclosed later)

#### **GLOBAL**

#### U.S. & EU Ph.I multiple dose cohorts complete

#### **Next steps**

- Evaluate efficacy signals using cumulative HMPL-689 data from both International and China studies, and RP2D selection
- Engage FDA in H2 2021 through End of Phase 1 meeting to confirm registrational path



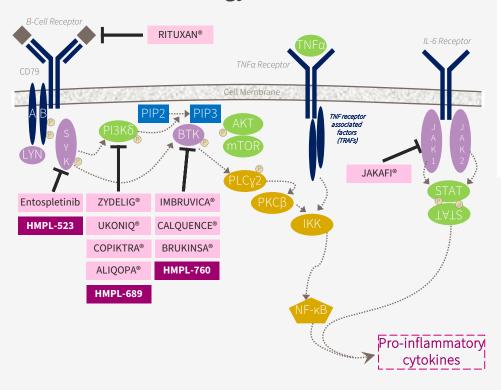
HUTCHMED

HMPL-523

## HMPL-523: Non-Hodgkin's Lymphoma (NHL)



## The B-cell signaling is critical in hematological cancers and immunology



#### **NHL DEVELOPMENT UPDATE**

- China / Australia Phase I complete
- Promising data in CLL/SLL post-BTK
- Conducting international Phase I study
- Initiate single global study including China in post-BTK



## **HMPL-523 Global NHL Development Overview**

International to build on China data, and explore additional subgroups

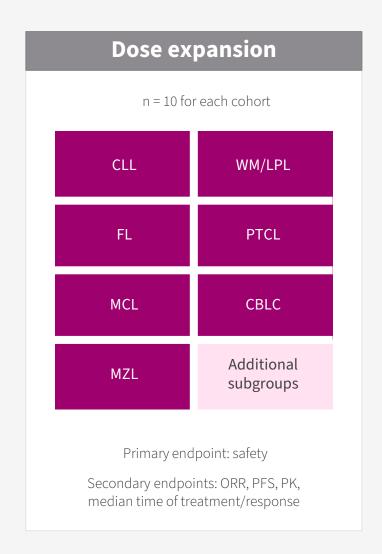
#### **Next step: Complete dose escalation in Q3 2021**

### Lymphoma study:

- Establish RP2D for international development
- International expansion cohorts to start
- Explore options to enrich for post-BTKi patients in the expansion phase

	Dose escalation	
	Relapsed/refractory lymphomas	
	100mg	
	200mg	
	400mg	
	600mg	
	700mg	
IJ	800mg	
	Primary endpoint: DLT, MTD, RP2D	
	Secondary endpoints: ORR, PFS, PK, median time of treatment/response	





## HMPL-523: Immune thrombocytopenia (ITP)



## Current treatments target Treg, magakaryocyte and B cells

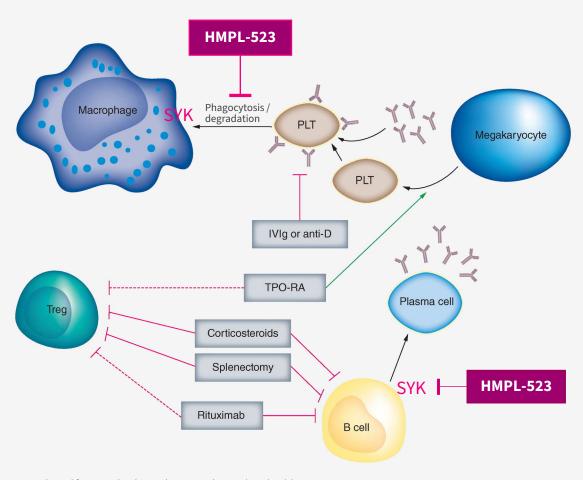
- Moderate efficacy
- All patients become refractory

#### SYK is a validated target for ITP

- Fostamatinib approved in the US
- Moderate efficacy, dose limited by tox
- Syk targets both B cells & macrophages

#### **HMPL-523**

- China Phase II complete –encouraging efficacy and good safety
- Phase III planned to initiate H2 2021



Adapted from Newland A, et al. Immunotherapy (2018) 10(1), 9–25

## **HMPL-523: development summary**



#### NHL

#### China / Australia Phase I complete

Promising data in CLL/SLL post-BTKi

#### **International Phase I**

- Moving into expansion cohorts Q3 2021
- Explore post-BTK CLL/SLL based on signal in China/Australia
- Could inform registration strategy
- A single study to support global filing, including China
- Plan to explore additional subgroups

#### **IMMUNOLOGY**

#### Immune thrombocytopenia (ITP)

- Phase I/Ib dose escalation and expansion complete
- Emerging data supports further development
- EOP2 meeting with China CDE being arranged
- Possible Phase III initiation H2 2021

#### Autoimmune hemolytic anemia (AIHA)

Initiating Phase II in China H2 2021



## **EARLY PROGRAMS**

Clinical: HMPL-306, HMPL-453 & HMPL-295

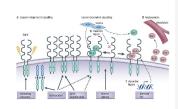
Preclinical: HMPL-760, HMPL-653, HMPL-A83

## Early programs summary



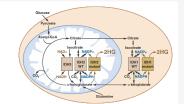
HMPL-453 (FGFR1/2/3)

- Phase II in iHCC with FGFR2 fusion enrolling
- Early signs of clinical activity
- Combinations study IND planned mid-2021:
   1L chemo & IO combos



HMPL-306 (IDH1/2)

- Potent IDH1/2 inhibitor with brain penetration
- Designed to overcome resistance due to isoform conversion in MDS/AML, and explore GBM



- Dose escalation in China ongoing in IDHm+ AML, targeting completion by YE 2021
- International dose escalation started Q2 2021 in both AML & solid tumors

HMPL-295 (ERK)

- First candidate in MAPK pathway, more to come from HUTCHMED
- Dose escalation initiated, targeting FPI in mid-2021



## Three new INDs planned for 2021



HMPL-760 (3<sup>rd</sup> gen BTK)

- Reversible, non-covalent, potent against both wild type & C481S mutant enzymes
- Improved potency in *in vivo* models vs. ibrutinib and ARQ-531
- Potential for combinations with HMPL-689 (PI3Kδ), HMPL-A83 (CD47)
- IND submission Q2/Q3 2021 in both China and US

HMPL-653 (CSF-1R)

- Potent and selective CSF-1R inhibitor
- Targeting CSF-1R driven tumors (TGCT, Histiocytic, AML) and possibly in adjuvant setting in solid tumors
- IND submission Q3 2021 in China

HMPL-A83 (CD47)

- CD47 mAb with unique epitope and high affinity, highly efficacious in animal tumor models
- Much reduced effect on RBC
- Potential for combinations with HMPL-689 (PI3Kδ), HMPL-760 (BTK)
- IND submission YE 2021 in China and US

## 2021: another busy year for HUTCHMED



10 new registration studies

Savolitinib: 5

**Surufatinib: 1** 

Fruquintinib: 1

**HMPL-689: 2** 

**HMPL-523: 1** 

 2L EGFR TKI refractory NSCLC, China; 2L EGFR TKI refractory NSCLC, global; 1L EGFRm+ with MET overexpression, China; MET driven PRCC, global; MET amplified GC

• 2L NEC, in combination with toripalimab

• 2L EMC, in combination with sintilimab

• 2L MZL; 3L FL

ITP

3 new INDs **HMPL-760** 

**HMPL-653** 

HMPL-A83

• Third generation BTK inhibitor: US, China

• CSF-1R inhibitor: China

CD47 monoclonal antibody: US, China



## **DISCOVERY STRATEGY**

Including upcoming 2021 INDs (HMPL-760, HMPL-653, HMPL-A83)

## What is next from discovery?



Differentiated assets against multiple targets

### **Priming & activations**

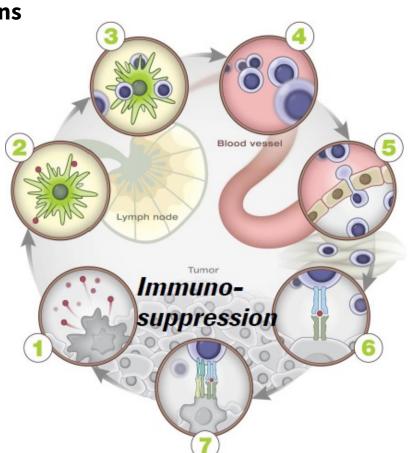
### Multiple mAb Programs

HMPL-A83 (CD47)

#### **Antigen release**

- MET (savolitinib)
- EGFR (epitinib)
- Syk (HMPL-523)
- PI3Kδ (HMPL-689)
- FGFR (HMPL-453)
- IDH 1/2 (HMPL-306)
- ERK 1/2 (HMPL-295)
- BTK (HMPL-760)

Multiple small molecule programs



### **Anti-angiogenesis**

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

#### **Negative regulators**

- Treg (HMPL-689)
- CSF-1R (surufatinib, HMPL-653)

Multiple small molecule & mAb programs

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

## **Discovery Project Overview**



01

02

03

### **Small molecules**

Six ongoing projects

Apoptosis

Cell signaling

Epigenetics

Protein translation

### Large molecules

Multiple mAb and bsAb projects ongoing

CD47-based antibody platform

### **New technology**

Initiating

PROTAC Antibody-Drug Conjugate

## HUTCHMED

## **Discovery Projects**

	Potential Indications	CAN Nomination	IND-Enabling (12~15 months)	Clinical Trials: Dose finding
HMPL-760 (BTK)	Hematological malignancies			
HMPL-653 (CSF1R)	TGCT, solid tumors		-	1~8 months to IND
HMPL-A83 (CD47 MAb)	Hematological malignancies			
Project (apoptosis)	Multiple myeloma, NHLs			
Project (oncoprotein)	Solid tumors			
Bispecific MAb	Hematologic malignancies		3~12 months to	
Bispecific MAb	Solid tumors		candidate nomination	
Project (epigenetics)	NHLs, Solid tumors			
Project (oncoprotein)	Solid tumors			
Project (MAPK pathway)	Solid tumors			
Project (mAb)	Hematologic malignancies			
Project (Bs Ab)	Hematologic malignancies			



# MARKET POTENTIAL & INTRODUCTION TO COMMERCIAL

Christian Hogg, CEO

## Savolitinib: key patients with MET alterations



Potential first-in-class selective METi in China – global studies planned in NSCLC & PRCC

	Est. Annual Incidence ('000)				Median	
	China	U.S.	EU5	Japan	Total	<b>DOT</b> <sup>[17]</sup>
CRC [1, 2]  MET+ EGFR ref.	4	4	4	1	13	TBD
Esophageal [3, 4, 5]  MET Gene Ampl.	16	1	1	1	20	TBD
GC <sup>[3, 4, 6]</sup> MET Gene Ampl.	19	1	2	6	28	8.0 mo. VIKTORY Ph.II
PRCC [3, 4, 7, 8, 9]  MET positive	5	5	5	2	16	10.5 mo. CALYPSO Ph.II
NSCLC EGFRm+ MET+	TBD	TBD	TBD	TBD	TBD	TBD
<b>NSCLC</b> [3, 4, 10, 11, 12, 13]  MET+ EGFR TKI ref. (3 <sup>rd</sup> gen.)	21 <sup>[5]</sup>	7	4	7	40	<b>5.4 mo.</b> TATTON Ph.II
<b>NSCLC</b> [3. 4, 10, 11, 12, 14]  MET+ EGFR TKI refractory (1 <sup>st</sup> /2 <sup>nd</sup> gen.)	12	3	2	3	20	9.0 mo.
NSCLC <sup>[3, 4, 15]</sup> MET Gene Ampl.	26	7	7	4	44	TBD
NSCLC [3, 4, 16]  MET Exon 14d	13	6	6	4	29	9.7 mo. Registr. Ph.II
	116	34	32	28	210	
	istration Stu lanning for 2				& only tralternative	

All figures are estimates for preliminary illustrative purposes only.

<sup>[1]</sup> IQVIA; Merck KGaA financial report; Eli Lilly financial report; Company estimates; [2] Kanwal Raghav, et al. Oncotarget 2016; [3] GLOBOCAN; [4] SEER; [5] Denis L. Fontes Jardim, et al. Oncotarget 2014; Yanqiu Wang, et al. BMC Cancer 2019; Jochen K. Lennerz, et al.; [6] Haidar El Darsa, et al. Journal of Experimental Pharmacology 2020; [7] Ricketts, C. J. et al. Cell Rep. 2018; [8] Pignot, G. et al. Urology 2007; [9] Cancer Genome Atlas Research Network et al. NEJM 2016; [10] Zhang YL, et al. Oncotarget. 2016; [11] IQVIA; [12] Frost & Sullivan, Company estimates; [13] Estimates 50% EGFR+ patients in U.S., EU5 and Japan are treated with 1st/2nd generation EGFR; [15] Ravi Salgia, Molecular Cancer Therapeutics, 2017; [16] Frampton GM, Ali SM, Rosenzweig M, et al. Cancer Discov. 2015; Company estimates; [17] DOT = duration of treatment in latest study.

## Fruquintinib: select patients may benefit from a best-in-class selective VEGFRi



Monotherapy in 3<sup>rd</sup> line CRC; expand through chemo/PD-1 combo in earlier line settings



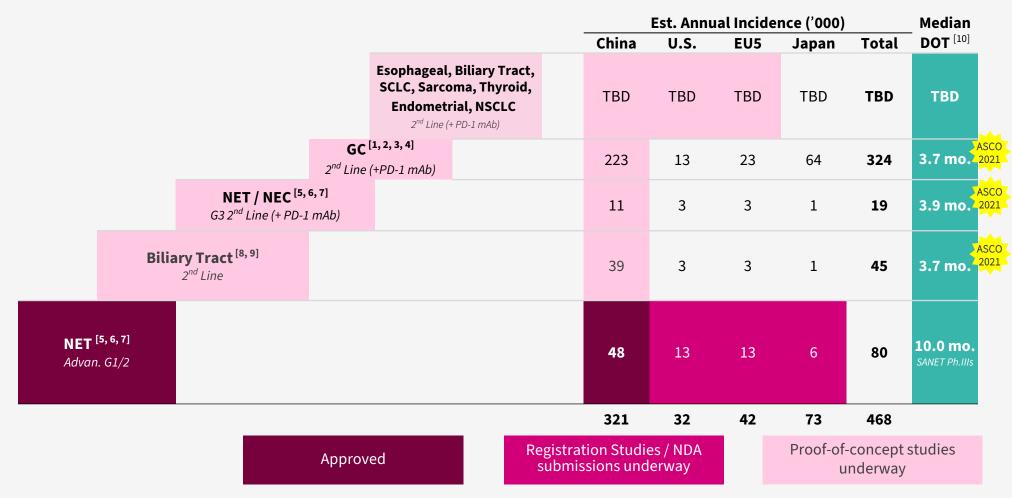
All figures are estimates for preliminary illustrative purposes only.

<sup>[1]</sup> Globocan; [2] SEER; [3] Markowitz, S. D., et al. NEJM 2009; [4] 3L estimated to be 50% of 1L and 2L estimated to be 30% of all CRC patients; [5] de Mello RA, et al. World J Gastroenterol 2013; [6] 2L estimated to be 70% of 1L and 1L estimated to be 70% of all gastric cancer patients; [7] DOT = duration of treatment in latest study.

## Surufatinib: select patients may benefit from VEGFRi/CSF-1Ri synergistic activity



Monotherapy in adv. Grade 1/2 NET; expand through PD-1 combos in earlier line settings



All figures are estimates for preliminary illustrative purposes only.

[10] DOT = duration of treatment in latest study.

<sup>[1]</sup> Globocan; [2] SEER; [3] de Mello RA, et al. World J Gastroenterol 2013; [4] 2L estimated to be 70% of 1L and 1L estimated to be 70% of all gastric cancer patients;

<sup>[5]</sup> China and U.S. NET patient numbers from Frost & Sullivan; [6] EU5 and Japan NET patient numbers estimated based on relative population versus the U.S.; [7] Daniel M Halperin, et al. The Lancet 2017;

<sup>[8]</sup> Supriya K. Saha, et a.l. The Oncologist 2016; Company estimates; [9] Estimates 40% BTC patients in 2L;

## **HMPL-689: iNHL patients may benefit**



**Emerging hematological malignancies asset** – global and China development moving now in parallel in multiple indolent NHL indications – combinations to follow



All figures are estimates for preliminary illustrative purposes only.

<sup>[1]</sup> Globocan; [2] SEER; [3] NCCN; [4] Estimates 80% of DLBCL patients receiving 1 lines of therapy. 50% of treated DLBCL patients are considered to be adequately managed with 1L therapy; [5] Estimates 70% of FL/MZL/MCL patients receiving 2 lines of therapy; [6] DOT = duration of treatment in latest study.

## HMPL-523: BTK-refractory NHL & immunology



**Emerging immunology and hematological malignancies asset** – first approval opportunity in ITP – global opportunity in BTKi refractory indolent NHL



All figures are estimates for preliminary illustrative purposes only.



## CHINA ONCOLOGY COMMERCIAL OPERATIONS

Hong Chen, Chief Commercial Officer – China

## Recap: 3 novel drugs launched / in review



2021 Oncology consolidated revenues guidance \$110-\$130 million (vs. 2020 \$30.2m actual)



## Fruquintinib China commercial responsibility assumed Oct 2020

Receiving 70-80% of in-market sales as revenues in China [1]

#### Surufatinib launched in China Jan 2021

**HUTCHMED** owns all China rights

## Savolitinib potential approval as early as Q2 2021

First sale milestone in China \$25 million

Eligible for 30% royalty on China sales [2]







## Revenues 2022 onwards

#### **Global registration study ongoing**

Potential NDA & MAA submissions in U.S., EU & Japan in 2022/2023

HUTCHMED owns all ex-China rights

#### US & EU filings to complete in 2021

Preparing for potential launch in 2022

HUTCHMED owns all ex-China rights

#### **AZ ex-China development**

Phase III development in RCC & NSCLC targeted to start in 2021

Eligible for 9-18% royalty ex-China

## **China Commercial operations infrastructure**



HUTCHMED leverages strong scale and capabilities from two organizations

#### Shanghai Hutchison Pharmaceuticals

Nationwide distribution & promotion

- √ 2,500+ sales reps
- √ 18,700+ hospitals
- √ 87,000+ physicians



## HUTCHMED

Oncology focus, deep disease expertise

- √ 480+ (and growing) sales reps
- ✓ 2,500+ hospitals
- √ 20,000+ oncology physicians



#### Hutchison Sinopharm Pharmaceuticals

Third-party distribution & logistics

- ✓ Nationwide support from Sinopharm in distribution/logistics
- ✓ Deep Shanghai coverage

### Strong capabilities and track record

#### **Market Access**

Multiple products on NRDL incl. ELUNATE®

#### **Product Registration**

ELUNATE®, SULANDA® & Savolitinib obtained China priority review status (from filing to launch)

#### Medical Affairs (MA)

National KOL networks & capabilities to conduct pre- & post-registration studies (IITs, Phase IV studies, etc.)

## HUTCHMED

## 480+ person oncology commercial team

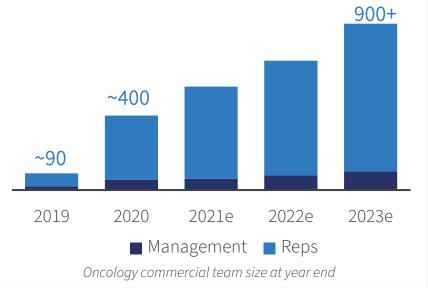
#### Expanding rapidly to support ELUNATE® and SULANDA® launches

## Broad drug marketing and distribution capabilities with long-standing operational track record

Gov't Medical Compli-**Affairs** Pharmaco-Marketing **Affairs Pricing &** vigilance ance **Policy Sales Management** & Administration Commercial **Pharmacy** Channel **Detailing Promotion and Management & Patient Education** Sales

## 2,500+ oncology hospitals and 20,000+ oncology physicians covered Fully in-place since mid-2020; in training until products launched

- Vast majority of new staff from successful China oncology companies
- Expansion planned for future product launches
- SF productivity will reach to US\$400k per year in 2023



## **China Oncology commercial team**

### Blend of multinational and local oncology expertise



**Chief Commercial Officer** 



NOVARTIS



VP, Sales & Marketing







Director, Commercial





Director, Sales Force Effectiveness & Training







Director, Marketing Research & New Business Development





Senior Marketing Director -Fruguintinib







**Associate Marketing** Director - Surufatinib





Associate Director, **Medical Marketing** 







Regional Sales Director North





Regional Sales Manager North I





Regional Sales Manager North II







Regional Sales Manager East I







Regional Sales Manager East II





Regional Sales Manager Central





Regional Sales Manager South





Regional Sales Manager South West





## HUTCHMED

## **Commercial capabilities - Market Access**

A strong Market Access team with a track record of delivering NRDL and hospital listings

## **Market Access Team** Government funds and projects **Nationwide** Bidding dossier preparation NRDL planning negotiation Regional supplement listing Regional Critical illnesses insurance Regional bidding Relationship with key hospitals **Provincial** and health authorities Local and Relationship with selected key Hospitals hospitals

#### Fruquintinib successful 2019 NRDL listing



#### **Exceptional results in access and price protection**

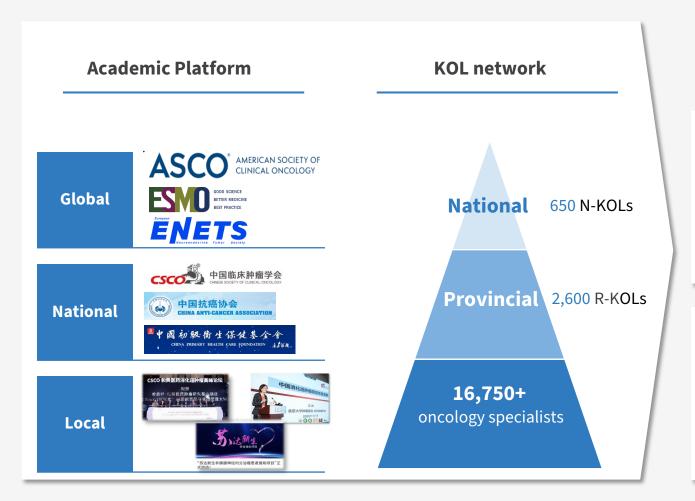


**Surufatinib NRDL negotiation preparation in 2021** 

## **Commercial capabilities - KOL Relationships**



Good relationships with KOLs in major academic associations, covering solid & hematological cancers



#### **Publications**



#### **Guideline inclusion**

Class I recommendation (Level 1A evidence) for the treatment of 3L CRC regardless of RAS and BRAF gene status

## Guidelines for the Diagnosis and Treatment of HUTCHMED Pancreatic Neuroendocrine Tumors in China (2020)



#### (三) 靶向治疗

pNET 的靶向治疗主要包括依维莫司(mTOR抑制剂)、舒尼替尼(酪氨酸激酶抑制剂)和索凡替尼(酪氨酸激酶抑制剂)。依维莫司适用于中、低级别的进展期pNET患者,其在抑制肿瘤生长、延长患者中位无进展生存期方面具有明确价值(1A, I级推荐)[142]。但依维莫司联合 SSA 可能无法进一步改善患者的远期预后 [143],且其在化疗、PRRT等失败的患者中可能引起更高的严重不良反应发生率 [144]。舒尼替尼通常适用于分化较好的进展期pNET患者,其能抑制肿瘤生长并延长患者的无进展生存期(1A, I级推荐)[145]。但对于亚洲人群,标准剂量(37.5 mg/d)的舒尼替尼常引起较严重的不良反应,而适当降低药物剂量(25 mg/d)并不影响舒尼替尼的临床有效性 [146]。索凡替尼同样适用于分化较好的进展期 pNET,其能延长患者的无病生存期,有望成为进展期pNET患者新的治疗选择(1A, I级推荐)[147]。

"Surufatinib is also suitable for well-differentiated advanced pNET, which can prolong disease-free survival in patients with advanced pNET and is expected to be a new treatment option for patients with advanced pNET (1A, grade I recommendation)."

## Commercial capabilities – Relationships with Patient advocacy groups



>2,000 mCRC pts benefited from fruquintinib PAP program; surufatinib program recently initiated







#### **Fruquintinib PAP program**

- √ A successful program: more than 2,000 mCRC patients benefited
- ✓ *Close collaboration:*with China Primary Health Care Foundation
  (Jan. 2019 Aug. 2020)
- ✓ Donation management: incl. label, tax, free goods management, etc.

#### **Surufatinib PAP program**

- ✓ Recently initiated with commercial launch
- ✓ Significant benefit for China NET patients expected given long survival period

## Commercial capabilities – academic promotion HUTCHMED



Diversified Academic Promotion platforms to deliver product value to stakeholders

















**Academic** promotion

Actively engaging physicians & patients to realize full product value









**Expert** consensus group











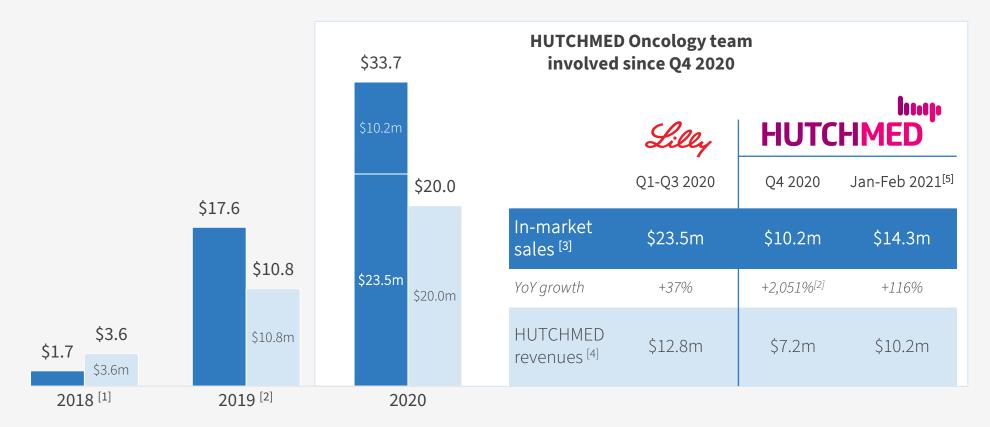


## **ELUNATE®** commercial update



Sales growth accelerating since HUTCHMED assumed commercial role in Q4 2020

#### In-market sales since launch



<sup>■</sup> In-Market sales [3] ■ HUTCHMED revenues [4]

<sup>[1]</sup> ELUNATE® was launched in late November 2018. HUTCHMED revenues in 2018 primarily relate to manufacturing fees and royalties paid by Lilly.

<sup>[2]</sup> During Q4 2019, ELUNATE® in-market sales were affected by rebates and downward price adjustments required in the distribution channel in the lead up to NRDL inclusion effective Jan 1, 2020

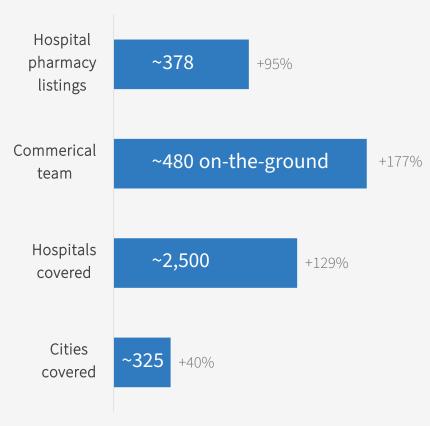
<sup>[3]</sup> Represents total sales to third parties as provided by Lilly; [4] Represents manufacturing fees, commercial service fees and royalties paid by Lilly to HUTCHMED and sales to other third parties invoiced by HUTCHMED. [5] Unaudited.

## **ELUNATE®** coverage and key opportunities



Sales benefitting from deeper coverage...

#### Increased on-the-ground activities April 30, 2021 vs. Sept 30, 2020



## ...with many potential growth opportunities for ELUNATE®

- CRC: 2<sup>nd</sup> highest cancer incidence in China, with up to 550,000 new patients in 2020<sup>1</sup>
- 3L CRC patients increasing quickly
- Promising ELUNATE® PD-1 combos data in 3L CRC at ASCO could greatly extend DOT of ELUNATE®
- Over 20 investigator initiated trials (IITs) ongoing exploring treatment of 2L CRC patients intolerant to chemotherapy
- Phase III in 2L gastric cancer (GC) ongoing

### SULANDA® launch



#### Executed within 3 weeks of NDA approval...just beginning

Dec 30, 2020 Jan 14, 2021 Jan 19, 2021 Jan 29, 2021

NDA Approved First order shipped



First Prescribed Prescription in 30 provinces



Jan-Feb 2021 \$4.9 million<sup>[1]</sup> in 1<sup>st</sup> two months on market

#### **Patient access**

 Eligible to negotiate for NRDL inclusion during 2021









# Potential growth opportunities for SULANDA®

- Covering all tumor origins: If the pNET NDA is approved, SULANDA® would be the first product to address all NET patients regardless the tumor origin
- Immunotherapy combinations: SULANDA's unique mechanism of action could make it a better choice for PD-1 combination therapy



# US COMMERCIAL ORGANIZATION & STRATEGY

Tom Held, Head of Commercial – U.S.

### **US Commercial leadership team in place**

# HUTCHMED

#### Deep Oncology and NET Commercial Experience



Tom Held, SVP
Commercial, Oct '20
30+ Years of Pharma Experience
20+ Oncology, incl. former Head of
US Oncology Rare Diseases & Global
Brand Lead on AFINITOR®







Ed Barnes, VP Sales and Training, Mar '21 25+ Years of Pharma Experience 20+ Oncology







Ushank Agarwal, VP Commercial Ops , Apr '21 14+ Years of Pharma Experience 10+ Oncology







Leslie Blair, VP
Marketing, Jan '21
25+ Years of Pharma Experience
20+ Oncology







Kapil Raina MD, VP Value, Access, Pricing Feb '21 15+ Years of Pharma Experience 5+ Oncology







# US Commercial / Medical Affairs critical capabilities

# Differentiated brand value propositions

- Actionable insights into the patient journey
- Building on key points of differentiation
- Well-funded Brand/Launch plans

# Robust operational frameworks and platforms

- Recruiting top talent
- Integrated and compliant Med Affairs-Commercial alignment around the customer
- IT systems to drive customer centricity

# Optimized go-to-market model

- Competitive share of voice
- Rare disease patient acquisition model
- Building Value / Access / Pricing models for the US and beyond
- Flexible fit-for purpose model to expand from GI Cancers (NET, CRC) to Hem indications

# **Surufatinib: US NET Market Landscape**

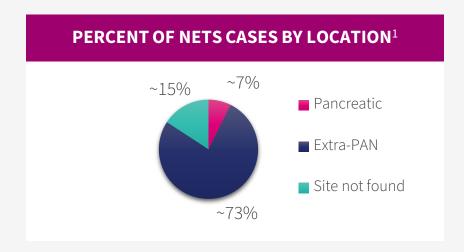


A rare heterogeneous tumor that presents in the metastatic stage in 40-50% of patients

NETs are relatively rare and heterogeneous tumor type, comprising ~2% of all malignancies<sup>1,2</sup>

#### US 2021 estimates: 1,3

- 140,000~170,000 living with NET
  - **17,000~20,000** diagnosed with *Extra-pancreatic* NET
  - 1,200~3,900 diagnosed with pancreatic NET
- ~30,000 patients under active treatment in the metastatic setting
- 40%–50% of overall NET patients present with distant metastases at initial diagnosis<sup>6,7</sup>
  - Metastatic disease generally incurable and current treatments offer palliation only
- 5-year survival is ~54% in Pancreatic NETs, ~94% in GI-NETs and ~89% in Lung NETs



#### TREATMENT LANDSCAPE

# Palliative systemic therapy is mainstay for adv. disease

- Somatostatin analogs
- Targeted Agents
  - Sunitinib
  - Everolimus
- Cytotoxics:
- Peptide receptor radionuclide therapy

# Surufatinib: US extrapancreatic NET Prescriber Level Data



< 10% of eligible patients are prescribed everolimus or sunitinib in 2018

IQVIA's medical claims and prescription data longitudinal databases track patients over time and not dependent on insurance carrier, pharmacy, or employer.

- 1.0 billion annual claims that contain diagnosis and visit information
- Represents >870,000 practitioners per month.

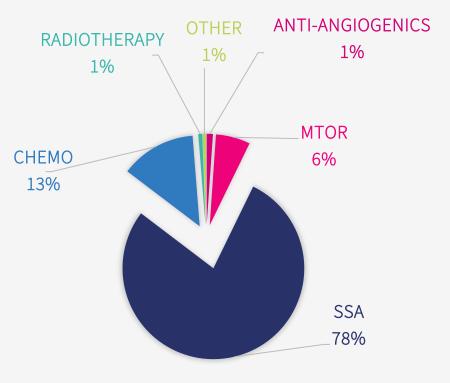


Office Based Medical Claims (Dx)



(LRx)

- Sourced from US office-based physicians, and other private practitioners through the CMS-1500 medical claims form/837 billing form
- Patient level diagnoses / procedures, and provider specialties
- Sourced by retail, mail order and specialty pharmacies across the U.S. through the NCPDP form
- Prescription details (drug brand/generic name, quantity, days supply) and prescriber/pharmacy data



## Fruquintinib: US CRC Landscape Overview [1]



Approved Stivarga (rego) & Lonsurf (TAS-102) used 20% to 30% in 3L+ patients Unmet need remains high in refractory setting

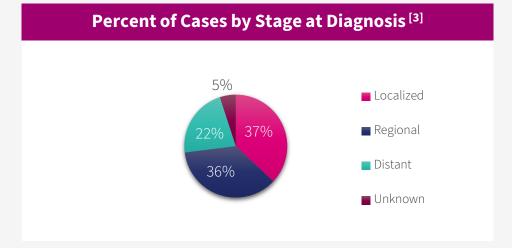
new cases of CRC diagnosed in **US in** 

2021[3]

#### **CRC Current and Future Market Situation**

- Total value of CRC market expected to increase from \$4.7bn in 2016 to \$7.5bn in 2025 (US, JPN and EU5) [2]
- US CRC market value growing from \$2.0bn in 2016 to \$3.5bn in 2025 (CAGR = 6.4%) due to high prevalence of CRC in the US and uptake of new targeted therapies [2]

  About 149.500
- Est. 149,500 CRC new cases diagnosed in US, 2021
  - 32,890 (or 22%) are metastatic at diagnosis
  - >67K patients treated for mCRC in 2018



#### **Fast Evolving Treatment Landscape**

- Chemotherapy, anti-VEGF, and anti-EGFR agents to continue as mainstay of treatment, novel MoAs provide more treatment options
  - Stivarga (regorafenib) and Lonsurf (TAS-102): SoC for 3L treatment
  - Stivarga: approved by the FDA with a liver toxicity black box warning: severe and sometimes hepatotoxicity observed
- Increasing number of options, treatment beyond 3<sup>rd</sup> line likely to increase

#### **Unmet needs and challenges**

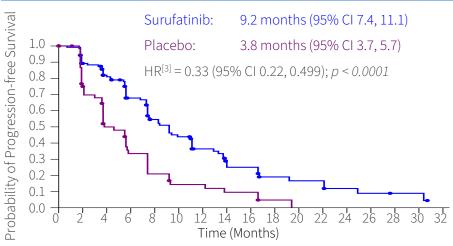
- Novel treatment options available for rarer subtypes; larger subsets are treated with traditional options
- Lack of treatment options that can significantly improve prognosis for metastatic patients
  - 5-year survival rate for mCRC remains only slightly over 14%
- Unmet Medical Need remains high for 4L and beyond
  - Fruquintinib shown strong data already in CRC 3L and beyond
  - Limited strategies for managing drug resistance

### **Surufatinib Phase III results in NETs**

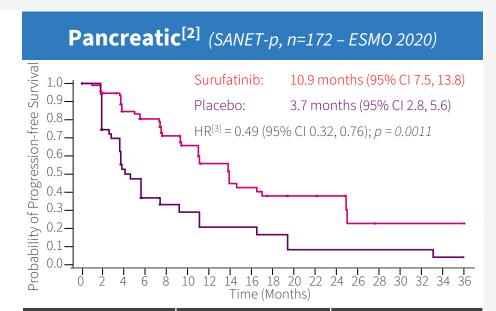


Both SANET-ep and SANET-p met superiority criteria for PFS at the pre-planned interim analysis; IDMC recommendation to stop study due to superior efficacy of surufatinib

#### Extra-Pancreatic<sup>[1]</sup> (SANET-ep, n=198 – ESMO 2019)



RADIANT 4 <sup>[4]</sup> (GEP NETS)	Everolimus	Placebo		
N	205	97		
PFS	11.0	3.9		
HR/p-value	0.48 (0.35, 0.67) p < 0.001			



RADIANT 3 <sup>[4]</sup> (PNET)	Everolimus	Placebo		
N	205	97		
PFS	11.0	4.6		
HR/p-value	0.35 (0.27, 0.45) p < 0.001			

# FRESCO China Phase III results compare favorably with current Western standards of care



Median OS of 9.3 months compares favorably with TAS-102 and Regorafenib

	Fruquintinib		TAS-102		Regorafenib		Nintedanib	
Metastatic Colorectal	FRESCO		RECOURSE		CORRECT		LUME Colon-1	
Cancer	3 <sup>rd</sup> line or later Mainland China		3 <sup>rd</sup> line Global		3 <sup>rd</sup> line Global		3/4 <sup>th</sup> line (40/60%) Global	
Treatment arms	Fruquintinib	Placebo	TAS-102	Placebo	Regorafenib	Placebo	Nintedanib	Placebo
Patients (n)	278	138	534	266	505	255	384	381
Complete Response, n (%)	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0%	0%
Partial Response, n (%)	4.3%	0.0%	1.6%	0.4%	1.0%	0.4%	0%	0%
Stable Disease, n (%)	57.6%	12.3%	N/A	N/A	42.8%	14.5%	26%	11%
Disease Control Rate, n (%)	62.2%	12.3%	44%	16%	41.0%	14.9%	26%	11%
Median PFS (mo.)	3.7	1.8	2.0	1.7	1.9	1.7	1.5	1.4
mPFS p-value	<0.00	01	<0	.001	<0.000	001	P<0.0	0001
mPFS Hazard Ratio	0.26	6	0	.48	0.49	)	0.5	58
Median OS (mo.)	9.3	6.6	7.1	5.3	6.4	5.0	6.4	6.0
mOS p-value	<0.00	)1	<0	.001	0.005	52	0.86	559
mOS Hazard Ratio	0.6	5	0	.68	0.77	7	1.0	)1



# MANUFACTURING EXPERTISE

Zhenping Wu, Head of Pharmaceutical Sciences



# **Manufacturing strategy**

Some we control, some we outsource

	Small Molecule Manufacturing	Large Molecule Manufacturing
	Global Manufacturing/ formulation (Suzhou / Shanghai)	Collaborate with CDMOs
	<ul> <li>Formulation supported by HUTCHMED Suzhou (≤\$500m revenue)</li> </ul>	<ul> <li>2020-22: outsource mAb manufacturing to CDMOs.</li> </ul>
Formulation	<ul> <li>Long-term formulation (\$0.5-\$2.5bn revenue) incl. China &amp; global product supply → HUTCHMED Shanghai new factory</li> <li>Established ≤\$0.5bn capacity Suzhou 2018, now at steady</li> </ul>	<ul> <li>In parallel, establish own small scale lab mftg facilities to support discovery.</li> </ul>
	state; ~\$2.0bn capacity new Shanghai factory by 2025	<ul> <li>Build scale-up mAb mftg facilities in Shanghai new factory as</li> </ul>
	Global API Manufacturing	necessary.
	• Continue to outsource API unless we determine IP risk.	Establish CDMO collaboration
API	Established Multiple 3 <sup>rd</sup> -party China-based API manufacturers have been established in past 10 years.	during 2020 - in mid- to long-term we will establish in-house mAb production.

# **CMC Development & Manufacturing**



#### Leadership



#### **Zhenping Wu, SVP**

- 13 years with HUTCHMED
- 30 years in pharma manufacturing including Roche and Pfizer



Process Research & Development

- 9 years with HUTCHMED
- 18 years in pharma manufacturing including Apotex and ChemPartner



Analytical Research & Development

- 8 years with HUTCHMED
- 25 years in pharma manufacturing including Merck and Sundia



Drug Product Manufacturing & Supply Chain

- 11 years with HUTCHMED
- 20 years in pharma manufacturing including Bright Future and Frontage



**Biologics CMC** 

- 1 year with HUTCHMED
- 9 years in pharma manufacturing including Pfizer

- API process development
- Solid form selection
- Clinical material manufacturing
- Commercial API supplies

- Analytical method development
- API & drug product stability
- Commercial specification
- Regulatory CMC

- Formulation development
- Clinical supplies
- Commercial supplies
- Supply chain management

- Biological process development
- Biological formulation
- Biological method development
- Clinical supplies

# **Outsourcing API manufacturing**

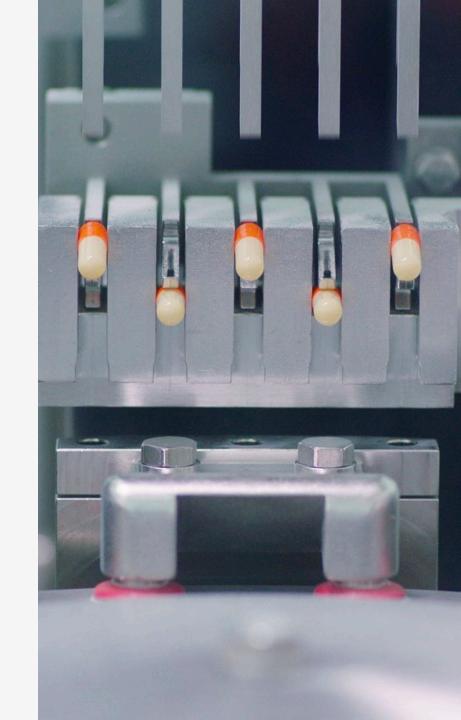
Advancing clinical pipeline and produce commercial supplies

Work with leading CMOs in China for API manufacturing





- Established strong relationships with CMOs from clinical manufacturing through commercialization
- Plan to have two sites qualified for each product for commercial manufacturing to mitigate supply risks



# HUTCHMED

### **Drug Product and Biological Facilities**

New Shanghai factory to support production for China and global post 2025

#### **SUZHOU FACTORY**

- Built to produce ELUNATE® and SULANDA®
- Manufacturing talent developed
- Suzhou is designed to U.S. GMP standards

#### **SHANGHAI FACTORY**

- Capex of \$130 million over 5 years
- Will fulfil additional global production requirements
- Additional capacity for expansion in large molecule production

Key Aspects	Suzhou Factory	New Shanghai Factory
Property Type	Leased	Owned
Land Size (sq.m.)	~1,800	~28,700 <b>(16x)</b>
Building Size (sq.m.)	~4,500 (Office: ~1,000)	~55,000 <b>(12x)</b> (Office: ~16,400)
Capacity (Cap & Tabs)	50 million	250 million (5x, Phase 1)
Growth Potential	No capacity for growth	Phase 2 for biologics









### **CMC Development and Manufacturing**

Advancing clinical pipeline and produce commercial supplies

API, formulation, and analytical development for small molecules and biologics

Clinical supplies, NDA filings, and commercial supplies for China and global

Broad experience with 100 scientists, most with MS or Ph.D.

Leverage leading CMOs in China for clinical manufacturing

Commercial API supplies at CMOs and drug product mostly in-house



# **SUMMARY**

Christian Hogg, CEO

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



Realizing the global potential of HUTCHMED's novel oncology assets



Building a fully integrated oncology business in China

### **HUTCHMED** footprint



Control operations in >50% of global pharma market

Capitalize on established discovery & manufacturing capabilities in China

Commercial partnerships to cover balance of global markets



- Global discovery
- Global manufacturing
- Clinical dev. & regulatory
- China commercial platform

#### EU, Japan & Australia

- Clinical development
- Regulatory expertise

#### **Partnerships**

Commercialization excluding China and U.S.

#### U.S.

- International HQ for clinical dev. & regulatory
- U.S. commercial platform

#### **HUTCHMED 2025**



#### **Ambitious targets with potential for transformation**

# Therapies launched



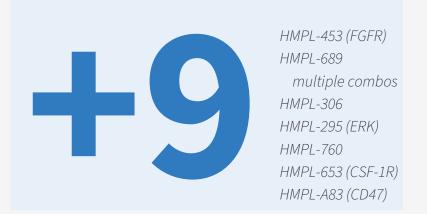


# Additional therapies in registration studies





Suru mono
Suru + PD-1 combo
Fruq mono
Fruq + PD-1 combo
Savo mono
Savo + Tagrisso
Savo + Imfinzi
HMPL-689
HMPL-523 (Syk)



HUTCHMED 1000

9. Q&A

### **Speakers**

# HUTCHMED

#### **HUTCHMED Management Team**



Christian Hogg Chief Executive Officer

P&G

32/21



31/16

Weiguo Su Chief Scientific Officer





25/11

Hong Chen Chief Commercial Officer, China

Bristol Myers Squibb

**U** NOVARTIS



30/1

Tom Held Head of Commercial. U.S.

O Daiichi-Sankyo

**b** NOVARTIS

27/3

Marek Kania Managing Director & Chief Medical Officer, International





27/13

Zhenping Wu Pharmaceutical Sciences



**Pfizer** 



Johnny Cheng Chief Financial Officer H Bristol Myers Squibb

Nestle Nestle

KPMG



General Manager, SHPL

Junjie Zhou

**SANOFI** 

32/13





May Wang Business Dev. & Strategic Alliances





Mark Lee Corporate Finance & Development





Charles Nixon General Counsel





Andrew Shih HR - Organization & Leadership Dev.





Thomas Fu

Global Quality





Yiling Cui Government Affairs







23/2

# **Thank you**

HUTCHMED Innep

www.hutch-med.com