HUTCHMED (China) Limited Supplemental and Updated Disclosures

We recently filed an application (the "Listing Application") with The Stock Exchange of Hong Kong Limited (the "Stock Exchange") in connection with a proposed listing (the "Listing") of our ordinary shares, par value US$0.10 per share ("Shares"), on the Main Board of the Stock Exchange.

The Listing Application contains supplemental and additional descriptions of certain aspects of our business and financial information as required by the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited as well as updated disclosure of certain information previously disclosed in our annual report on Form 20-F for the year ended December 31, 2020 filed on March 4, 2021 (the "2020 Annual Report"). This exhibit sets forth such new, supplemental and updated information and disclosures as described below. The disclosure herein supplements and should be read in conjunction with the disclosure in our 2020 Annual Report and other disclosures furnished on Form 6-K.

There is no assurance as to if or when such Listing will take place. This communication is neither an offer to sell nor a solicitation of an offer to buy, nor shall there be any offer, solicitation or sale of our securities in any jurisdiction in which such offer, solicitation or sale would be unlawful.

FORWARD LOOKING STATEMENTS

This Exhibit contains forward-looking statements that involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. The words "anticipate," "assume," "believe," "contemplate," "continue," "could," "estimate," "expect," "goal," "intend," "may," "might," "objective," "plan," "potential," "predict," "project," "positioned," "seek," "should," "target," "will," "would," or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are based on current expectations, estimates, forecasts and projections about our business and the industry in which we operate and management's beliefs and assumptions, are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors.

Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. As a result, any or all of our forward-looking statements in this Exhibit may turn out to be inaccurate. We have included important factors in the cautionary statements included in this Exhibit and in the 2020 Annual Report, particularly in the section of the 2020 Annual Report titled "*Risk Factors*", that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Moreover, we operate in a highly competitive and rapidly changing environment in which new risks often emerge. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make.

The forward-looking statements contained herein are made as of the date of the filing of this Exhibit, and we do not assume any obligation to update any forward-looking statements except as required by applicable law. We undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date on which the statements are made or to reflect the occurrence of unanticipated events. You should read this Exhibit completely in conjunction with our annual reports on Form 20-F and other documents filed with or furnished to the SEC and with the understanding that our actual future results may be materially different from what we expect.

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RECENT DEVELOPMENTS

The following sets forth updated information subsequent to the filing of our 2020 Annual Report.

For our unaudited consolidated financial statements as of March 31, 2021 and for the three months ended March 31, 2020 and 2021, please refer to the document available on our company website titled "Unaudited First Quarter 2021 Financial Information" and the related disclosures contained herein and therein.

SUMMARY OF FIRST QUARTER 2021 HIGHLIGHTS

Cash and cash equivalents and short-term investments were US$396.1 million as of March 31, 2021 compared to US$435.2 million as of December 31, 2020.

Revenues increased by 58.1% to US$81.6 million for the three months ended March 31, 2021 from US$51.6 million for the three months ended March 31, 2020.

- **Oncology/Immunology revenues** increased by 227.3% to US$21.7 million for the three months ended March 31, 2021 from US$6.6 million for the three months ended March 31, 2020.
  - **Accelerating Sales Growth of Elunate –** Sales of Elunate generated revenues of US$13.4 million for the three months ended March 31, 2021 compared to US$2.9 million for the three months ended March 31, 2020. In-market sales of Elunate were US$20.2 million for the three months ended March 31, 2021 compared to US$7.3 million for the three months ended March 31, 2020, as provided by Eli Lilly.
  - **Launch of Sulanda –** We commercially launched Sulanda as a treatment for patients with advanced non-pancreatic NET in China in mid-January 2021 within three weeks of approval from China's National Medical Products Administration (the "NMPA"). We had revenues of US$5.5 million from sales of Sulanda for the three months ended March 31, 2021.
- **Other Ventures revenues** increased by 33.2% to US$59.9 million for the three months ended March 31, 2021 from US$45.0 million for the three months ended March 31, 2020.

Research and development expenses incurred by Oncology/Immunology increased by 87.0% to US$57.1 million for the three months ended March 31, 2021 from US$30.5 million for the three months ended March 31, 2020, primarily due to a significant expansion of clinical activities in the United States and rapid organizational growth to support such expansion. In particular, this increase was attributable to the expansion of the fruquintinib, surufatinib, HMPL-689 and HMPL-306 development programs. Our international clinical and regulatory operations in the United States and Europe incurred research and development expenses of US$30.6 million for the three months ended March 31, 2021 compared to US$8.0 million for the three months ended March 31, 2020. We expect to incur significant expenses, particularly research and development expenses, for the foreseeable future as we expand our development of, and seek regulatory approvals for, our drug candidates.

Net loss attributable to our Company was US$41.1 million for the three months ended March 31, 2021 compared to US$16.1 million for the three months ended March 31, 2020. Net loss attributable to our Company was US$0.06 per ordinary share for the three months ended March 31, 2021 compared to US$0.02 per ordinary share for the three months ended March 31, 2020.

BUSINESS UPDATES

Recent Disposal

On March 24, 2021, we entered into a sale and purchase agreement with GL Mountrose Investment Two Limited, a company controlled and managed by GL Capital Group, to sell our entire investment in

Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Company Limited, our non-consolidated joint venture ("Hutchison Baiyunshan"). GL Capital Group is an investment firm that focuses on buyout and growth opportunities in China's healthcare industry and is an independent third party which has a minority interest in the Company and is not a connected person of the Company. The disposal is subject to regulatory approval in China and is expected to be completed in the second half of 2021.

The aggregate amounts to be received attributable to the Company are approximately US$169 million, of which approximately US$127 million is related to our shareholding in Hutchison Baiyunshan and approximately US$42 million is related to distributions of the land compensation and the prior year's undistributed profits. A deposit of approximately US$15.9 million paid upon signing of the agreement will be credited against the proceeds due on completion of the disposal.

Following the completion of the disposal, the Group will cease equity accounting of the financial results of Hutchison Baiyunshan, and will derecognize the carrying value of the Company's investment in Hutchison Baiyunshan and recognize a disposal gain attributable to the Company estimated at approximately US$80-90 million, net of taxes. The Group will exit from the over-the-counter drug arena upon the disposal. As our focus is the discovery and development of novel therapies in oncology and immunology, the sale of our interest in Hutchison Baiyunshan will allow us to focus resources on our primary aim of accelerating investment in our Oncology/Immunology assets.

Baring Private Placement

On April 14, 2021, the Company completed the sale of US$100 million of Shares at a price of US$6.10 per Share (equivalent to an ADR price of US$30.50 per ADS) via a private placement to Pachytene Limited, an investment holding company wholly owned by Baring Asia Private Equity Fund VII.

FINANCIAL UPDATES

Our unaudited condensed consolidated statements of operations and cash flows presented below for the three months ended March 31, 2020 and 2021 and our unaudited condensed consolidated balance sheet as of March 31, 2021 have been derived from our unaudited consolidated financial statements as of March 31, 2021 and for the three months ended March 31, 2020 and 2021("Unaudited First Quarter 2021 Financial Information"), which are available on our company website. The unaudited interim financial information for the three months ended March 31, 2021 has been prepared on the same basis as our audited consolidated financial data and has been reviewed by our reporting accountant in accordance with Hong Kong Standard on Review Engagements 2410. Please refer to our Unaudited First Quarter 2021 Financial Information for a discussion of the effect of material differences between the financial information of the Company prepared under U.S. GAAP and IFRS.

The consolidated financial information below should be read in conjunction with, and is qualified in its entirety by reference to, our audited consolidated financial statements for the years ended December 31, 2018, 2019 and 2020 and as of December 31, 2018, 2019 and 2020 and related notes contained in our 2020 Annual Report. Our historical results do not necessarily indicate results expected for any future periods, and the results of operations for the three months ended March 31, 2021 are not necessarily indicative of the results to be expected for the full fiscal year ending December 31, 2021.

Condensed Consolidated Statements of Operations

	Three Months Ended March 31,	
	2020	2021
	US$'000 (Unaudited)	
Revenues		
Goods – third parties	45,971	67,060
– related parties	767	1,306
Services		
– commercialization – third parties	—	7,406
– collaboration research and development – third parties	3,618	2,706
– research and development – related parties	121	130
Other collaboration revenue – royalties – third parties	1,093	2,948
Total revenues	**51,570**	**81,556**
Operating expenses		
Costs of goods – third parties	(40,778)	(54,872)
Costs of goods – related parties	(512)	(954)
Costs of services – commercialization – third parties	—	(9,114)
Research and development expenses	(30,511)	(57,059)
Selling expenses	(2,594)	(5,733)
Administrative expenses	(9,667)	(17,024)
Total operating expenses	**(84,062)**	**(144,756)**
	(32,492)	**(63,200)**
Other income, net of other expenses	1,172	293
Loss before income taxes and equity in earnings of equity investees	**(31,320)**	**(62,907)**
Income tax expense	(1,045)	(1,939)
Equity in earnings of equity investees, net of tax	16,939	24,993
Net loss	**(15,426)**	**(39,853)**
Less: Net income attributable to non-controlling interests	(715)	(1,290)
Net loss attributable to our Company	**(16,141)**	**(41,143)**
Losses per share attributable to our Company – basic and diluted (US$ per share)	(0.02)	(0.06)
Number of shares used in per share calculation – basic and diluted	683,855,237	723,176,387

Condensed Consolidated Balance Sheets

	December 31, 2020	March 31, 2021
	US$'000	
		(Unaudited)
Assets		
Current assets		
Cash and cash equivalents	235,630	346,133
Short-term investments	199,546	49,939
Accounts receivable – third parties	46,648	53,128
Inventories	19,766	19,757
Other current assets	29,150	27,273
Total current assets	**530,740**	**496,230**
Property, plant and equipment	24,170	26,257
Right-of-use assets	8,016	9,849
Investments in equity investees	139,505	133,816
Other non-current assets	21,687	26,965
Total assets	**724,118**	**693,117**
Liabilities and shareholders' equity		
Current liabilities		
Accounts payable	31,612	28,636
Other payables, accruals and advance receipts	120,882	150,332
Lease liabilities	2,785	3,970
Other current liabilities	3,118	5,577
Total current liabilities	**158,397**	**188,515**
Lease liabilities	6,064	6,529
Long-term bank borrowings	26,861	26,872
Other non-current liabilities	13,847	6,806
Total liabilities	**205,169**	**228,722**
Commitments and contingencies		
Company's shareholders' equity		
Ordinary shares	72,772	72,812
Additional paid-in capital	822,458	808,776
Accumulated losses	(415,591)	(456,742)
Accumulated other comprehensive income	4,477	3,425
Total Company's shareholders' equity	**484,116**	**428,271**
Non-controlling interests	34,833	36,124
Total shareholders' equity	**518,949**	**464,395**
Total liabilities and shareholders' equity	**724,118**	**693,117**

Condensed Consolidated Statements of Cash Flows

	Three Months Ended March 31,	
	2020	2021
	US$'000 (Unaudited)	
Net cash used in operating activities	(1,757)	(22,356)
Investing activities		
Purchases of property, plant and equipment	(2,087)	(6,057)
Deposits in short-term investments	(191,764)	(49,943)
Proceeds from short-term investments	96,011	199,549
Deposit received for divestment of Hutchison Baiyunshan	—	15,912
Purchase of leasehold land	—	(355)
Refund of leasehold land deposit	—	930
Net cash (used in)/generated from investing activities	(97,840)	160,036
Financing activities		
Proceeds from issuance of ordinary shares	118,341	242
Purchases of treasury shares	—	(26,758)
Payment of issuance costs	(7,643)	(231)
Net cash generated from/(used in) financing activities	110,698	(26,747)
Net increase in cash and cash equivalents	11,101	110,933
Effect of exchange rate changes on cash and cash equivalents	(18)	(430)
	11,083	110,503
Cash and cash equivalents		
Cash and cash equivalents at beginning of period	121,157	235,630
Cash and cash equivalents at end of period	132,240	346,133

Three Months Ended March 31, 2020 Compared to Three Months Ended March 31, 2021

Set forth below is a discussion of our unaudited consolidated statements of operations for the three months ended March 31, 2020 and 2021:

Revenues. Our revenue increased by 58.1% from US$51.6 million for the three months ended March 31, 2020 to US$81.6 million for the three months ended March 31, 2021, which was caused by increased revenue from both Oncology/Immunology and Other Ventures operations.

Revenue from Oncology/Immunology increased by 227.3% from US$6.6 million for the three months ended March 31, 2020 to US$21.7 million for the three months ended March 31, 2021, primarily due to the commercial launch of Sulanda in January 2021 which generated revenue of US$5.5 million for the three months ended March 31, 2021. Furthermore, there was an increase in revenue related to the sale of Elunate from US$2.9 million for the three months ended March 31, 2020 to US$13.4 million for the three months ended March 31, 2021 which was mainly comprised US$7.4 million in service revenue from promotion and marketing services to Eli Lilly and an increase in manufacturing sales and royalties of US$3.1 million across these periods.

Revenue from our Other Ventures increased by 33.2% from US$45.0 million for the three months ended March 31, 2020 to US$59.9 million for the three months ended March 31, 2021, primarily due to an increase in sales of prescription drug products which increased by 28.7% from US$38.0 million for the three months ended March 31, 2020 to US$49.0 million for the three months ended March 31, 2021 resulting from increased sales by our consolidated joint venture Hutchison Sinopharm. Revenues from our consumer health products also increased by 58.0% from US$7.0 million for the three months ended

March 31, 2020 to US$10.9 million for the three months ended March 31, 2021, primarily due to an increase in sales of infant nutrition products.

Cost of Revenues. Our cost of revenues increased by 57.3% from US$41.3 million for the three months ended March 31, 2020 to US$64.9 million for the three months ended March 31, 2021. This increase was primarily due to increased sales by our Other Ventures as well as the cost of promotion and marketing services to Eli Lilly which commenced in October 2020. Cost of revenues as a percentage of revenue was relatively stable at 80.1% for the three months ended March 31, 2020 and 79.6% for the three months ended March 31, 2021.

Research and Development Expenses. Our research and development expenses incurred by Oncology/Immunology increased by 87.0% from US$30.5 million for the three months ended March 31, 2020 to US$57.1 million for the three months ended March 31, 2021, which was primarily attributable to a US$17.2 million increase in CRO and other clinical trial related costs and a US$6.0 million increase in employee compensation related costs. These increased costs were due to a significant expansion of clinical activities in the United States and rapid organizational growth to support such expansion. In particular, this increase was attributable to the expansion of the fruquintinib, surufatinib, HMPL-689 and HMPL-306 development programs. As a result, research and development expenses as a percentage of our revenue increased from 59.2% to 70.0% across these periods.

Selling Expenses. Our selling expenses increased by 121.0% from US$2.6 million for the three months ended March 31, 2020 to US$5.7 million for the three months ended March 31, 2021, primarily due to promotion and marketing expenses incurred for the sale of Sulanda in China which launched in January 2021. As a result, selling expenses as a percentage of our revenues increased from 5.0% to 7.0% across these periods.

Administrative Expenses. Our administrative expenses increased by 76.1% from US$9.7 million for the three months ended March 31, 2020 to US$17.0 million for the three months ended March 31, 2021. This was primarily due to US$3.8 million increase in administrative expenses incurred by Oncology/Immunology, which was mainly related to increased staff cost to support the expansion of our clinical activities. There was also an increase of US$2.9 million in administrative expenses incurred by our corporate head office for organizational expansion. Administrative expenses as a percentage of our revenues increased from 18.7% to 20.9% across these periods.

Other Income, net. We had net other income of US$1.2 million for the three months ended March 31, 2020, compared to net other income of US$0.3 million for the three months ended March 31, 2021. The decrease was primarily due to a decline in interest income of US$0.5 million mainly due to lower bank deposit rates and an increase of exchange loss of US$0.6 million. Such decrease was partly offset by a decrease in interest expenses of US$0.2 million due to lower bank borrowing rates.

Income Tax Expense. Our income tax expense increased from US$1.0 million for the three months ended March 31, 2020 to US$1.9 million for the three months ended March 31, 2021, primarily due to higher withholding taxes accrued as a result of an increase in net income of Shanghai Hutchison Pharmaceuticals and higher taxable income in relation to commercial activities.

Equity in Earnings of Equity Investees. Our equity in earnings of equity investees, net of tax, increased by 47.5% from US$16.9 million for the three months ended March 31, 2020 to US$25.0 million for the three months ended March 31, 2021. This change was primarily due to an increase in net income of Shanghai Hutchison Pharmaceuticals.

Net Loss. As a result of the foregoing, our net loss increased from US$15.4 million for the three months ended March 31, 2020 to US$39.9 million for the three months ended March 31, 2021. Net loss attributable to our Company increased from US$16.1 million for the three months ended March 31, 2020 to US$41.1 million for the three months ended March 31, 2021. The increase in net losses is primarily due to an increase in research and development expenses, as a result of a significant expansion of clinical activities.

Cash Flows and Capital Commitments

Set forth below is a discussion of our unaudited consolidated cash flows for the three months ended March 31, 2020 and 2021:

Net Cash used in Operating Activities. Net cash used in operating activities was US$1.8 million for the three months ended March 31, 2020, compared to net cash used in operating activities of US$22.4 million for the three months ended March 31, 2021. The net change of US$20.6 million was primarily attributable to an increase in research and development expenses of US$26.6 million from US$30.5 million for three months ended March 31, 2020 to US$57.1 million for the three months ended March 31, 2021.

Net Cash (used in)/generated from Investing Activities. Net cash used in investing activities was US$97.8 million for the three months ended March 31, 2020, compared to net cash generated from investing activities of US$160.0 million for the three months ended March 31, 2021. The net change of US$257.8 million was primarily attributable to net deposits in short-term investments of US$95.8 million for the three months ended March 31, 2020 compared to the net withdrawal of deposits in short-term investments of US$149.6 million for the three months ended March 31, 2021. The net change was also due to our receipt of a US$15.9 million deposit in March 2021 in connection with our planned divestment of Hutchison Baiyunshan.

Net Cash generated from/(used in) Financing Activities. Net cash generated from financing activities was US$110.7 million for the three months ended March 31, 2020, compared to net cash used in financing activities of US$26.7 million for the three months ended March 31, 2021. The net change of US$137.4 million was primarily attributable to net proceeds of US$110.7 million from our follow-on offering in the United States in January and February 2020. This net change was also due to the purchases of treasury shares of US$26.8 million for the three months ended March 31, 2021.

Capital Expenditures. We had capital expenditures of US$2.1 million and US$6.1 million for the three months ended March 31, 2020 and 2021, respectively. Our capital expenditures for the three months ended March 31, 2021 were primarily used for the construction of our new manufacturing facility in Shanghai. Our capital expenditures have been primarily funded by cash flows from operations and proceeds from our initial public and follow-on offerings in the United States and other equity offerings.

As of March 31, 2021, we had commitments for capital expenditures of approximately US$44.2 million, primarily for the construction of our new manufacturing facility in Shanghai. We expect to fund these capital expenditures through cash flows from operations, bank borrowings and existing cash resources.

INFORMATION ABOUT THE LISTING

The following section sets forth certain information relating to the Global Offering, including information concerning stamp duty, the establishment of a Hong Kong Share Registrar, and the conversion between our ADSs listed on the Nasdaq and our Shares proposed to be listed on the Main Board of the Stock Exchange.

Register of Members and Stamp Duty

Our principal register of members will be maintained by our principal share registrar in the Cayman Islands, and our Hong Kong register of members will be maintained by the Hong Kong Share Registrar, Computershare Hong Kong Investor Services Limited, in Hong Kong.

Dealings in our Shares which are registered on our Hong Kong share register will be subject to Hong Kong stamp duty. The stamp duty is charged to each of the seller and purchaser at the ad valorem rate of 0.1% (which is proposed to be increased to 0.13% as announced by the Hong Kong Government in its Budget for 2021/22 and to be effective upon approval by the Legislative Council and the enactment of amendments to the Stamp Duty Ordinance) of the consideration or, if higher, the fair value of the Shares transferred. In other words, a total of 0.2% (which is proposed to be increased to 0.26% as announced by the Hong Kong Government in its Budget for 2021/22 and to be effective upon approval by the Legislative Council and the enactment of amendments to the Stamp Duty Ordinance) is currently payable on a typical sale and purchase transaction of our Shares. In addition, a fixed duty of HK$5.00 is charged on each instrument of transfer (if required).

Dealings and Settlement of Shares in Hong Kong

Our Shares will trade on the Stock Exchange in board lots of 500 Shares. Dealings in our Shares on the Stock Exchange will be conducted in Hong Kong dollars.

The transaction costs of dealings in our Shares on the Stock Exchange include:

(a) The Stock Exchange trading fee of 0.005% of the consideration of the transaction, charged to each of the buyer and seller;

(b) Securities and Futures Commission of Hong Kong transaction levy of 0.0027% of the consideration of the transaction, charged to each of the buyer and seller;

(c) trading tariff of HK$0.50 on each and every purchase or sale transaction. The decision on whether or not to pass the trading tariff onto investors is at the discretion of brokers;

(d) transfer deed stamp duty of HK$5.00 per transfer deed (if applicable), payable by the seller;

(e) ad valorem stamp duty at a total rate of 0.2% of the value of the transaction, with 0.1% payable by each of the buyer and the seller (which is proposed to be increased to 0.13% payable by each of the buyer and the seller);

(f) stock settlement fee, which is currently 0.002% of the gross transaction value, subject to a minimum fee of HK$2.00 and a maximum fee of HK$100.00 per side per trade;

(g) brokerage commission, which is freely negotiable with the broker (other than brokerage commissions for IPO transactions which are currently set at 1% of the subscription or purchase price and will be payable by the person subscribing for or purchasing the securities); and

(h) the Hong Kong share registrar will charge between HK$2.50 to HK$20, depending on the speed of service (or such higher fee as may from time to time be permitted under the Rules Governing the Listing of Securities on The Stock Exchange ("Listing Rules"), for each transfer of Shares

from one registered owner to another, each share certificate canceled or issued by it and any applicable fee as stated in the share transfer forms used in Hong Kong.

Investors must settle their trades executed on the Hong Kong Stock Exchange through their brokers directly or through custodians. For an investor who has deposited his/her Shares in his/her stock account or in his/her designated CCASS (Central Clearing and Settlement System established and operated by Hong Kong Securities Clearing Company Limited) participant's stock account maintained with CCASS, settlement will be effected in CCASS in accordance with the General Rules of CCASS and CCASS Operational Procedures in effect from time to time. For an investor who holds the physical certificates, settlement certificates and the duly executed transfer forms must be delivered to his/her broker or custodian before the settlement date.

Exchanges Between Shares Trading in Hong Kong and ADSs

In connection with the initial public offering of our Shares in Hong Kong, or the Hong Kong Public Offering, we have established a branch register of members in Hong Kong, or the Hong Kong share register, which will be maintained by our Hong Kong Share Registrar, Computershare Hong Kong Investor Services Limited. Our principal register of members, or the Cayman share register, will continue to be maintained by our Principal Share Registrar, Computershare Investor Services (Jersey) Limited.

All Shares offered in the Hong Kong Public Offering will be registered on the Hong Kong share register in order to be listed and traded on the Hong Kong Stock Exchange. Holders of Shares registered on the Hong Kong share register will be able to exchange those Shares for ADSs and vice versa.

The following sets forth certain risks factors that have been updated and/or supplemented to reflect changes since the filing of our 2020 Annual Report as well as additional new risk factors related to the Listing.

RISKS RELATING TO OUR FINANCIAL POSITION AND NEED FOR CAPITAL

We have incurred significant net operating cash outflows during the three financial years ended December 31, 2020, and may continue to experience net cash outflow from operating activities.

Investment in biopharmaceutical drug development is highly speculative. It entails substantial upfront expenditures and significant risk that a drug candidate might fail to gain regulatory approval or become commercially viable. We continue to incur significant expenses related to our ongoing operations. Net cash used in operating activities was US$32.8 million, US$80.9 million and US$62.1 million for the years ended December 31, 2018, 2019 and 2020, respectively. We expect to incur significant expenses, particularly research and development expenses, for the foreseeable future as we expand our development of, and seek regulatory approvals for, our drug candidates. Typically, it takes many years to develop one new drug from the drug discovery stage to the time it is available for treating patients. Our ability to improve our cash flow depends on a number of variables, including the number and scope of our drug development programs and the associated costs of those programs, the cost of commercializing any approved products, our ability to generate revenues and the timing and amount of milestones and other payments we make or receive through arrangements with third parties. Our failure to generate positive cash flow from operations may adversely affect our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. There is no assurance that we will be able to generate sufficient net cash inflows from operating activities, which could have adverse effects on our long-term viability.

We face risks with our short-term investments and in collecting our accounts receivables.

Our short-term investments are bank deposits with maturities of more than three months but less than one year. Our short-term investments were US$214.9 million, US$96.0 million and US$199.5 million as of December 31, 2018, 2019 and 2020, respectively, and are placed with major financial institutions. These investments may earn yields substantially lower than expected. Failure to realize the benefits we expected from these investments may materially and adversely affect our business and financial results. To date, we have experienced no loss or lack of access to our invested cash or cash equivalents; however, we can provide no assurance that access to our invested cash and cash equivalents will not be impacted by adverse conditions in the financial and credit markets.

Our accounts receivable – third parties balance, net of allowance for credit losses, totaled US$40.2 million, US$41.4 million and US$46.6 million as of December 31, 2018, 2019 and 2020, respectively. We have policies and procedures in place to ensure that sales are made to customers with an appropriate credit history. We perform periodic credit evaluations of our customers and monitor risk factors and forward-looking information, such as country risk, when determining credit limits for customers. However, there can be no assurance such policies and procedures will effectively limit our credit risk and enable us to avoid losses, which could adversely affect our financial condition and results of operations. In addition, amounts due to us are not covered by collateral or credit insurance. As of April 30, 2021, US$41.4 million, or 89%, of the total accounts receivable – third parties outstanding as of December 31, 2020 had been settled. If we fail to collect all or part of such accounts receivable in a timely manner, or at all, our financial condition may be materially and adversely affected.

RISKS RELATING TO OUR ONCOLOGY/IMMUNOLOGY OPERATIONS AND DEVELOPMENT OF OUR DRUG CANDIDATES

If we participate in compassionate-use programs, discrepancies among the regulations in different countries may lead to increased risk of adverse drug reactions and serious adverse events arising from the use of our drug candidates.

Compassionate-use programs are regulatory programs that facilitate access to investigational drugs for the treatment of patients with serious or immediately life-threatening diseases or conditions that lack therapeutic alternatives. Currently, there is no unified approach or standard practice to regulate compassionate-use programs or access to investigational drugs across countries. In China, the NMPA and the National Health Commission issued the Promulgation of the Administrative Provisions on Extended Clinical Trials of Medical Devices (for Trial Implementation) on March 14, 2020, with immediate effect, providing a route for patients suffering from life-threatening diseases without existing effective treatments to engage treatment that is yet to be approved for marketing. In the United States, compassionate-use programs are limited to patients who have a life-threatening disease or serious disease or condition, who may gain access to an investigational medical product for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available. Additionally, the U.S. Right to Try Act provides a separate pathway for patients with a life-threatening disease or condition who have exhausted all other treatment options and who are unable to participate in clinical trials to access investigational drugs that have passed Phase I clinical trials under a more expedited process.

The regulatory discrepancy for compassionate-use programs among countries may lead to uneven patient entry criteria and protocols for compassionate-use programs. This may create increased risk of serious adverse events because of enrolled patients' advanced disease or comorbidities. In addition, because the products in compassionate-use programs are investigational drugs, many of which are still in experimental stages and have not received marketing approval, patients in compassionate-use program may exhibit adverse drug reactions from using these products. If we participate in compassionate-use programs, we may be subject to the risk of enrolled patients exhibiting adverse drug reactions or serious adverse events being produced from the use of our future drug products. Such occurrences can potentially lead to clinical holds of our ongoing clinical trials or complicate the determination of the safety profile of a drug candidate under regulatory review for commercial marketing, or expose us to tort liability. Changes in government regulations or in practices relating to the pharmaceutical and biopharmaceutical industries, including healthcare reform in China, and compliance with new regulations may result in additional costs.

RISKS RELATING TO SALES OF OUR INTERNALLY DEVELOPED DRUGS AND OTHER DRUGS

As a significant portion of the operations of our Other Ventures is conducted through joint ventures, we are dependent on the success of our joint ventures and our receipt of dividends or other payments from our joint ventures for cash to fund our operations and our investments in our joint ventures are subject to liquidity risk.

We are party to joint venture agreements with Shanghai Traditional Chinese Medicine Co., Ltd. ("Shanghai Pharmaceuticals") and Guangzhou Baiyunshan Pharmaceutical Holdings Company Limited ("Guangzhou Baiyunshan"), relating to our non-consolidated joint ventures, which together form part of the operations of our Other Ventures. Our equity in the earnings of these non-consolidated joint ventures, net of tax, was US$38.3 million, US$40.6 million and US$79.1 million for the years ended December 31, 2018, 2019 and 2020, respectively, as recorded in our consolidated financial statements. Equity in earnings of Hutchison Baiyunshan for the year ended December 31, 2020 included a one-time gain of US$36.0 million from land compensation for a return of land use rights to the Guangzhou government. As such, our results of operations and financial performance have been, and will continue to be, affected by the financial performance of these joint ventures as well as any other equity investees we have or may have in the future. We may also be required to recognize an impairment charge in our consolidated financial statements if there is a decline in the fair market value of our investments in such

businesses below their carrying amounts for whatever reason that is determined to be other-than-temporary. Furthermore, we have consolidated joint ventures with each of Sinopharm and Hain Celestial which accounted for substantially all of our Other Ventures' consolidated revenue for the years ended December 31, 2018, 2019 and 2020.

As a result, our ability to fund our operations and pay our expenses or to make future dividend payments, if any, is largely dependent on the earnings of our joint ventures and the payment of those earnings to us in the form of dividends. Payments to us by our joint ventures will be contingent upon our joint ventures' earnings and other business considerations and may be subject to statutory or contractual restrictions. Each joint venture's ability to distribute dividends to us is subject to approval by their respective boards of directors, which in the case of Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan are comprised of an equal number of representatives from each party. Furthermore, our ability to promptly sell one or more of our interests in our joint ventures in response to changing corporate strategy or economic, financial and investment conditions is limited. The market for such investments can be affected by various factors, such as general economic and market conditions, availability of financing, interest rates and investor demand, many of which are beyond our control. If we determine to sell any of our joint venture investments, we cannot predict if we will be successful or whether any price or other terms offered by a prospective purchaser would be acceptable to us.

Operationally, our joint venture partners have certain responsibilities and/or certain rights to exercise control or influence over operations and decision-making under the joint venture arrangements. Therefore, the success of our joint ventures depends on the efforts and abilities of our joint venture parties to varying degrees. For example, we share the ability to appoint the general manager of our joint venture with Guangzhou Baiyunshan, with each of us having a rotating four-year right, and therefore, our ability to manage the day-to-day operations of this joint venture is more limited. On the other hand, we appoint the general managers of Hutchison Sinopharm and Shanghai Hutchison Pharmaceuticals pursuant to the respective joint venture agreements governing these entities and therefore oversee the day-to-day management of these joint ventures. However, we still rely on our joint venture partners Sinopharm and Shanghai Pharmaceuticals to provide certain distribution and logistics services.

We may not be successful in building a commercial team to successfully manufacture, sell and market our approved drugs, and we may not be able to generate any revenue from such products.

We have leveraged our experience operating our prescription drugs business to commercialize certain of our approved, internally developed drug candidates in China. We must adapt our know-how to build a specific oncology and/or immunology focused sales and marketing team. As of December 31, 2020, we had an oncology commercial team with about 390 staff in China to support the commercialization of fruquintinib, surufatinib and our other drug candidates, if approved.

There are risks involved in establishing an in-house oncology commercial team. For example, recruiting and/or training a sales force to detail our approved drug candidates is time consuming and could delay any drug launch. Factors that may inhibit our efforts to commercialize our drug candidates include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- our inability to effectively manage the expansion of our operations and train additional qualified personnel in the relevant areas of oncology and/or immunology;
- the inability of our sales personnel to obtain access to physicians or educate adequate numbers of physicians who then prescribe any future drugs; and
- the lack of complementary drugs to be offered by our sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines.

In such case, our business, results of operations, financial condition and prospects will be materially and adversely affected.

We may engage in strategic transactions, including acquisitions, investments, joint ventures or divestitures that may have an adverse effect on our business. If we engage in a strategic transaction, there is no assurance that the transaction will be consummated.

We may pursue transactions as part of our business strategy, including continuing to actively evaluate non-core assets divestment opportunities. For instance, on March 24, 2021, we entered into a sale and purchase agreement with GL Mountrose Investment Two Limited, a company controlled and managed by GL Capital Group, to sell our entire investment in Hutchison Baiyunshan. See "*Recent Developments*" for more information.

Acquisitions and investments involve numerous risks such as difficulties in finding suitable partners or acquisition candidates, difficulties in obtaining financing on favorable terms, if at all, the assumption of certain known and unknown liabilities of acquired companies and difficulties in integrating operations, services products and personnel. Divestitures also involve numerous risks. Any divestiture could result in a dilutive impact to our future earnings and significant write-offs, including those related to goodwill and other intangible assets, which could have a material adverse effect on our results of operations and financial condition. Divestitures could involve additional risks, including difficulties in the separation of operations, services, products and personnel, the diversion of management's attention from other business concerns, the disruption of our business and the potential loss of key employees.

We may not complete strategic transactions in a timely manner, on a cost-effective basis, or at all, and we may not realize the expected benefits of any transaction. For instance, the disposal of Hutchison Baiyunshan is subject to regulatory approval in China. We may not be successful in managing these or any other significant risks that we encounter if we engage in a strategic transaction. If we are not successful in managing the risks, uncertainties and potential disruptions, a strategic transaction could have a negative impact on our business, results of operations or financial position.

OTHER RISKS AND RISKS RELATING TO DOING BUSINESS IN CHINA

We have granted, and may continue to grant, options, awards under our long-term incentive scheme adopted by the Shareholders in April 2015 and other types of awards under our Schemes, which may result in increased share-based compensation expenses and give rise to potential employment related disputes.

We and Hutchison MediPharma have adopted share option schemes in June 2005, December 2014 and April 2015 and long-term incentive scheme in April 2015 (together, the "Schemes") for the purpose of granting share-based compensation awards to certain management, Directors, employees and other eligible grantees as a means to retain, incentivize, reward, remunerate, compensate and/or provide benefits to eligible grantees. We recognized share-based compensation expenses of US$10.1 million, US$11.6 million and US$19.6 million for the years ended December 31, 2018, 2019 and 2020, respectively, in our consolidated financial statements in accordance with U.S. GAAP.

We believe the granting of share-based compensation is of significant importance to our ability to attract and retain key personnel and employees, and we will continue to grant share-based compensation in the future. As a result, our expenses associated with share-based compensation may increase, which may have an adverse effect on our results of operations. We may re-evaluate the vesting schedules, exercise price or other key terms applicable to the grants under our currently effective Schemes from time to time. If we choose to do so, we may experience a substantial change in our share-based compensation expenses in the reporting periods following the offer of the Shares to the public in Hong Kong, in the United States or to certain investors who are U.S. Persons, and to non-U.S. Persons outside of the United States (together, the "Global Offering"). In addition, we could in the future become involved in disputes or legal proceedings with our employees or former employees on employment related matters (including disputes on the entitlement of options, awards and other share-based compensation or in connection with the employees incentive or compensation arrangements). If such disputes or legal proceedings arise, there can be no assurance that we will prevail in them, and in any event defending against these disputes or

legal proceedings could cause us to incur legal and other costs. Any adverse outcome of these disputes or legal proceedings could have a material adverse effect on our reputation, business and results of operations.

RISKS RELATING TO THE GLOBAL OFFERING AND OUR LISTINGS IN HONG KONG, THE UNITED STATES AND UNITED KINGDOM

Our audit report and the audit reports of our non-consolidated joint ventures are prepared by auditors who are not inspected by the PCAOB. In addition, various legislative and regulatory developments related to U.S.-listed China-based companies due to lack of PCAOB inspection and other developments may have a material adverse impact on our listing and trading in the U.S. and the trading prices of our ADSs and Shares. We could be delisted from the Nasdaq if the PCAOB continues to be unable to inspect our independent registered public accounting firm for three consecutive years.

Our auditor and the auditors for our non-consolidated joint ventures are registered with the Public Company Accounting Oversight Board ("PCAOB"). Pursuant to laws in the United States, the PCAOB has authority to conduct regular inspections over independent registered public accounting firms registered with the PCAOB to assess their compliance with the applicable professional standards. Our auditor is located in Hong Kong, a special administrative region of China, a jurisdiction where the PCAOB is currently unable to conduct full inspections without the approval of the Chinese authorities. The auditors of our non-consolidated joint ventures are located in China. As a result, we understand that our auditor and the auditors for our non-consolidated joint ventures are not currently inspected by the PCAOB.

This lack of PCAOB inspections in China prevents the PCAOB from fully evaluating audits and quality control procedures of our auditor and the auditors of our non-consolidated joint ventures. As a result, we and investors in our securities are deprived of the benefits of such PCAOB inspections. The inability of the PCAOB to conduct inspections of auditors in China makes it more difficult to evaluate the effectiveness of the audit procedures or quality control procedures of our auditor and the auditors of our non-consolidated joint ventures as compared to auditors outside of China that are subject to the PCAOB inspections, which could cause investors and potential investors in our securities to lose confidence in our audit procedures and reported financial information and the quality of our financial statements.

In May 2013, the PCAOB announced that it had entered into a Memorandum of Understanding on Enforcement Cooperation with the China Securities Regulatory Commission, or the CSRC, and the PRC Ministry of Finance, which established a cooperative framework between the parties for the production and exchange of audit documents relevant to investigations undertaken by the PCAOB, the CSRC or the PRC Ministry of Finance in the United States and the PRC. The PCAOB continued to discuss with the CSRC and the PRC Ministry of Finance on joint inspections in the PRC of PCAOB-registered audit firms that provide auditing services to Chinese companies that trade on U.S. stock exchanges. In December 2018, the SEC and the PCAOB issued a joint statement on regulatory access to audit and other information internationally that cites the ongoing challenges faced by them in overseeing the financial reporting of companies listed in the United States with operations in China, the absence of satisfactory progress in discussions on these issues with Chinese authorities and the potential for remedial action if significant information barriers persist. In April 2020, the SEC and the PCAOB issued another joint statement reiterating the greater risks of insufficient disclosures from companies in many emerging markets, including China, compared to those from U.S. domestic companies. In discussing the specific issues related to these risks, the statement again highlighted the PCAOB's inability to inspect audit work and practices of accounting firms in China with respect to U.S. reporting companies. In June 2020, the former President Trump issued a memorandum ordering the President's Working Group on Financial Markets, or the PWG, to submit a report to the President within 60 days of the memorandum that includes recommendations for actions that can be taken by the executive branch and by the SEC or the PCAOB on Chinese companies listed on U.S. stock exchanges and their audit firms. In August 2020, the PWG released the report. In particular, with respect to jurisdictions that do not grant the PCAOB

sufficient access to fulfill its statutory mandate, or NCJs, the PWG recommended that enhanced listing standards be applied to companies from NCJs for seeking initial listing and remaining listed on U.S. stock exchanges. Under the enhanced listing standards, if the PCAOB does not have access to work papers of the principal audit firm located in a NCJ for the audit of a U.S.-listed company as a result of governmental restrictions, the U.S.-listed company may satisfy this standard by providing a co-audit from an audit firm with comparable resources and experience where the PCAOB determines that it has sufficient access to the firm's audit work papers and practices to inspect the co-audit; there is currently no legal framework under which such a co-audit may be conducted for China-based companies. The report recommended a transition period until January 1, 2022 before the new listing standards apply to companies already listed on U.S. stock exchanges. Under the PWG recommendations, if we fail to meet the enhanced listing standards before January 1, 2022, we could face de-listing from the Nasdaq, deregistration from the SEC and/or other risks, which may materially and adversely affect, or effectively terminate, our ADS trading in the United States. There were recent media reports about the SEC's proposed rulemaking in this regard. It is uncertain whether the PWG recommendations will be adopted, in whole or in part, and the impact of any new rule on us cannot be estimated at this time.

As part of a continued regulatory focus in the United States on access to audit and other information currently protected by national law, in particular China's, in June 2019, a bipartisan group of lawmakers introduced bills in both houses of Congress that would require the SEC to maintain a list of issuers for which the PCAOB is not able to inspect or investigate an auditor's report issued by a foreign public accounting firm. The Ensuring Quality Information and Transparency for Abroad-Based Listings on our Exchanges Act, or EQUITABLE, prescribes increased disclosure requirements for such issuers and, beginning in 2025, the delisting from national securities exchanges such as Nasdaq of issuers included for three consecutive years on the SEC's list. On May 20, 2020, the U.S. Senate passed S. 945, the Holding Foreign Companies Accountable Act, or the Act. The Act was approved by the U.S. House of Representatives on December 2, 2020. The Act was signed into law by the President of the United States on December 18, 2020. In essence, the Act requires the SEC to prohibit foreign companies from listing securities on U.S. securities exchanges if a company retains a foreign accounting firm that cannot be inspected by the PCAOB for three consecutive years, beginning in 2021. On March 24, 2021, the SEC adopted interim final rules relating to the implementation of certain disclosure and documentation requirements of the Act. We will be required to comply with these rules if the SEC identifies us as having a "non-inspection" year under a process to be subsequently established by the SEC. The SEC is assessing how to implement other requirements of the Act, including the listing and trading prohibition requirements described above. On May 13, 2021, the PCAOB proposed a new rule, PCAOB Rule 6100, *Board Determinations Under the Holding Foreign Companies Accountable Act,* to provide a framework for its determinations under the Act that the PCAOB is unable to inspect or investigate completely registered public accounting firms located in a foreign jurisdiction because of a position taken by one or more authorities in that jurisdiction. The enactment of the Act and any additional rulemaking efforts to increase U.S. regulatory access to audit information in China could cause investor uncertainty for affected SEC registrants, including us, the market price of our securities could be materially adversely affected, and we could be delisted from Nasdaq if we are unable to meet the PCAOB inspection requirement in time.

An active trading market for the Shares on the Stock Exchange of Hong Kong Limited might not develop or be sustained, their trading prices might fluctuate significantly and the effectiveness of the liquidity arrangements might be limited.

Following the completion of the Global Offering, we cannot assure you that an active trading market for the Shares on the Stock Exchange will develop or be sustained. In particular, the Stock Exchange only implemented changes to the Listing Rules to facilitate the listing of biotech companies in 2018, and investors in Hong Kong listed securities may not be as familiar with investing in biotech companies as investors in other markets. If an active trading market for the Shares on the Stock Exchange of Hong Kong Limited does not develop or is not sustained after the Global Offering, the market price and liquidity of the Shares could be materially and adversely affected. As a result, the market price of our

Shares in Hong Kong following the completion of the Global Offering might not be indicative of the historical market prices of our Shares on the AIM and our ADSs on Nasdaq.

We may also seek further listings on other stock exchanges such as the Shanghai Stock Exchange. If such a listing materializes, PRC investors who previously traded on the Stock Exchange through the Shanghai-Hong Kong Stock Connect and similar arrangements may no longer do so, which could result in a significant reduction in the trading activities of the Shares on the Stock Exchange.

If we pursue and complete a listing of our Shares on the Star Market, the Shares issued in connection with such listing would cause the shareholding of our Shareholders immediately prior to such listing to be diluted.

We continue to monitor market conditions for, and evaluate, the possibility of, seeking a listing on the Shanghai Stock Exchange Science and Technology Innovation Board ("STAR Market"). While the evaluation is ongoing, no decision has been made as to whether any such further listings will be sought and, if so, whether any application for such further listings will be successful. If we proceed with and complete a listing on the STAR Market (a "STAR Listing"), we currently expect to issue new shares (including pursuant to any over-allotment option granted in connection with such potential STAR Listing) representing no more than 20% of the issued share capital of the Company immediately following the completion of such potential STAR Listing (taking into account the Shares to be issued pursuant to the Global Offering but without taking into account any Shares to be issued pursuant to any (a) exercise of the Over-allotment Option in connection with the Global Offering, (b) exercise of share options granted or to be granted under the share option schemes adopted by the Shareholders in June 2005 and April 2015 or (c) exercise of the ordinary shares subscription warrant entered into between the Company and General Atlantic on July 2, 2020). The issue of shares pursuant to a potential STAR Listing would result in the shareholding of our Shareholders immediately prior to the completion of such potential STAR Listing being diluted by no more than 20%. Any STAR Listing and the size of any offering of new shares in our Company in connection with a STAR Listing (and consequently, the dilution impact on the shareholding of the then existing Shareholders) will be subject to a number of factors, including market conditions, our funding needs, approval of the Shareholders and approval of the Shanghai Stock Exchange, the CSRC and all relevant regulators.

The following section sets forth new information and statistics relating to the industry in which we operate. Certain information and statistics were derived from the Frost & Sullivan Report, prepared by Frost & Sullivan, an independent industry consultant which was commissioned by us in respect of the Global Offering.

WHAT IS CANCER?

Cancer is a broad group of diseases in which cells undergo changes that allow them to divide and grow in an uncontrolled fashion, forming malignant tissues known as tumors , which can adversely affect normal bodily functions. Oncology is the study and treatment of tumors. Cancer is the second leading cause of death globally, causing approximately one in six deaths.

The global market for oncology treatment grew from US$93.7 billion in 2016 to US$150.3 billion in 2020, and is expected to further grow to US$482.5 billion by 2030, with a CAGR of 15.2% between 2020 and 2025 and 9.6% between 2025 and 2030. The oncology drug market in China is expected to grow at a faster pace than the global market. In 2016, the China oncology market was US$19.2 billion and increased to US$30.4 billion in 2020. Double-digit annual growth of 16.1% and 10.4% is expected between 2020 and 2025 and 2025 and 2030, respectively, with the market in China expected to reach US$105.1 billion by 2030.

OVERVIEW OF ONCOLOGY TREATMENT

The field of cancer treatment has advanced rapidly in recent decades, progressing from surgery and radiotherapy, to chemotherapy and, more recently, to molecularly targeted drugs and immunotherapies.

Oncology Treatment

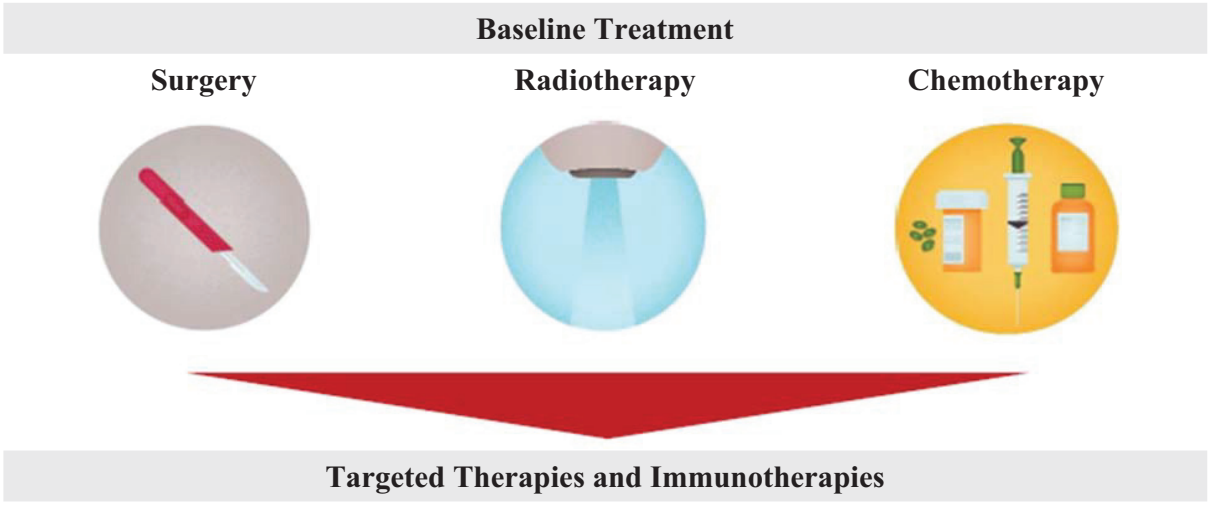
Traditional Cancer Treatments			New Era of Cancer Treatments	
Surgery	Radiotherapy	Chemotherapy	Targeted Therapies	Immunotherapies
▪ A procedure in which a surgeon removes cancer from a patient's body ▪ Best for early stage tumors that are contained in one area but is limited for cancers that have metastasized	▪ High doses of radiation to kill cancer cells and shrink tumors including solid tumors and leukemia ▪ Affects nearby healthy cells, causing side effects such as fatigue, hair loss and skin changes	▪ Uses one or more anti-cancer drugs to stop or slow the growth of cancer cells ▪ Targets all fast growing cells, causing side effects such as fatigue, hair loss, easy bruising and bleeding, and infection	▪ Act on specific targets that are associated with cancer growth ▪ Less harmful to normal cells than traditional therapies ▪ Include both small molecule drugs and monoclonal antibodies	▪ Induce the patient's own immune system to fight cancer ▪ Include cytokines, monoclonal antibodies, checkpoint inhibitors, adoptive T-cell therapy and cancer vaccines

Source: Frost & Sullivan analysis.

Although molecularly targeted therapies and immunotherapies are becoming more available, the traditional cancer treatments noted above currently remain the essential or first-line treatments for most types of cancers globally, and, in particular, surgery is the primary treatment for patients whose cancer is resectable or in early stages.

THE FUTURE OF CANCER TREATMENT IS A BALANCED, MULTIPRONGED STRATEGY

We believe that the future of cancer treatment will continue to be a multipronged strategy, which treats cancer through the multiple modalities and mechanisms by which it develops, including by targeting the tumor microenvironment, cancer cell signaling processes and the body's immune system.



Cancer cell signaling

- Cells interact with their environment and cells around them. This process is known as cell signaling.
- Usually these signals help regulate a normal cycle of cell growth and death, but sometimes cells mutate and lose the ability to respond properly to cell signals. When this happens, they can grow out of control, resulting in the expansion of a tumor.
- Certain targeted therapies, such as those targeting MET, Syk, EGFR and PI3Kδ, aim to interrupt the messages inside and outside of the cells to stop cancer cells from proliferating and tumors from growing.
- Other targeted therapies aim to interrupt messages generated by cancer cells which help to power or feed the cell. If a drug can interrupt the messaging, it may be possible to starve tumors of energy and nutrients.

Tumor microenvironment

- The growth and spread of a tumor involve not just the cancer cells themselves, but also other healthy cells, tissues and molecules in the environment around them. This surrounding area is known as the tumor microenvironment.
- Many tumors produce chemical signals that change their surroundings around them to help them thrive and certain targeted therapies aim at disrupting these microenvironments. For instance, some tumors create signals that establish a network of blood vessels to supply the tumor with nutrients and oxygen, known as angiogenesis.

- If a targeted therapy can interrupt the microenvironment by, for example, inhibiting VEGFR or FGFR, kinases which are known to play a role in angiogenesis, it may be possible to reduce or cut off the flow of nutrients and oxygen to certain tumors.
- Targeted therapies may also act on the tumor environment to boost the immune response to cancer. For example, it may be possible to enable T cells to infiltrate the tumor microenvironment by inhibiting VEGFR.

Immuno-oncology

- The immune system is the body's natural defense system. Because cancer cells are different from normal cells, the immune system should find and attack them, but sometimes cancer cells can hide from or trick the immune system. Other times a person's immune system is not strong enough to fight off cancer cells.
- Immuno-oncology is a developing area of research that seeks to activate or support the immune system, making it possible for a patient's body to find and attack cancer cells.
- The immune system has several checkpoints that stop it from attacking healthy cells. Some cancer cells turn on these checkpoints to avoid destruction. To prevent this, immunotherapies such as anti-PD-1 antibodies aim to turn off these checkpoints.
- Targeted therapies may also act on tumor-associated macrophages and tumor-associated neutrophils thereby boosting a patient's immune response to cancer.

Source: Frost & Sullivan analysis.

Advent of Personalized Medicine Through Targeted Therapies and Immunotherapies

Over the past 20 years, cancer treatments have seen an increased focus on newer treatment methods, including targeted therapies, which target specific biological molecules, generally proteins or enzymes, or genetic changes that play a role in the spread of cancer, and immunotherapies, which use the patient's own immune system to help fight cancer.

With a better understanding of cancer biology, new therapies and diagnostic tests, cancer treatment is becoming increasingly personalized. In many cases, cancer is no longer a single tumor-type diagnosis. Rather, it is defined by a combination of personalized factors such as the biomarkers or gene mutations exhibited by a patient's tumor. The molecular characteristics of individual tumors are starting to be used to guide the choice of treatment.

The personalized medicine approach to cancer aims to optimize a patient's chances of responding to a particular targeted therapy treatment based on identified biomarkers or gene mutations. For example, it is now recommended that all NSCLC patients have their tumors tested for the presence of specific genetic abnormalities. Patients who test positive for an EGFR mutation are then typically treated with an EGFR inhibitor such as Tagrisso.

Next-Generation Kinase-targeted Therapies as a Critical Component of Combination Therapies

Human cells have many different kinases, and they help control important functions associated with cellular growth and survival. Some cancer cells have genetic alterations which cause certain kinases to be more active and blocking those kinases can keep the cancer cells from abnormal proliferation.

The cancer treatment landscape was transformed beginning with the introduction of small molecule targeted therapies such as tyrosine kinase inhibitors. The first tyrosine kinase inhibitor was approved for the treatment of cancer in the United States in 2001. Approved tyrosine kinase inhibitors have demonstrated significant benefits to patients.

The first generation of tyrosine kinase inhibitors to be discovered were multi-kinase inhibitors, targeting a wide range of kinases, one or more of which were intended target(s). Today, many approved tyrosine kinase inhibitors are multi-kinase inhibitors. Unfortunately, the benefits afforded by these first-generation molecules are accompanied by off-target toxicity, which in turn can lead to insufficient dosage with a short therapeutic window:

- *Off-target toxicity*. Off-target toxicities occur when a drug inhibits unintended targets due to similarities with the intended target. Off-target toxicities cause adverse side effects such as kidney and liver damage. For example, Stivarga was approved with a black box warning for liver toxicity on its FDA label. Off-target toxicities limit dosage levels and duration of treatment, thereby reducing efficacy. Off-target toxicities also limit the potential to use multi-kinase inhibitors in combination with other therapies, due to intolerable cumulative toxicities.
- *Insufficient dosage*. To prevent the adverse effects of off-target toxicities from being too intolerable for patients, many multi-kinase inhibitors are administered at dosages far below the optimal quantities to inhibit an intended target. These lower dosages can reduce the efficacy and therapeutic window of the drug.

Moreover, most patients who initially benefit from targeted therapies eventually relapse due to the development of new aberrations. For instance, studies suggest that when patients with metastatic lung cancers who initially benefit from anti-EGFR therapies like Tagrisso relapse, their tumors develop new aberrations such as MET amplification and further EGFR mutations. Off-target toxicities, as well as other adverse events such as undesirable drug-drug interactions, make management of subsequently acquired resistance difficult. One of our core strategies is to focus on next-generation, highly selective tyrosine kinase inhibitors which have the potential to address the problems described above by limiting off-target toxicity, increasing tolerability and efficacy and enabling combinations with other therapies to address acquired resistance. Furthermore, if multiple kinases do need to be targeted to provide clinical benefit, a personalized combination of multiple highly selective kinase inhibitors could be the optimal approach. In addition, highly selective kinase inhibitors may be well-suited to be used in combination with chemotherapies or immunotherapies for the same reasons. For further discussion of the use of highly selective inhibitors in combination therapies, see "*– The Use of Targeted Therapies in Combination Therapies*."

Key Benefits of Highly Selective Kinase Inhibitors Versus Multi-targeted Kinase Inhibitors

- The consideration to determine whether highly selective kinase inhibitors or multi-targeted kinase inhibitors are preferable in cancer therapy based on aspects concerning stability, efficacy, toxicity, resistance and drug combination.

	Highly Selective Kinase Inhibitor	Multi-targeted Kinase Inhibitor
Toxicity	✓ Unique selectivity and low IC_{50} of the inhibitor for the specific target limit off-target toxicity.	× The combination of different targets with high IC_{50} is more likely to generate off-target toxicity.
Resistance	✓ More flexibility exists thanks to the possibility of switching to other highly selective kinase inhibitors when resistance by this mechanism is detected.	× Mutations may decrease the affinity of the kinase to the inhibitor, causing potential ineffectiveness of multi-targeted kinase inhibitor.
Efficacy	✓ Unique selectivity and lower toxicity makes the treatment more tolerable, leading to better target coverage and more durable response.	× Increasing off-target toxicity can lead to less durable response, consequently reducing the efficacy of drugs.
Drug Combination	✓ Combinations of multiple single-targeted kinase inhibitors will trigger synergistic antitumor effects to enable the titration of the dose of either agent to optimize target inhibition with less concern about toxicity.	× Combinations of multi-targeted kinase inhibitors might lead to enhanced toxicity because cumulative target and off-target inhibition has a broader and less predictable effect on cellular functions.

Source: Frost & Sullivan analysis.

The Use of Targeted Therapies in Combination Therapies

Combination therapy is the use of two or more medications or therapies to treat the same disease or condition. Often, the use of two or more oncology treatments is more efficacious than a single oncology treatment, also known as a monotherapy, because the combination therapy treats the cancer from multiple angles at the same time.

Highly selective therapies are optimal for use in combination therapies because they can be tailored to address biological processes that are most relevant to each cancer's molecular profile. By using multiple therapies that simultaneously work via different mechanisms, combination therapies can decrease the likelihood that resistant cancer cells will develop. Moreover, when drugs with different effects are combined, each drug can be used at its optimal dose. Meanwhile, reducing unnecessary kinase inhibition can also reduce unnecessary toxicity.

Targeted therapies have been approved and are being studied in clinical trials for use in combination with several types of oncology drugs or therapies, including:

- *Combination with chemotherapy*. Studies have shown significant improvements in the overall outcome of certain cancer patients when a targeted therapy is used in combination with chemotherapy. For example, the addition of a VEGFR inhibitor to chemotherapy has been demonstrated to show an increase in PFS and overall survival in certain types of cancers, and we are studying a similar combination in a Phase III clinical trial of fruquintinib in combination with Taxol in second-line gastric cancer patients in China.
- *Combination with other targeted therapies*. The use of two targeted therapies that affect different cancer pathways can slow disease progression and address, delay or prevent acquired resistance to a greater extent than using just one targeted therapy. Highly selective tyrosine kinase

inhibitors are ideal candidates for use together in combination therapies because, due to their high selectivity, each drug can be used at its maximum dose without intolerable side effects. For example, in a Phase II clinical trial we are studying our drug candidate savolitinib, a MET inhibitor, in combination with Tagrisso, AstraZeneca's approved EGFR inhibitor, for the treatment of a certain type of metastatic NSCLC.

- *Combination with immunotherapies*. Immunotherapies are one of the fastest- growing areas within oncology research. Combinations of targeted therapies and immunotherapies have shown great potential in ongoing clinical trials. Early evidence in Phase III clinical trials in certain cancer types suggests that using immunotherapies, such as PD-1 and PD-L1 checkpoint inhibitors, in combination with tyrosine kinase inhibitors, may result in an enhanced response compared to the use of either agent alone. We are focusing on the clinical development of savolitinib in combination with immunotherapy (Imfinzi). We are also focusing on the clinical development of our drug candidate fruquintinib in combination with anti PD-1 antibodies (Tyvyt, Tuoyi and tislelizumab) and chemotherapy (Taxol). In addition, we are currently focusing on the clinical development of surufatinib in combination with immunotherapies (Tuoyi, Tyvyt and tislelizumab).

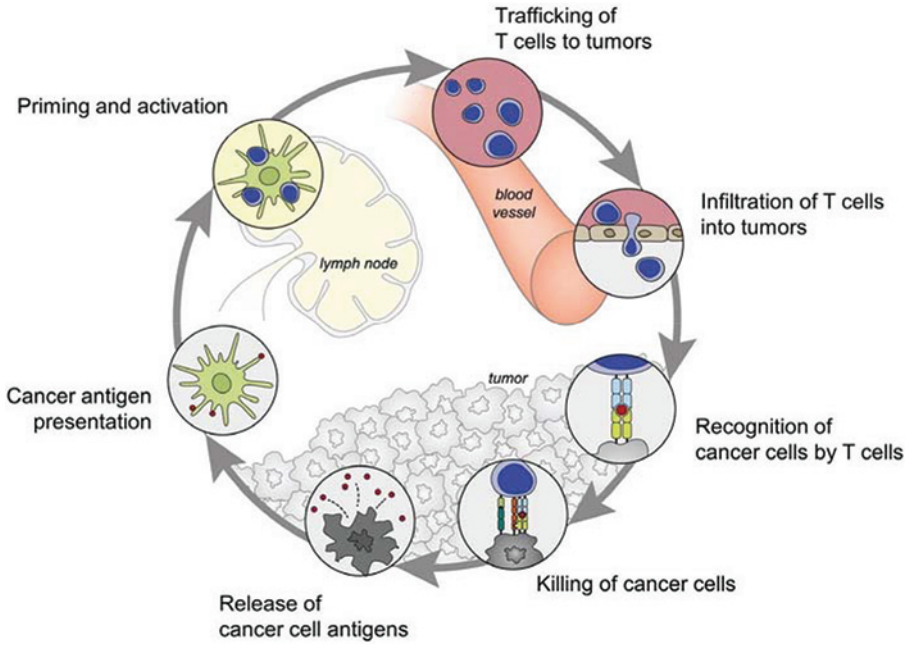
Many Angles of Attack Within the Cancer-Immunity Cycle

There are several processes involved when an immune response is effective in killing cancer cells. These steps are referred to as the cancer-immunity cycle. Combination treatments aim to be effective against cancer by addressing different parts of this cycle. Key parts of the cycle that targeted drugs can address include:

- *Release of cancer cell antigens*. Parts of aberrant cancer cells, particularly when they are killed by targeted therapies, are released into the bloodstream, allowing the immune system to recognize cancerous cells. Therapy targets being developed include MET, ERK, FGFR, IDH, RIP1K, ROS1 and Syk, among others.
- *Priming and activation*. Immune cells that specialize in antigen detection present antigens to T cells, priming them to look for and kill cells displaying those antigens. Stimulatory therapies being developed are designed to improve insufficient T cell response. Targets include OX40 and 4-1BB.
- *Trafficking and infiltration of T cells into tumors*. Activated T cells travel in the bloodstream to find and infiltrate the tumor microenvironment. Therapies in development aim to aid T cells in this process, including anti-angiogenic therapies such as VEGFR and FGFR inhibitors.
- *Recognition, and killing, of cancer cells by T cells*. T cells look for and kill cells displaying the cancer antigen. However, tumors often utilize various natural checkpoints that hinder T cells' ability to recognize and kill them. Therapy targets being developed include PD-1/PD-L1, CTLA4, Treg, CSF-1R, TIGIT, AhR, TIM3 and TCBs. Chimeric antigen receptor T cells, or CAR-T cells, are T cells that have been artificially encoded to recognize tumors.

Once the cancer cells are successfully killed by T cells, the cancer cells release antigens, and the cycle can repeat itself thereafter.

Steps in Activating the Immune Response for the Treatment of Cancer



Source: Adapted from Chen DS et al. Oncology Meets Immunology: The Cancer-Immunity Cycle. Immunity, Volume 39, Issue 1, 1 – 10; Frost & Sullivan analysis.

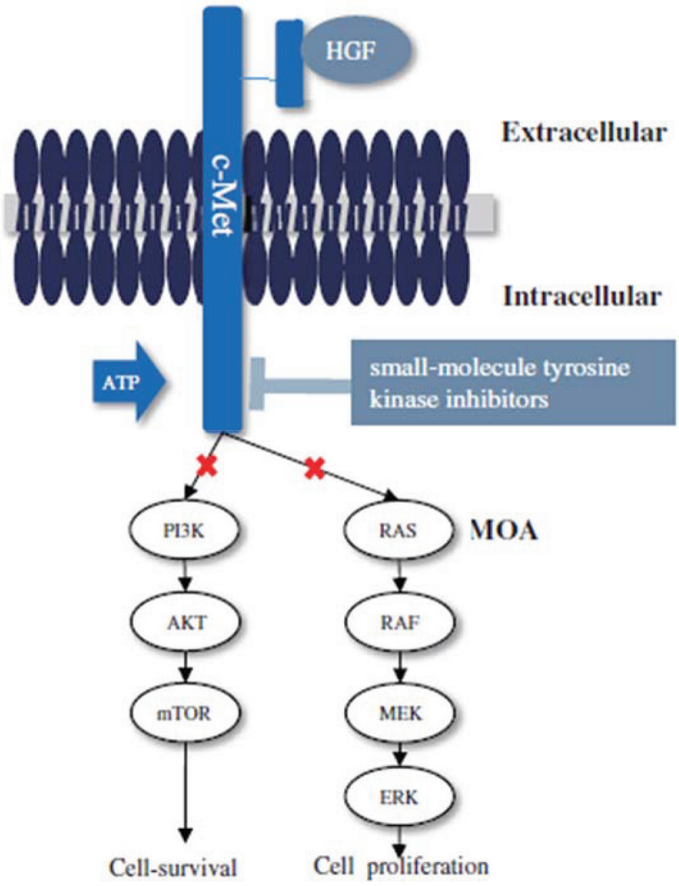
OVERVIEW OF MOLECULAR TARGETS AND MARKET LANDSCAPE

Our approved and clinical-stage drug candidates are highly selective therapies targeting a variety of novel and validated targets, including the MET, VEGFR, FGFR, CSF-1R, PI3Kδ, Syk, IDH, ERK and EGFR pathways, as described below. The drugs shown in the competitive landscape tables are small molecule therapies or biologic therapies.

MET Pathway

Overview of MET Inhibitors

MET is a receptor tyrosine kinase and its signaling pathway has specific roles in normal mammalian growth and development. However, the MET pathway has also been shown to function abnormally in a range of different cancers, primarily through MET gene amplification, overexpression and gene mutations. As a result, MET has become a widely investigated oncology target in recent years. The diagram below illustrates the mechanism of action of MET inhibitors.



Source: Frost & Sullivan.

Notes: After binding with c-Met's ATP, the ligand activates a wide range of cellular signaling pathways, including those involved in cell proliferation, motility, migration and invasion. By targeting the binding site of c-Met's ATP, c-Met Inhibitors block the phosphorylation and transduction of downstream signaling pathways, further suppressing the growth of tumors.

See "*Business – Our Clinical Pipeline – 1. Savolitinib MET Inhibitor – Mechanism of Action*" for more details.

Market Landscape

The following table sets out the incidence of different types of aberrant activation of MET in different primary tumor settings as well as the incidence of new cancer cases by tumor type globally and in China in 2020.

Aberrant Activation of MET in Different Tumor Settings

Indication	MET			New Cases (2020)	
	Amplification	Mutation	Over-expression	Global	China
Gastric	10%	1%	41%	1,089,100	469,600
Non-small Cell Lung Cancer (NSCLC)	4%/16%/30%[a]	2%[b]	39%	1,875,800	785,500
Head and Neck	17-39%	11%[c]	46%[d]	931,900	143,100
Colorectal	10%	3%	65%	1,880,700	453,400
Papillary Renal Cell Carcinoma (PRCC)	64%	17-33%[e]	55%	48,500	3,839
Clear Cell Renal Cell Carcinoma (CCRCC)	54%	N.A.[e]	35%	300,900	60,030
Esophagus	8%	1.4%[g]	92%	604,100	289,600
Prostate	0%[h]	1.06%[g]	54%/83%[f]	1,414,300	114,300

Notes:

(a) MET amplification for NSCLC occurs in approximately 4% of patients not previously exposed to systemic therapies and in up to 16% and 30% of patients with acquired resistance to 1st generation and 3rd generation EGFR TKIs, respectively.

(b) MET exon 14 skipping mutation only.

(c) Oropharynx squamous cell cancer only.

(d) Head and neck squamous cell cancer only.

(e) Mutations in renal cell carcinoma, Volume 38, Issue 10, October 2020, Pages 763-773.

(f) MET expression is increased with progression of prostate cancer, which is 54% of lymph node metastases and 83% of bone metastases.

(g) The AACR Project GENIE Consortium. AACR Project GENIE: powering precision medicine through an international consortium. Cancer Discovery. 2017;7(8):818-831. Dataset Version 8.

(h) MET expression during prostate cancer progression, Oncotarget, Vol. 7, No. 21.

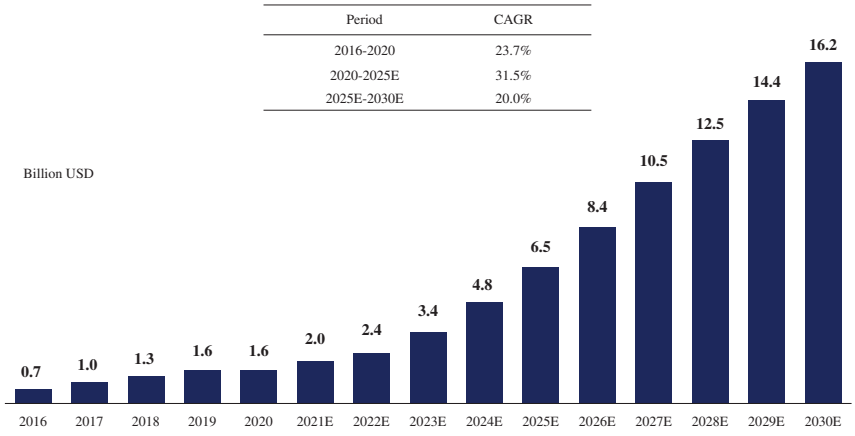
N.A. = data not available

Source: Frost & Sullivan analysis.

There is a highly unmet need for treatments that can overcome acquired resistance to anti-EGFR therapy. We believe this is the largest potential market for MET inhibitors. For example, the savolitinib and Tagrisso combination, if approved, could potentially be the first treatment option available for the approximately 16% to 30% of EGFRm+ inhibitor-resistant NSCLC patients whose tumors have MET amplification. Both overexpression and amplification are associated with MET pathway activation, and there can be heterogeneity within tumors or across metastatic sites. Generally, MET overexpression overlaps extensively with MET amplification, but there are some tumors that overexpress MET without MET amplification and vice versa. MET amplification is recognized as an effective driver of acquired resistance of EGFR therapy. MET overexpression can be responsible for the cancer formation by activating MET signaling pathway to promote tumor cell growth, survival, migration and invasion as well as tumor angiogenesis.

While there are currently no approved selective MET inhibitors on the market in China, two selective MET inhibitors are on the market in the United States and Japan: Tepmetko (tepotinib) and Tabrecta (capmatinib) are approved for MET exon 14 skipping NSCLC with additional programs focused on lung cancer underway. The global and China markets for small molecule MET inhibitors are expected to grow to US$16.2 billion and US$4.8 billion by 2030, respectively, with the majority of the growth occurring after 2021 when the first highly selective MET inhibitor is expected to launch, as shown in the charts below:

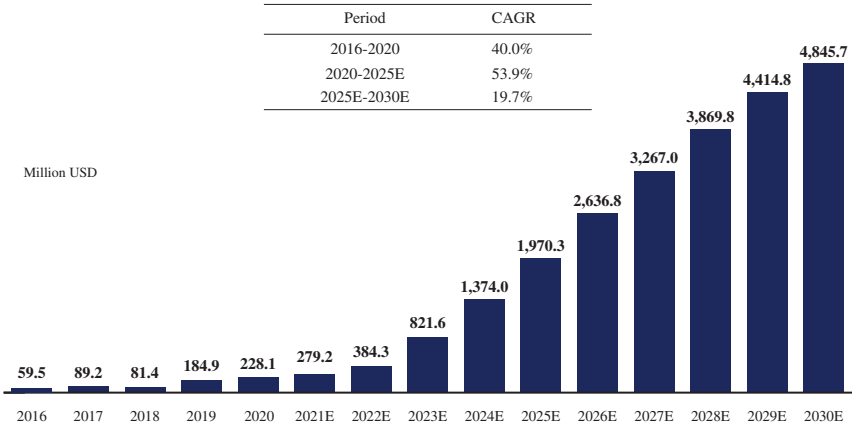
Global Market for Small Molecule MET Inhibitors, 2016-2030E



Note: E = estimated.

Source: Frost & Sullivan analysis.

China Market for Small Molecule MET Inhibitors, 2016-2030E



Notes: US$1 = RMB6.5; and E = estimated.

Source: Frost & Sullivan analysis.

Our drug candidate savolitinib is a selective MET inhibitor in global development for the treatment of lung cancer, kidney cancer, gastric cancer and CRC. As evidenced by the recently published final data analysis from our TATTON (Part B) study, savolitinib demonstrated meaningful clinical benefits to patients with a certain type of metastatic NSCLC patients in combination with Tagrisso.

We are not aware of any other selective MET inhibitors in late-stage clinical development.

A summary of the competitive landscape of approved MET inhibitors and drug candidates in development in China and globally is set out below.

Marketed Small Molecule MET Targeted Therapies for Cancer Treatment Globally

Brand Name	Generic Name	Company	FDA Approval	Indication
Tabrecta	Capmatinib	Novartis/Incyte	2020-05-06	• Adult patients with metastatic NSCLC whose tumors have a mutation that leads to MET 14 skipping
Tepmetko	Tepotinib	EMD Serono (a Merck KGaA subsidiary)	2021-02-03	• Adult patients with metastatic NSCLC whose tumors have a mutation that leads to MET 14 skipping

Small Molecule MET Targeted Therapies for Cancer Treatment under Clinical Development Globally

TherapDrug Name	Company	Indication	Clinical Stage	Mono/Combo Therapy
Bozitinib APL-101	Apollomics	• NSCLC	Phase II	Mono
TPX-0022	Turning Point Therapeutics	• Solid Tumors	Phase I	Mono

Source: Clinicaltrials.gov, FDA, Frost & Sullivan Analysis

Small Molecule MET Targeted Therapies for Cancer Treatment Under Clinical Development in China

INN/Drug Code	Company	Indication	Clinical Stage	Mono/Combo Therapy
Cabozantinib	Simcere	• Advanced RCC, Hepatocellular Carcinoma	ANDA	Mono
	Jiangsu Vcare Pharmatech	• Advanced RCC, Hepatocellular Carcinoma	Biologics Evaluation	Mono
	Jiangsu Aosaikang Pharmaceutical			
	Jiangsu Hansoh Pharmaceutical			
Bozitinib	Beijing Pearl Bio-Science	• NSCLC	Phase II	Mono
		• Neuroglioma	PhaseII/III	Mono
Glumetinib	TopAlliance Biosciences	• Relapsed Metastatic NSCLC	Phase Ib/II	Combo
	Shanghai Institute of Materia Medica. Chinese Academy of Sciences/ GreenValley/Haihe Biopharma	• Relapsed Metastatic NSCLC	Phase Ib/II	Combo
		• Advanced NSCLC with MET Mutation		Mono
Tepotinib	Beijing Merck Serono (a Merck KGaA Subsidiary)	• NSCLC with MET Amplification	PhaseII	Mono
		• Local/Advanced/Metastatic NSCLC	PhaseII	Mono
AL2846	CTTQ (a Sino Biopharma subsidiary)	• Advanced NSCLC with Bone Metastasis	PhaseII	Mono
Capmatinib	Novartis Pharmaceuticals	• Advanced NSCLC Harboring MET Exon 14 Skipping Mutation	PhaseII	Mono

Source: NMPA, Chinadrugtrials.org.cn, CDE, Frost & Sullivan Analysis

MET mAbs for Cancer Treatment under Clinical Development Globally

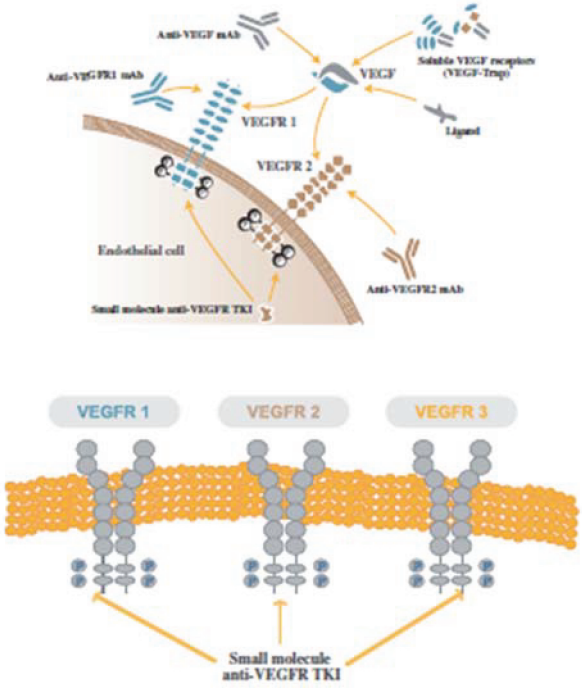
Drug Code	Company	Indication	Clinical Stage	Mono/Combo Therapy
Amivantamab	Genmab, Janssen (a J&J subsidiary)	• Metastatic NSCLC with EGFR Exon 20 Insertion Mutations	Biologics License Applications	N/A
Telisotuzumab ABBV-399	AbbVie	• NSCLC	Phase II	Mono
MCLA-129	Merus	• NSCLC and other Solid Tumors	Phase I/II	Mono

Source: NMPA, Clinicaltrials.gov, CDE, Frost & Sullivan Analysis

VEGFR Pathway

Overview of VEGFR Inhibitors

During the development of cancer, tumors at an advanced stage can secrete large amounts of VEGF, a protein ligand, to stimulate formation of excessive vasculature (angiogenesis) around the tumor in order to provide greater blood flow, oxygen and nutrients to fuel the rapid growth of the tumor. Inhibition of the VEGF/VEGFR signaling pathway can act to stop the growth of the vasculature around the tumor and thereby starve the tumor of the nutrients and oxygen it needs to grow rapidly. The diagram below illustrates the mechanism of action of VEGFR inhibitors.



Source: Frost & Sullivan.

Notes: During the development of cancer, tumors at an advanced stage can secrete large amounts of VEGF, a protein ligand, to stimulate formation of excessive vasculature (angiogenesis) around the tumor in order to provide greater blood flow, oxygen and nutrients to fuel the rapid growth of the tumor. VEGF and other ligands can bind to three VEGF receptors, VEGFR 1, 2 and 3, each of which has been shown to play a role in angiogenesis. Therefore, inhibition of the VEGF/VEGFR signaling pathway can act to stop the growth of the vasculature around the tumor and thereby starve the tumor of the nutrients and oxygen it needs to grow rapidly.

See "*Business – Our Clinical Pipeline – 3. Fruquintinib VEGFR 1, 2 and 3 Inhibitor – Mechanism of Action" and "Business – Our Clinical Pipeline – 2. Surufatinib VEGFR 1, 2 and 3, FGFR1 and CSF-1R Inhibitor – Mechanism of Action*" for more details.

Potential for Combination with Immunotherapies

It is theorized that targeting VEGFR may help restore part of the cancer-immunity cycle by enhancing T-cell infiltration into the tumor microenvironment. Therefore, simultaneous inhibition of VEGF and immune checkpoints such as PD-L1 and PD-1 may be a rational combination therapy. Multiple clinical studies have demonstrated that the combination of VEGF/R inhibitor with a PD-1 or PD-L1 inhibitor results in a better outcome than either agent alone. Recently, the FDA approved Roche's Tecentriq, a monoclonal antibody against PD-L1, in combination with Avastin, a VEGF inhibitor, and chemotherapy for first-line treatment of metastatic NSCLC without EGFR or ALK mutations.

The FDA has approved the following three filings for combination in clear cell renal cell carcinoma: (i) Inlyta with Keytruda (based on the 861-patient KEYNOTE-426 study), (ii) Inlyta with Bavencio (based on the 886-patient JAVELIN Renal 101 study) and (iii) Opdivo with Cabometyx (based on the 651-patient CHECKMATE-9ER study). The Inlyta and Keytruda combination therapy showed that the patients receiving such therapy had a higher objective response rate than patients in the monotherapy arms, as described in the chart below:

Comparison of Response Rates between VEGFR Inhibitor Monotherapy, PD-1 Inhibitor Monotherapy, and VEGFR Inhibitor and PD-1 Inhibitor Combination Therapy in First-line Clear Cell Kidney Cancer

Sources:

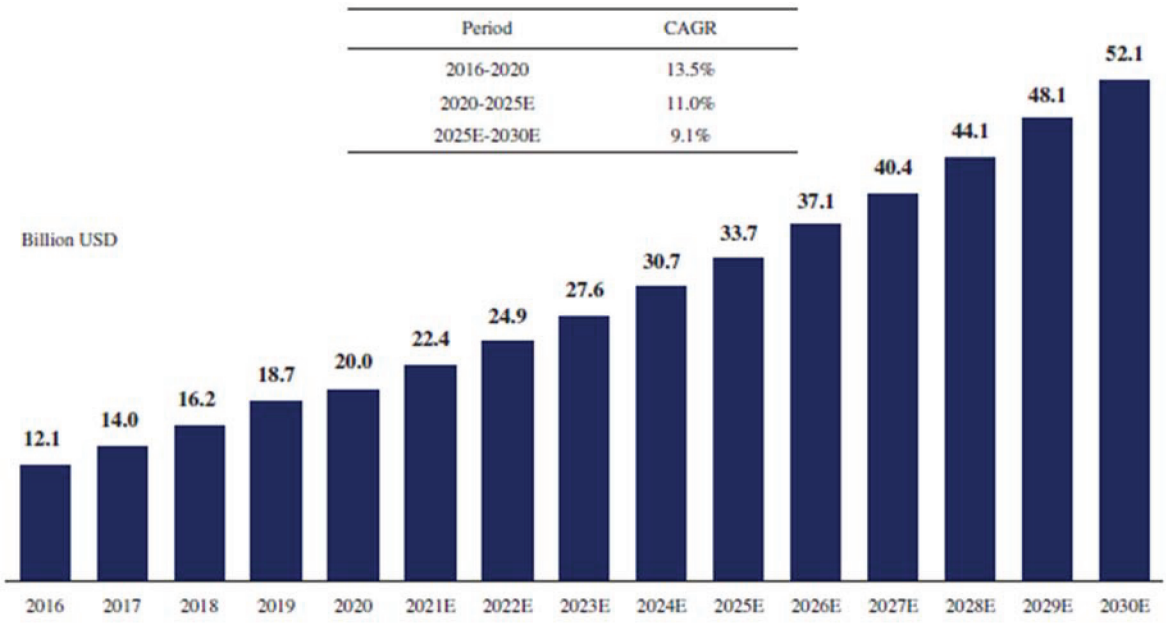
(1) B. Rini et al, for the KEYNOTE-426 Investigators, NEJM 2019 Feb 16. doi: 10.1056/NEJMoa1816714, Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma.

(2) D.F. McDermott et al, ASCO 2018 #4500, Pembrolizumab monotherapy as first-line therapy in advanced clear cell renal cell carcinoma (accRCC): Results from cohort A of KEYNOTE-427.

Market Landscape

The global market for VEGFR therapies was estimated at approximately US$20.0 billion in 2020, including both monoclonal antibodies and small molecules approved in around 26 tumor settings. The global market for VEGFR therapies is expected to grow to US$52.1 billion by 2030, as shown in the chart below.

Global Market for VEGFR Therapies, 2016-2030E



Note: E = estimated.

Source: Frost & Sullivan analysis.

Fruquintinib capsules, self-discovered and developed by our Company and sold under the brand name Elunate in China, were approved for marketing in China by the NMPA in September 2018 and commercially launched in late November 2018 for third-line treatment of mCRC. Fruquintinib is a VEGFR 1, 2 and 3 inhibitor that has the potential to be a VEGFR inhibitor with the best selectivity for its targets in global Phase III development due to its superior kinase selectivity compared to other small molecule VEGFR inhibitors, which can be prone to excessive off-target toxicities. A global registration study of Fruquintinib is ongoing in the United States, Europe and Japan in refractory mCRC. Fruquintinib is in clinical development for the treatment of CRC, gastric cancer, NSCLC and other solid tumors.

Our self-discovered and developed drug candidate surufatinib is an oral small molecule inhibitor targeting VEGFR 1, 2 and 3, FGFR1 and CSF-1R. Targeting CSF-1R, in addition to VEGFR 1, 2 and 3 and FGFR1, gives surufatinib a unique angio-immune profile. See "*– Overview of CSF-1R Inhibitors*" for more details.

A summary of the competitive landscape of approved VEGFR inhibitors and drug candidates in development in China and globally is set out below.

Marketed Small Molecule Targeted VEGFR Therapies for Cancer Treatment in the U.S.

Brand Name	INN	Company	FDA Approval	Indication
Nexavar	Sorafenib	Bayer	2005-12-01	• Unresectable hepatocellular carcinoma (HCC) • Advanced RCC • Locally recurrent or metastatic, progressive, differentiated thyroid carcinoma (DTC) refractory to radioactive iodine treatment

Brand Name	INN	Company	FDA Approval	Indication
Sutent	Sunitinib	CPPI CV (a Pfizer subsidiary)	2006-01-26	• Gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate advanced RCC • Adjuvant treatment of adult patients at high risk of recurrent RCC following nephrectomy progressive, well-differentiated pancreatic NET in patients with unresectable locally advanced or metastatic disease
Votrient	Pazopanib	Novartis	2009-10-19	• Advanced RCC • Advanced soft tissue sarcoma who have received prior chemotherapy
Caprelsa	Vandetanib	Genzyme (a Sanofi subsidiary)	2011-04-06	• Symptomatic or progressive medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease
Inlyta	Axitinib	PF Prism CV (a Pfizer subsidiary)	2012-01-27	• Advanced RCC after failure of one prior systemic therapy
Stivarga	Regorafenib	Bayer	2012-09-27	• mCRC previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if RAS wild-type, an anti-EGFR therapy • Locally advanced, unresectable or metastatic GIST who have been previously treated with imatinib mesylate and sunitinib malate • HCC previously treated with sorafenib
Cometriq	Cabozantinib	Exelixis	2012-11-29	• Patients with progressive, metastatic MTC
Vargatef[(1)]	Nintedanib	Boehringer Ingelheim	—	• For the treatment of adult patients with locally advanced, metastatic or locally recurrent NSCLC of adenocarcinoma tumor histology after first-line chemotherapy
Lenvima	Lenvatinib	Eisai	2015-02-13	• For the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory DTC • In combination with everolimus, for the treatment of patients with advanced RCC following one prior anti-angiogenic therapy • For the first-line treatment of patients with unresectable HCC

Brand Name	INN	Company	FDA Approval	Indication
Cabometyx	Cabozantinib	Exelixis	2016-04-25	• patients with advanced RCC • patients with HCC who have been previously treated with sorafenib
Fotivda	Tivozanib	Aveo Oncology	2021-03-10	• Patients with relapsed or refractory advanced RCC

Note:

(1) EMA approval on November 21, 2014.

Source: Clinicaltrials.gov, Frost & Sullivan Analysis

Marketed Small Molecule Targeted VEGFR Therapies for Cancer Treatment in China

Brand Name	INN	Company	CFDA Approval	Indication	Approximate Average Monthly Cost(based on the latest bidding price)[1]	NRDL
Nexavar	Sorafenib	Bayer	2006-09-12	• Unresectable or distant metastatic hepatocellular carcinoma (HCC)	USD1,754	√
				• Unresectable advanced RCC		
				• Gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate	USD2,862	
Sutent	Sunitinib	Pfizer	2007-10-30	• Unresectable RCC	USD2,862	√
				• Adjuvant treatment of adult patients at high risk of recurrent RCC following nephrectomy progressive, well-differentiated pancreatic NET in patients with unresectable locally advanced or metastatic disease	USD2,146	
Aitan	Apatinib	Hengrui	2014-10-17	• Patients with recurrent or advanced gastric adenocarcinoma or gastric esophageal junction adenocarcinoma who have received at least two types of systemic chemotherapy before	USD1,594	√
				• HCC		
Inlyta	Axitinib	Pfizer	2015-04-29	• Advanced RCC after failure of one prior systemic therapy	USD1,815	√
Votrient	Pazopanib	Novartis	2017-02-21	• Firstline treatment for advanced RCC and advance RCC patients who has been treated with cytokines before	USD2,954	√

Brand Name	INN	Company	CFDA Approval	Indication	Approximate Average Monthly Cost(based on the latest bidding price)[1]	NRDL
Stivarga	Regorafenib	Bayer	2017-03-22	• mCRC previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if RAS wild-type, an anti-EGFR therapy • Locally advanced, unresectable or metastatic GIST previously treated with imatinib mesylate and sunitinib • HCC who have been previously treated with sorafenib	USD2,381	√
Focus V	Anlotinib	CTTQ (a Sino Biopharma subsidiary)	2018-05-08	• Small Cell Lung Cancer, Advanced/Metastatic NSCLC, Advanced/Metastatic Medullary Thyroid Carcinoma, Advanced/ Metastatic Soft Tissue Sarcoma	USD991	√
Lenvima	Lenvatinib	Eisai	2018-09-04	• Patients with unresectable HCC who have not previously received systemic therapy	USD1,495	√

Source: CDE, FDA, Frost & Sullivan Analysis

Note: The pricing and reimbursement coverage is only available for China and is set by the MoHRSS.

VEGFR Small Molecule Targeted VEGFR Therapies for Cancer Treatment Under Clinical Development in China

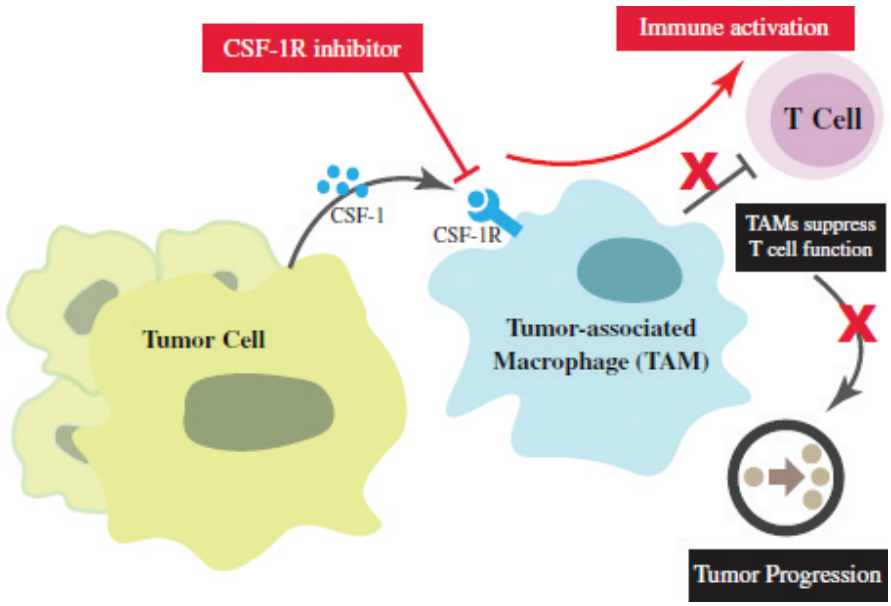
Drug Name	Company	Indication	Clinical Stage	Combo/Mono Therapy
Donafenib	Suzhou Zelgen Biopharmaceuticals	• Advanced Hepatocellular Carcinoma	NDA	Mono
Famitinib	Jiangsu Hengrui Medicine	• Advanced gastrointestinal stromal tumor	Phase III	Mono
		• Recurrent or Metastatic Cervical Cancer	Phase II	Combo
		• Advanced NSCLC	Phase II	Mono
		• Advanced urinary system tumors	Phase II	Mono
		• Intrahepatic cholangiocarcinoma	Phase II	Mono
CM082	Canaanji Medical Science (a Betta Pharma subsidiary)	• Metastatic Kidney Cancer	Phase II	Combo
EOC315	Taizhou Edding Group	• Gastric Cancer	Phase II	Combo
Sitravatinib	BeiGene	• Advanced/Metastatic Hepatocellular Carcinoma/ Gastroesophageal Junction Carcinoma	Phase I/II	Mono/Combo

Source: Chinadrugtrials.org.cn, CDE, Frost & Sullivan Analysis

CSF-1R Pathway

Overview of CSF-1R Inhibitors

CSF-1R plays an important role in the functions of macrophages. The CSF-1R signaling pathway promotes recruitment of M2 macrophages to the tumor microenvironment. This type of tumor-associated macrophage facilitates the development of tumors by secreting proangiogenic and growth factors and suppressing T-cell effector function by releasing immune-suppressive cytokines. Several tumor types have been shown to overexpress the CSF-1 ligand. The diagram below illustrates the mechanism of action of CSF-1R inhibitors.



Source: Frost & Sullivan.

Notes: Colony-stimulating factor (CSF-1) is a cytokine that controls the proliferation, differentiation, migration and survival of tumor-associated macrophages (TAMs) via its receptor, CSF-1R. The presence of TAMs appears to be an adverse prognostic factor in many types of cancers, as TAMs suppress T cell proliferation and activation and cause immunosuppression in the tumor microenvironment. Inhibition of the CSF-1/CSF-1R pathway may therefore represent an appealing therapeutic strategy to regulate tumor microenvironment and improve efficacy of cancer treatment.

See "*Business – Our Clinical Pipeline – 2. Surufatinib VEGFR 1, 2 and 3, FGFR1 and CSF-1R Inhibitor – Mechanism of Action*" for more details.

Market Landscape

Our self-discovered and developed drug candidate surufatinib is an oral small molecule angio-immuno kinase inhibitor targeting VEGFR 1, 2 and 3, FGFR1 and CSF-1R. We believe that its unique angio-immuno kinase profile represents market opportunities as a monotherapy and in combinations with checkpoint inhibitors against various cancers.

Currently, Turalio is the only FDA approved CSF-1R inhibitor drug, and Sulanda is the only CSF-1R inhibitor drug that has been marketed in China. As such, this represents an unmet medical need and large potential market opportunity. A variety of small molecules and monoclonal antibodies directed at CSF-1R or its ligand CSF-1, are in clinical development both as monotherapy and in combination with standard treatments.

A summary of the competitive landscape of approved CSF-1R inhibitors and drug candidates in development in China and globally is set out below.

Marketed CSF-1R Targeted Therapies for Cancer Treatment Globally

Brand Name	INN	Company	FDA Approval	Indication
Turalio	Pexidartinib	Daiichi Sankyo	2019-08-02	• For the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery

Source: Clinicaltrials.gov, FDA, Frost & Sullivan Analysis

CSF-1R Targeted Therapies for Cancer Treatment under Clinical Development Globally

Drug Name	Company	Clinical Stage	Indication	Mono/ Combo Therapy
AMB05X	AmMax Bio	Phase II	• Tenosynovial Giant Cell Tumor	Mono
BLZ945	Novartis	Phase II	• Amyotrophic Lateral Sclerosis	Mono
NMS-03592088	Nerviano	Phase I/II	• Acute myeloid leukemia, Chronic myelomonocytic leukemia	Mono
DCC-3014	Deciphera Pharmaceuticals	Phase I/II	• Advanced Malignant Neoplasm	Mono
			• Giant Cell Tumor of Tendon Sheath	
			• Tenosynovial Giant Cell Tumor	
Axatilimab SNDX-6352	Syndax	Phase II	• Chronic Graft-versus-host-disease	Mono
		Phase II	• Unresectable Intrahepatic Cholangiocarcinoma	Combo

Source: Clinicaltrials.gov, FDA, Frost & Sullivan Analysis

Syk and PI3Kδ/B-cell Signaling Pathways

B-cell Signaling Pathways

Targeting the B-cell signaling pathway is emerging as a potential means to treat both hematological cancer and immunological diseases. Inhibiting PI3Kδ and BTK, two kinases found along the B-cell signaling pathway, has proven to have clinical efficacy in hematological cancers, with three breakthrough therapies having been recently approved by the FDA. Syk is a key kinase upstream to PI3Kδ and BTK within the B-cell signaling pathway and therefore thought to be an important target for modulating B-cell signaling.

Overview of PI3Kδ Inhibitors

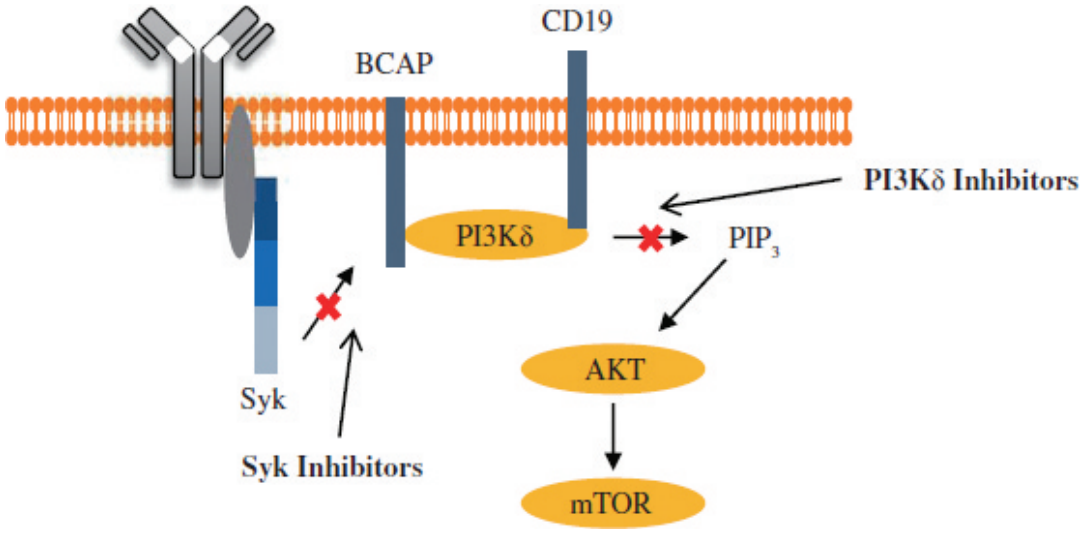
PI3Kδ is a lipid kinase that, through a series of intermediate processes, controls the activation of several important signaling proteins, including the serine/threonine kinase AKT. In most cells, AKT is a key PI3Kδ effector that regulates cell proliferation, carbohydrate metabolism, cell motility and apoptosis and other cellular processes.

Aberrant B-cell function has been observed in multiple immunological diseases and B-cell mediated malignancies. Therefore, PI3Kδ is considered to be a promising target for drugs that aim to prevent or

treat hematologic cancer, autoimmunity and transplant-organ rejection and other related inflammation diseases. See "*Business – Our Clinical Pipeline – 4. HMPL-689 PI3Kδ Inhibitor – Mechanism of Action*" for more details.

Overview of Syk Inhibitors

Syk is a tyrosine kinase expressed primarily in hematopoietic cells like B cells, monocytes, macrophages, mast cells and neutrophils and is recognized as a critical element in the B-cell signaling pathway upstream to PI3Kδ and BTK. The diagram below illustrates the mechanism of action of Syk and PI3Kδ inhibitors.



Source: Frost & Sullivan.

Notes: PI3Kδ participates in the signal transduction of B-cell receptor (BCR) in B cells and controls the development and maturation of B cells in the body. BCR is a membrane immunoglobulin. When the body is stimulated by an antigen, the specific surface immunoglobulin Ig on the surface of the BCR can bind to the antigen, leading to the phosphorylation of ITAM in the intracellular segment of the Igα/Igβ complex and the phosphorylated ITAM can recruit and activate Syk, and further activate BTK and its downstream pathways. Activated Syk can bind to the p85 subunit of PI3Kδ, activate PI3Kδ, and promote the generation of PIP3. The generated PIP3 can recognize and interact with the N-terminal domain of BTK to mediate the recruitment of BTK to the membrane, thereby activating BTK-mediated Guided B cell signal transduction, inducing the expression of many related genes. In addition, phosphorylated CD19 can also recruit PI3Kδ on the cell membrane, thereby activating PI3Kδ, catalyzing PIP2 to generate PIP3, promoting AKT activation, and regulating cell proliferation, migration, and apoptosis. Syk couples the B cell receptor for antigen (BCR) to the activation of mTOR.

See "*Business – Our Clinical Pipeline – 5. HMPL-523 Syk Inhibitor – Mechanism of Action*" for more details.

The safety threshold for a Syk inhibitor in chronic immunological diseases is extremely high, with no room for material toxicity. Our self-discovered and developed drug candidate HMPL-523, if approved, potentially could be the first selective Syk inhibitor for oncology that offers important safety advantages due to a unique pharmacokinetic profile based on promising early clinical results.

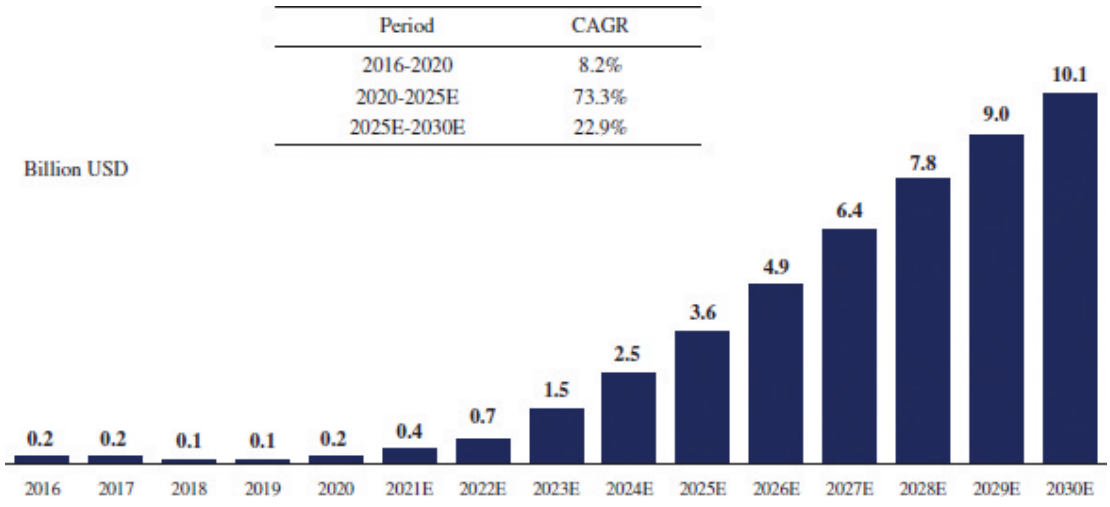
Although Syk has a specific inhibition profile, it may also affect other kinase pathways by identifying not only substrates of the kinase of interest but also substrates of off-target kinases. Off-target effects of Syk inhibitors include adverse events like diarrhea, nausea, and fatigue if the dosage is not properly controlled.

Market Landscape

Syk and PI3Kδ inhibitors have significant potential due to the large number of patients affected by hematological malignancies and immunological diseases. Safety needs to be balanced against efficacy as these patients live longer with their disease compared to many other types of cancers.

The market for PI3K therapies is expected to rise to US$10.1 billion globally by 2030 as shown in the chart below. There has not been significant growth in the global PI3K drug market in the past several years. However, as there was a recent new launch of a new PI3K inhibitor and several active late-stage programs, the global market is expected to experience an expansion.

Global Market for PI3K Therapies, 2016-2030E

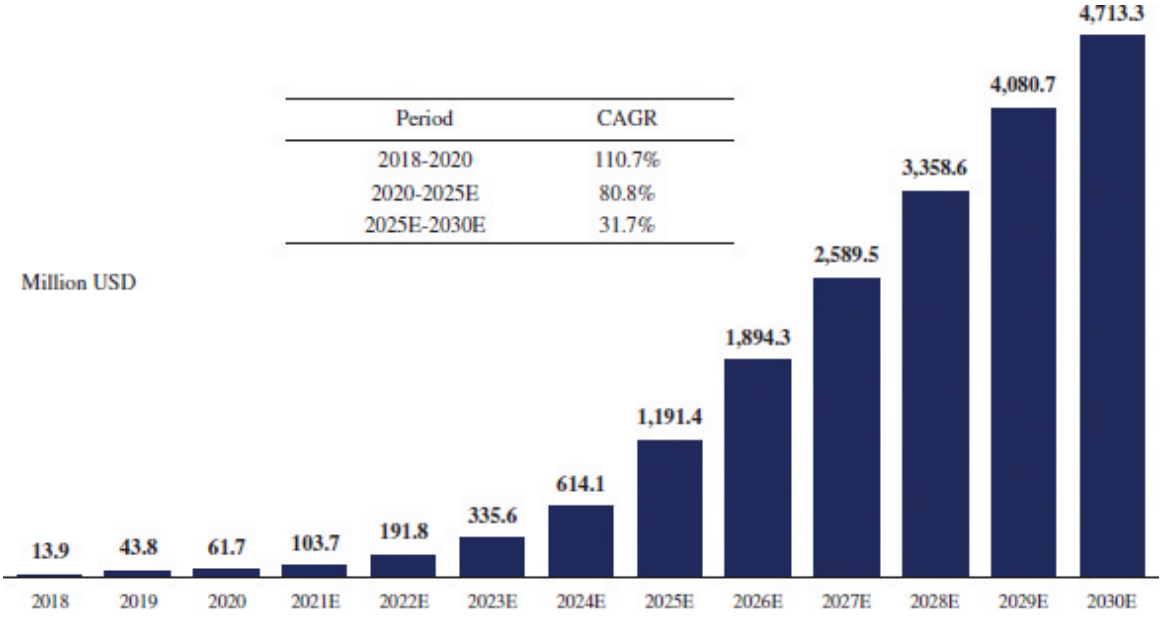


Note: E = estimated.

Source: Frost & Sullivan analysis.

The market for Syk therapies is expected to meet US$4.7 billion globally by 2030 as shown in the chart below. The global Syk drug market is still at a limited size since there is only one approved drug. As there are several drug candidates under Phase II studies, the market is expected to grow at an increased pace in the future.

Global Market for Syk Therapies, 2018-2030E



Note: E = estimated.

Source: Frost & Sullivan analysis.

A summary of the competitive landscape of approved Syk inhibitors and drug candidates in development in China and globally is set out below.

Marketed Small Molecule Syk Targeted Therapies for Cancer Treatment in the U.S.

Brand Name	INN	Company	FDA Approval	Indication
Tavalisse	Fostamatinib	Rigel	2018-04-17	• For the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment.

Source: FDA, Frost & Sullivan Analysis

Small Molecule Syk Targeted Therapies under Clinical Development Globally

Drug Name	Company	Clinical Stage	Indication	Mono/Combo Therapy
Gusacitinib ASN002	Asana BioScience	Phase II	• Chronic Hand Eczema	Mono
Entospletinib	Kronos Bio	Phase I/II	• Acute myeloid leukemia with NMP1 or FLT3 mutations	Combo
Cerdulatinib	Alexion Pharmaceuticals (being acquired by AZ)	Phase I/II	• Follicular lymphoma, non-Hodgkin lymphomas (NHL), small lymphocytic lymphoma • Peripheral T-cell lymphoma • B-Cell NHL	Mono
SKI-O-703	Oscotec	Phase II	• ITP	Mono

Source: Clinicaltrials.gov, Frost & Sullivan Analysis

Our self-discovered and developed drug candidate HMPL-689 is potentially selective PI3Kδ inhibitor with the best PI3Kδ isoform selectivity which we believe may offer advantages over currently approved drugs to minimize the risk of serious infection caused by immune suppression and compound-related toxicity.

Despite proven efficacy of other Syk inhibitors in clinical trials, the only small molecule drug candidate targeting Syk specifically that has been approved to date is Tavalisse for the treatment of chronic immune thrombocytopenia. Most Syk inhibitors studied have shown high levels of off-target toxicity as a result of lower kinase selectivity and their possibly poor pharmacokinetic properties.

We see potential for our Syk and PI3Kδ inhibitors to be combined with targeted therapies.

A summary of the competitive landscape of approved PI3Kδ inhibitors and drug candidates in development in China and globally is set out below.

Marketed Small Molecule PI3Kδ Targeted Therapies for Cancer Treatment in the U.S.

Brand Name	INN	Company	FDA Approval	Indication
Zydelig	Idelalisib	Gilead	2014-07-23	• Relapsed chronic lymphocytic leukemia (CLL), in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities • Relapsed follicular lymphoma (FL) in patients who have received at least two prior systemic therapies • Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior systemic therapies
Aliqopa(1)	Copanlisib(1)	Bayer	2017-09-14	• Adult patients with relapsed FL who have received at least two prior systemic therapies
Copiktra(2)	Duvelisib(2)	Secura Bio	2018-09-24	• Relapsed or refractory CLL or SLL after at least two prior therapies • Relapsed or refractory FL after at least two prior systemic therapies
Ukoniq	Umbralisib	TG Therapeutics	2021-02-05	• Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen. • Relapsed or refractory FL who have received at least three prior lines of systemic therapy.

Notes:

(1) Copanlisib is PI3Kα and PI3Kδ targeted.

(2) Duvelisib is PI3Kδ and PI3Kγ targeted.

Source: FDA, Frost & Sullivan Analysis

Small Molecule PI3Kδ Targeted Therapies for Cancer Treatment Under Clinical Development Globally

Drug Name	Company	Clinical Stage	Indication	Mono/Combo Therapy
ME-401 (Zandelisib)	MEI Pharma	Phase III	• Follicular lymphoma, non-Hodgkin lymphomas (NHL), marginal zone lymphoma	Combo
HEC68498 (Parsaclisib)	Incyte	Phase II	• B cell malignant tumour	Mono/ Combo
Tenalisib	Rhizen Pharmaceuticals	Phase II	• Hematological malignancy, NHL	Combo

Source: Clinicaltrials.gov, Frost & Sullivan Analysis

Small Molecule PI3Kδ Targeted Therapies for Cancer Treatment Under Clinical Development in China

Drug Name	Company	Clinical Stage	Indication	Mono/Combo Therapy
Duvelisib	CSPC (licensed from Secura Bio)	NDA	• Relapsed / Refractory Follicular Lymphoma	Mono
TQB3525[(1)]	CTTQ (a Sino Biopharma subsidiary)	Phase II	• Relapsed/Refractory Follicular Lymphoma	Mono
			• Relapsed/Refractory Mantle Cell Lymphoma (MCL)	Mono
SHC014748M	Nanjing Sanhome Pharmaceutical	Phase II	• Peripheral T cell lymphoma	Mono
			• Follicular lymphoma, marginal zone lymphoma	Mono
Linperlisib YY-20394	Shanghai YingLi Pharmaceutical and Hengrui	Phase II	• Relapsed and/or refractory peripheral T/NK cell lymphoma	Mono
			• Peripheral T-cell lymphoma	Mono
			• Follicular Lymphoma	

Notes:

(1) TQB3525 is PI3Kα and PI3Kδ targeted.

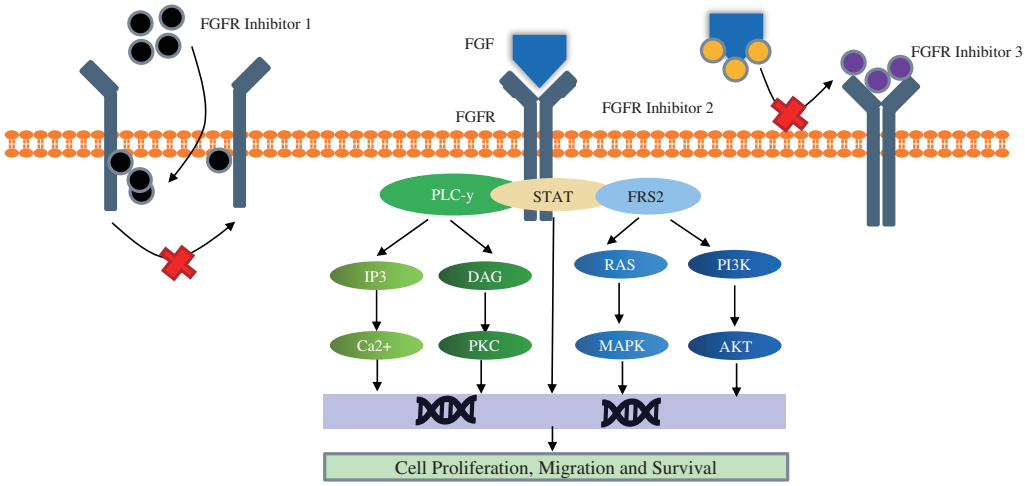
(2) Duvelisib is PI3Kδ and PI3Kγ targeted.

Source: Chinadrugtrials.org.cn, CDE, Frost & Sullivan Analysis

FGFR Pathway

Overview of FGFR Inhibitors

FGFR belongs to a subfamily of receptor tyrosine kinases. FGF/FGFR signaling regulates a wide range of basic biological processes, including tissue development, angiogenesis and tissue regeneration. Given the inherent complexity and critical roles in physiological processes, dysfunction in the FGF/FGFR signaling leads to a number of developmental disorders and is consistently found to be a driving force in cancer. The diagram below illustrates the mechanism of action of FGFR inhibitors.



Source: Frost & Sullivan.

Notes: As implied by their name, these receptors bind fibroblast growth factors which are members of the largest family of growth factor ligands comprising 22 members.

Phosphorylation of different downstream molecules activates the FGFR pathway and ultimately leads to cell proliferation, migration and survival.

See "*Business – Our Clinical Pipeline – 2. Surufatinib VEGFR 1, 2 and 3, FGFR1 and CSF-1R Inhibitor – Mechanism of Action*" and "*Business – Our Clinical Pipeline – 6. HMPL-453 FGFR Inhibitor – Mechanism of Action*" for more details.

Market Landscape

The global market for small molecule FGFR inhibitors is still at a size of US$84.1 million as there are only two drugs approved by FDA but is expected to grow to US$15.6 billion by 2030.

There is an unmet medical need and large potential market opportunity with respect to FGFR inhibitors. There are only two FGFR inhibitors approved for marketing, which are Balversa and Pemazyre, and such drugs have not been listed in China. Several small molecule FGFR tyrosine kinase inhibitors are in clinical trials for solid tumors, including our drug candidate HMPL-453.

A summary of the competitive landscape of approved FGFR inhibitors and drug candidates in development in China and globally is set out below.

Marketed FGFR Targeted Therapies for Cancer Treatment Globally

Brand Name	INN	Company	Indication	FDA Approval	NMPA Approval
Balversa	Erdafitinib	Janssen (a J&J subsidiary)	• Urothelial Cancer	2019-04-12	—
Pemazyre	Pemigatinib	Incyte	• Cholangiocarcinoma	2020-04-17	—

Source: Clinicaltrials.gov, FDA, Frost & Sullivan analysis

FGFR Targeted Therapies for Cancer Treatment under Clinical Development Globally

Drug Name	Company	Clinical Stage	Indication	Mono/Combo Therapy
Futinatinib TAS-120	Taiho Oncology (an Otsuka Holdings subsidary)	Phase III	• Advanced Cholangiocarcinoma	Mono
		Phase II	• Hepatocellular Carcinoma	Combo
		Phase II	• Advanced or Urothelial Cancer	Combo
		Phase II	• Gastric Cancer or Gastroesophageal Cancer	Mono
		Phase II	• Breast Cancer	Combo
Infigratinib BGJ398	QED Therapeutics	Phase III	• Advanced cholangiocarcinoma	Mono
		Phase III	• Urothelial Cancer	Mono
ABSK-091 AZD4547	AstraZeneca (out-licensed to Abbisko)	Phase II	• NSCLC	Combo
Derazantinib ARQ 087	Basilea	Phase II	• Intrahepatic cholangiocarcinoma	Mono
Bemarituzumab FPA144	Five Prime Therapeutics (an Amgen	Phase II	• Gastric Cancer	Combo

Drug Name	Company	Clinical Stage	Indication	Mono/Combo Therapy
	subsidiary)			
CH-5183284 Debio1347	Debiopharm	Phase II	• Solid tumor	Mono
E-7090	Eisai	Phase II	• Cholangiocarcinoma	Mono
Gunagratinib ICP-192	Beijing Innocare Pharm Tech	Phase II	• Bladder Urothelial Cancer	Mono
		Phase I/II	• Urothelial Carcinoma Cholangiocarcinoma	Mono
Roblitinib FGF401	Novartis/ Everest Medicines	Phase I/II	• Hepatocellular carcinoma	Mono
Fisogatinib BLU-554	CStone	Phase I/II	• Hepatocellular carcinoma	Combo

Source: Chinadrugtrials.gov, CDE, Frost & Sullivan Analysis

FGFR Targeted Therapies for Cancer Treatment under Clinical Development in China

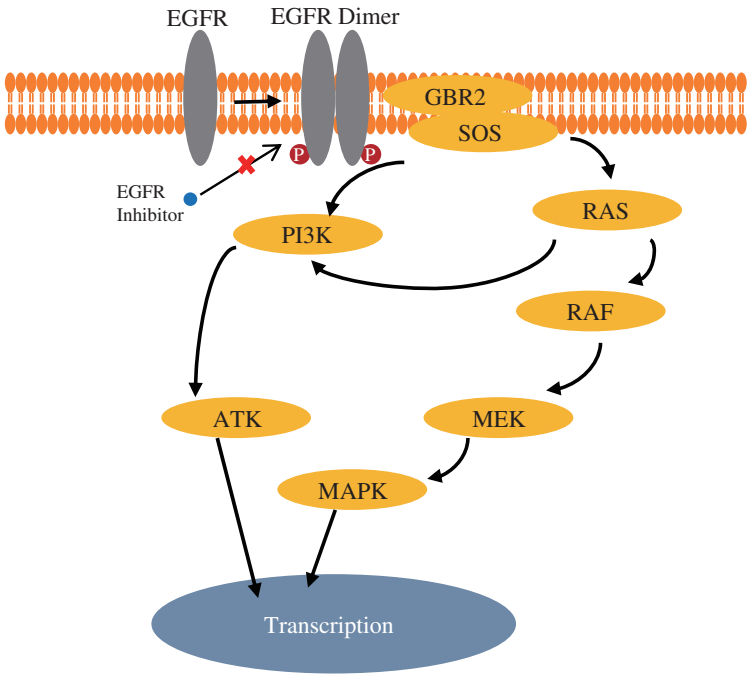
Drug Name	Company	Clinical trial	Indication	Mono/Combo Therapy
Erdafitinib	Xian Janssen (a J&J subsidiary)	Phase III	• Advanced urothelial carcinoma	Mono
Pemigatinib	Innovent (licensed from Incyte)	Phase III	• Cholangiocarcinoma	Mono
Gunagratinib ICP-192	Tiancheng/ InnoCare	Phase II	• Bladder urothelial carcinoma	Mono
Bemarituzumab FPA144	Zai Lab/Five Prime Therapeutics (an Amgen subdisiary)	Phase II	• Gastric Cancer, GEJC	Combo
Roblitinib FGF401	Novartis/ Everest Medicines	Phase I/II	• Hepatocellular carcinoma or solid malignant tumor	Mono
Fisogatinib BLU-554	CStone	Phase Ib/II	• Hepatocellular carcinoma	Combo

Source: Chinadrugtrials.org.cn, CDE, Frost & Sullivan Analysis

EGFR Pathway

Overview of EGFR Inhibitors

EGFR is a protein that is a cell surface receptor tyrosine kinase for epidermal growth factor. Activation of EGFR can lead to a series of downstream signaling activities that activate tumor cell growth, survival, invasion, metastasis and inhibition of apoptosis. Treatment strategies for certain cancers involve inhibiting EGFRs with small molecule tyrosine kinase inhibitors. The diagram below illustrates the mechanism of action of EGFR inhibitors.



Source: Frost & Sullivan.

Notes: Activation of EGFR can lead to a series of downstream signaling activities that activate tumor cell growth, survival, invasion, metastasis and inhibition of apoptosis. Tumor cell division can happen uncontrollably when the pathway is abnormally activated through EGFRm+, gene amplification of wild type EGFR or over expression of wild type EGFR. Treatment strategies for certain cancers involve inhibiting EGFRs with small molecule tyrosine kinase inhibitors. Once the tyrosine kinase is disabled, it cannot activate the EGFR pathway and trigger downstream signaling activities, thereby suppressing cancer cell growth.

See "*Business – Our Clinical Pipeline – 9. Epitinib EGFR Inhibitor*".

Market Landscape

The global and China markets for small molecule EGFR inhibitors are expected to grow to US$23.3 billion and US$9.3 billion by 2030, respectively.

There are successful examples of clinical efficacy among patients with EGFR overexpression in tumor types such as CRC and head and neck cancer. Many EGFR inhibitors have been approved for the treatment of NSCLC with EGFR activating mutations.

A summary of the competitive landscape of approved EGFR inhibitors and drug candidates in development in China and globally is set out below.

Marketed EGFR Targeted Therapies for Cancer Treatment in China and Globally

Brand Name	INN	Company	FDA Approval	NMPA Approval	Indication	Approximate Average Monthly Cost (based on the latest bidding price)[1]	NRDL
Iressa	Gefitinib	AstraZeneca	2003-05-05	2004-12-06	• Advanced EGFR Mutation	USD230	√
					• Metastatic NSCLC		
Conmana	Icotinib	Betta Pharma	—	2016-05-31	• Advanced EGFR Mutation	USD887	√
					• Metastatic NSCLC		
Tarceva	Erlotinib	Roche and OSI Pharma (an Astellas Pharma subsidiary)	2004-11-18	2006-04-06	• Pancreatic Cancer	USD274	√
					• NSCLC	USD328	
Gilotrif	Afatinib	Boehringer Ingelheim	2013-07-12	2017-02-21	• Advanced EGFR Mutation	USD766	√
					• Metastatic NSCLC		
Vizimpro	Dacomitinib	Pfizer	2018-09-27	2019-05-15	• Advanced EGFR Mutation	USD2,612	x
					• Metastatic NSCLC		
Tagrisso	Osimertinib	AstraZeneca	2015-11-13	2017-03-22	• Advanced EGFR Mutation	USD858	√
					• Metastatic NSCLC		
Ameile	Almonertinib/ Aumolertinib	Jiangsu Hansoh Pharmaceutical	—	2020-03-17	• Metastatic NSCLC	USD1,625	√
Olita[2]	Olmutinib	Hanmi Pharmaceutical	—	—	• NSCLC	—	x
Aifusha	Furmonertinib	Allist Pharmaceutical	—	2021-03-02	• NSCLC	USD5,275	x
Leclaza[3]	Lazertinib	J&J (exclude Korea)	—	—	• NSCLC	—	x

Notes:

(1) The pricing and reimbursement coverage is only available for China and is set by the MoHRSS.

(2) Ministry of Food and Drug Safety ("MFDS") Approval in May 2016.

(3) MFDS Approval in Jan 2021, developed by Yuhan, bought by Janssen for the development in the worldwide excluding the Republic of South Korea.

Source: FDA, NMPA, Frost & Sullivan Analysis

EGFR Targeted Therapies for Cancer Treatment Under Clinical Development Globally

Drug Name	Company	Clinical Stage	Indications	Mono/Combo Therapy
Mobocertinib TAK-788	Takeda	Phase III	• Advanced/ Metastatic NSCLC	Mono
FCN-411	Ahon Pharmaceutical	Phase I/II	• Lung Cancer	Mono
DZD-9008	Dizal Pharmaceuticals	Phase I/II	• NSCLC	Mono

Source: Clinicaltrials.gov, CDE, Frost & Sullivan Analysis

EGFR Targeted Therapies for Cancer Treatment Under Clinical Development in China

Drug Name/Code	Company	Clinical Stage	Indication	Mono/Combo Therapy
Osimertinib	Wanbang Pharma	ANDA	• NSCLC	Mono
BPI-D0316	Betta Pharma	NDA	• NSCLC	Mono
RX518/ CK-101	Neu Pharma	Phase III	• Advanced NSCLC	Mono
Larotinib	HEC	Phase III	• Esophageal Squamous Cell Carcinoma	Mono
Mobocertinib TAK-788	Takeda	Phase III	• Locally advanced or metastatic NSCLC	Mono
SH-1028	Sanhome	Phase III	• Locally advanced or metastatic NSCLC	Mono
Mefatinib	Huadong Medicine	Phase III	• Locally advanced or metastatic NSCLC	Mono
ASK120067	Jiangsu Aosaikang Pharmaceutical	Phase III	• Locally advanced or metastatic NSCLC	Mono
BPI-7711	Betta Pharma	Phase III	• Advanced or metastatic NSCLC	Mono
D-0316/ BPI-D0316	InventisBio/ Betta	Phase II/ III	• Locally advanced or metastatic NSCLC	Mono
Zorifertinib AZD3759	Alpha Biopharma	Phase II/ III	• Advanced NSCLC	Mono
TL007	Jiangsu Medolution	Phase II	• Advanced NSCLC with brain metastasis or brain metastasis progression after EGFR-TKI treatment	Mono

Drug Name/Code	Company	Clinical Stage	Indication	Mono/Combo Therapy
SZMD4	Jiangsu Medolution/ Teligene	Phase II	• Locally advanced or metastatic NSCLC, specialized on rare mutations without resistance	Mono
XZP-5809-TT1	Xuanzhu Biopharm	Phase I/II	• Locally advanced or metastatic NSCLC	Mono
FHND9041	CTFH	Phase I/II	• NSCLC	Mono
DZD-9008	Dizal Pharma	Phase I/II	• Advanced NSCLC With EGFR/ HER2	Mono

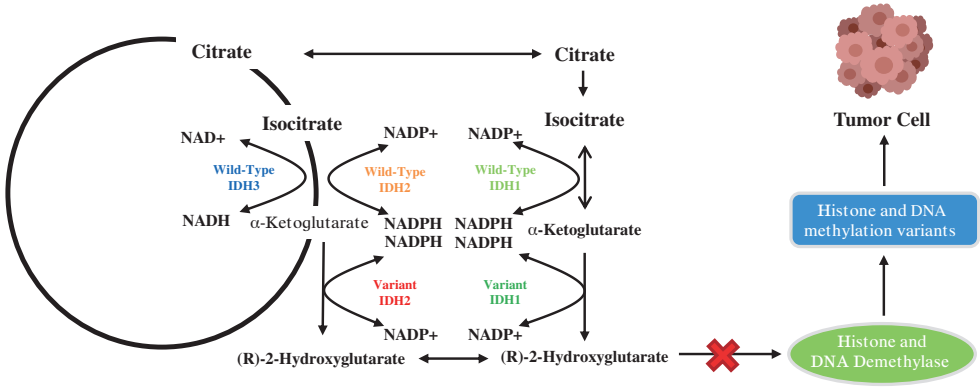
Source: Chinadrugtrials.org.cn, CDE, Frost & Sullivan Analysis

IDH

Overview of IDH1 and IDH2 Inhibition

IDH is a digestive enzyme used in the citric acid cycle. The reaction catalyzed by IDH is one of the most important sources of NADPH/NADH and other substances in cells. It also plays an important role in maintaining the steady state of cell redox balance. IDH1 and IDH2 are subtypes of IDH in the human body. IDH1 and IDH2 mutations have been implicated as drivers of certain hematological malignancies, gliomas and solid tumors, particularly among acute myeloid leukemia patients. The diagram below illustrates the mechanism of action of IDH inhibitors.

IDH1/2 Inhibitor Mechanism



Source: Frost & Sullivan.

Notes: The IDH family converts isocitrate to a-KG via oxidative decarboxylation, an important process for normal cellular metabolism. However, mutant IDH1/2 catalyze the reaction of a-KG to 2-HG, leading to accumulation of 2-HG in tumor cells. IDH inhibitors could restore 2-HG levels to normal physiological levels, induce tumor cell differentiation and ultimately stop tumor cell progression. Mutant IDH isoform switching, either from cytoplasmic mutant IDH1 to mitochondrial mutant IDH2, or vice versa, is a mechanism of acquired resistance to IDH inhibition.

See "*Business – Our Clinical Pipeline – 7. HMPL-306*".

Market Landscape

Currently, there are only two IDH inhibitor drugs (ivosidenib and enasidenib) approved by the FDA. Tibsovo is an approved therapy that specifically inhibits IDH1, while Idhifa is an approved therapy that specifically inhibits IDH2. Both of these drugs are for the treatment of adult patients with relapsed

or refractory acute myeloid leukemia. To date, there are no approved therapies that inhibit both IDH1 and IDH2. Our drug candidate HMPL-306 currently in development is a novel small molecule dual-inhibitor of IDH1 and IDH2. A pan-IDH inhibitor, vorasidenib, is currently in late-stage development for glioma.

A summary of the competitive landscape of approved IDH inhibitors and drug candidates in development in China and globally is set out below.

Marketed IDH1&2 Targeted Therapies for Cancer Treatment in the U.S.

Brand Name	INN	Company	FDA Approval	Target	Indication
Tibsovo	Ivosidenib	Agios (divested to Servier)	2018-07-20	IDH1	• For the treatment of adult patients with relapsed or refractory acute myeloid leukemia with a susceptible IDH1 mutation
Idhifa	Enasidenib	Celgene (acquired by BMS)	2017-08-01	IDH2	• For the treatment of adult patients with relapsed or refractory acute myeloid leukemia with an IDH2 mutation

Source: FDA, Frost & Sullivan Analysis

IDH1&2 Targeted Therapies for Cancer Treatment Under Clinical Development Globally

Drug Name	Company	Clinical Stage	Indication	Target	Mono/Combo Therapy
AG-881 (Vorasidenib)	Agios (divested to Servier)	Phase III	• Grade 2 Glioma • Residual Glioma • Recurrent Glioma	IDH1/2	Mono
Mobocertinib DS-1001b	Daiichi Sankyo	Phase II	• WHO Grade II Glioma	IDH1	Mono
FT-2102 (Olutasidenib)	Forma	Phase I/II	• Acute Myeloid Leukemia (AML) • Myelodysplastic Syndrome	IDH1	Combo

Source: Clinicaltrials.gov, Frost & Sullivan Analysis

IDH1&2 Targeted Therapies for Cancer Treatment Under Clinical Development in China

Drug Name	Company	Clinical Stage	Indication	Target	Mono/Combo Therapy
Enasidenib AG-221	Celgene (acquired by BMS)	Phase III	• Avanced Acute Myeloid Leukemia (AML)	IDH2	Mono

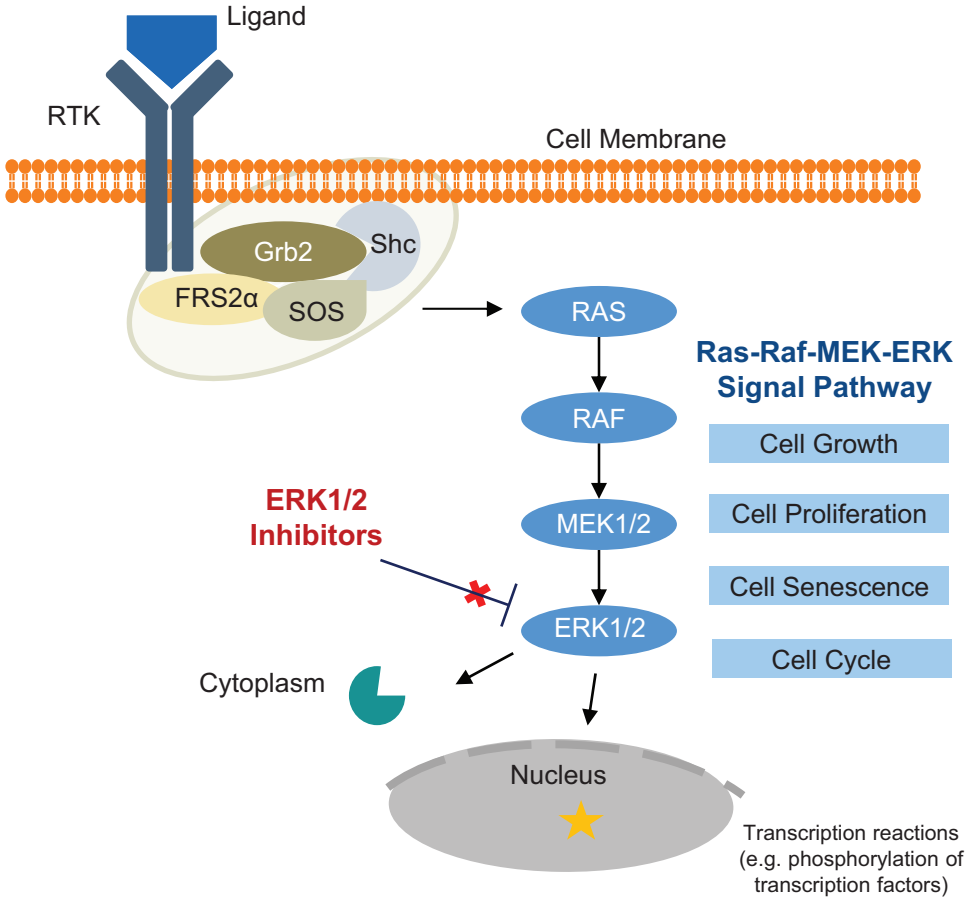
Source: Chinadrugtrials.org.cn, Frost & Sullivan Analysis

ERK

Overview of ERK Inhibition

ERK is a downstream component of the RAS-RAF-MEK-ERK signaling cascade (MAPK pathway). RAS-MAPK pathway is dysregulated in human diseases, particularly cancer, in which

mutations or nongenetic events hyperactivate the pathway in more than 50% of cancers. Activating mutations in RAS genes occur in more than 30% of cancers. They predict worse clinical prognosis in a wide variety of tumor types, mediate resistance to targeted therapies and decrease the response to standard of care, target therapy and immunotherapy. On the MAPK pathway, KRAS inhibitors are under clinical evaluation, and acquired resistance develops for RAF/MEK targeted therapies. ERK inhibition has the potential to overcome or avoid the intrinsic or acquired resistance from upstream mechanisms. The diagram below illustrates the mechanism of action of ERK inhibitors.



Source: Frost & Sullivan.

Notes: Once a mutation is activated in RAS genes, ERK1/2 will phosphorylate a series of substrates in the cytoplasm and nucleus, including phosphoric acid, kinases, cytoskeletal proteins and transcription factors, which play an indispensable role in cell death and cell proliferation. After the constitutive phosphorylation of upstream effectors, ERK1/2 is activated to phosphorylate its cytoplasm and nuclear substrates, thereby promoting tumor growth. ERK1/2 inhibitors prevent the normal interaction between proteins and their substrates through ATP-related or non-ATP-related pathways, thereby inhibiting the activity of ERK1/2, thereby inhibiting tumor growth.

See "*Business – Our Clinical Pipeline – 8. HMPL-295*".

Market Landscape

Several ERK 1&2 inhibitor drugs are in clinical trials. Our drug candidate HMPL-295 is an investigative and highly selective small molecule inhibitor of ERK in the MAPK pathway with the potential to address intrinsic or acquired resistance from upstream mechanisms such as RAS-RAF-MEK.

A summary of the competitive landscape of approved ERK inhibitor drug candidates in development in globally is set out below.

ERK1&2 Targeted Therapies for Cancer Treatment Under Clinical Development Globally

Drug Name	Company	Clinical Stage	Indications	Mono/Combo Therapy
Ulixertinib (BVD-523)	BioMed Valley Discoveries	Phase II	• Advanced Solid Tumor • BRAF Gene Mutation • BRAF Gene Alteration • MEK Mutation • MEK Alteration • MAP2K1 Gene Mutation • MAP2K1 Gene Alteration • MAP2K2 Gene Mutation • MAP2K2 Gene Alteration	Mono/Combo
HH2710	Shanghai Haihe Pharmaceutical	Phase I/II	• Advanced Tumors • Melanoma • NSCLC • Erdheim-Chester Disease • Other RAS/RAF/MEK/ERK • Mutated Tumors	Mono
ASTX029	Astex (an Otsuka subsidiary)	Phase I/II	• Solid Tumor, Adult	Mono

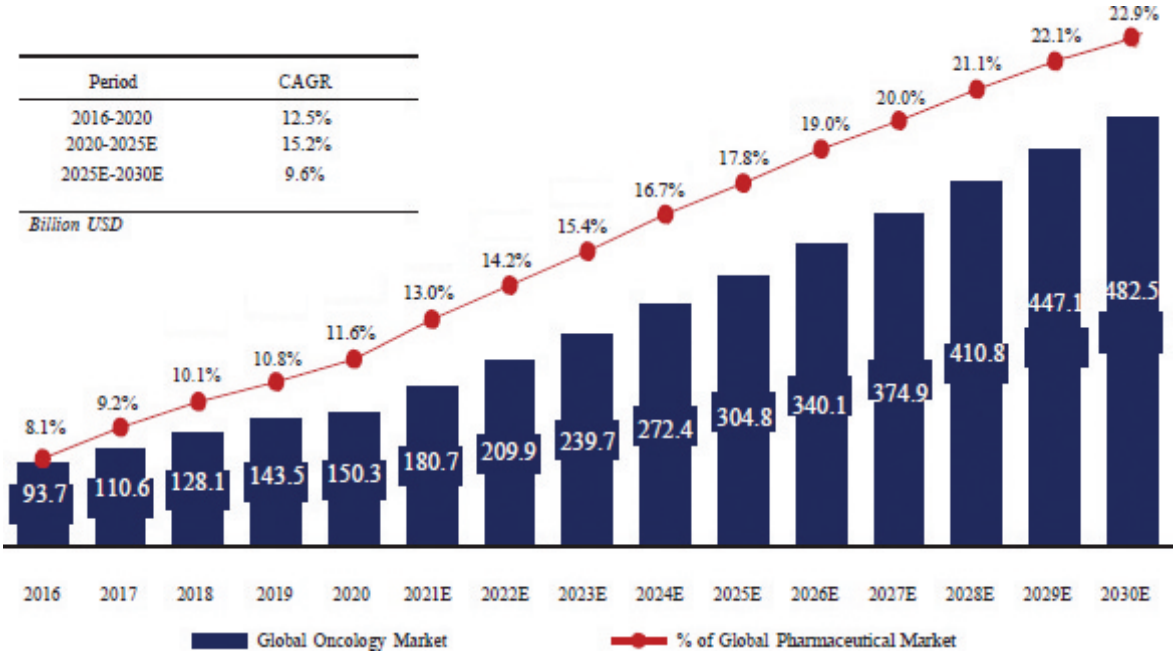
Source: Clinicaltrials.gov, CDE, Frost & Sullivan Analysis

OVERVIEW OF THE ONCOLOGY DRUG MARKET

Global Oncology Drug Market

The global oncology drug market is growing rapidly and expected to outpace growth in the overall pharmaceutical market. The market grew from US$93.7 billion in 2016 to US$150.3 billion in 2020, representing a CAGR of 12.5% during this period as compared to 3.0% growth in the overall pharmaceutical market during the period. Between 2020 and 2025, the global oncology market is expected to grow at a CAGR of 15.2% while the overall global pharmaceutical market is expected to grow at a CAGR of 5.7%. Between 2025 and 2030, the global oncology market is expected to grow at a CAGR of 9.6% while the overall pharmaceutical market is expected to grow at a CAGR of 4.2%. By 2030, the global oncology market is expected to grow to US$482.5 billion by 2030, representing 22.9% of the global pharmaceutical market compared to 11.6% in 2020, as shown in the following chart:

Global Oncology Drug Market, 2016-2030E



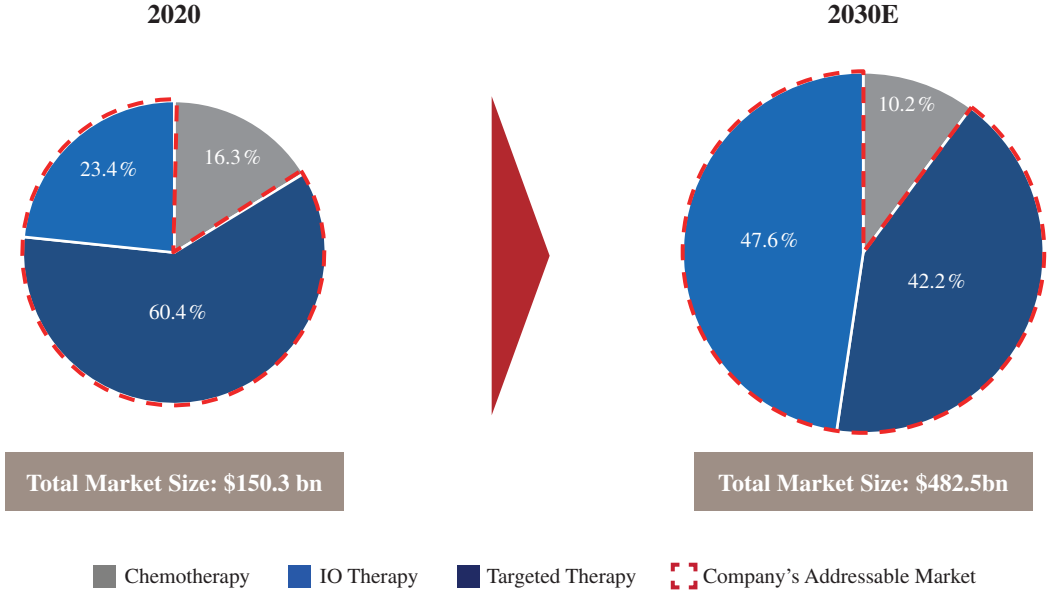
Note: E = estimated.

Source: Frost & Sullivan analysis.

Global Market for Targeted Therapies and Immunotherapies

In 2020, the global market for targeted therapies and immunotherapies reached a combined US$125.8 billion. The market is expected to grow to US$433.3 billion by 2030. Currently, targeted therapies and immunotherapies comprise 83.8% of the global market and are expected to comprise 89.8% by 2030 as shown in the chart below:

Breakdown of the Global Oncology Market by Therapy, 2020 and 2030E



Notes: bn = billion; IO Therapy = Immunotherapy; and E = estimated.

Source: Frost & Sullivan analysis.

Trends affecting growth in the U.S. oncology market generally foreshadow the development of the market globally, in particular the following factors:

Innovative oncology therapies are key growth drivers. Sales of new oncology drugs launched in the United States from 2013 to 2018 represented over 64% of the U.S. oncology market's growth during the period according to IQVIA Institute's Global Oncology Trends 2019 report.

Growth driven by earlier access to novel therapies. A key reason growth within the U.S. oncology market is seen as emblematic of the changing cancer treatment landscape in other developed countries is that it tends to have access to medicines earlier than the rest of the world. Other developed countries use centralized government price-setting and reimbursement coverage decisions, resulting in significantly slower reimbursement coverage.

Targeted indications command premium pricing. Median prices for new targeted therapy drugs have increased to US$175,000 in 2018, from a mean of US$144,000 during the period from 2012 to 2018 according to IQVIA Institute's Global Oncology Trends 2019 report. This is attributable to the large number of drugs being approved for a small number of patients and the significant clinical benefits brought by many new treatments.

Longer duration of treatment with novel therapies. Newer treatments extend survival and active treatment time frames. Furthermore, patients unable to take current cancer therapies or who have developed resistance to initial therapies may be able to take advantage of new options and lines of therapy.

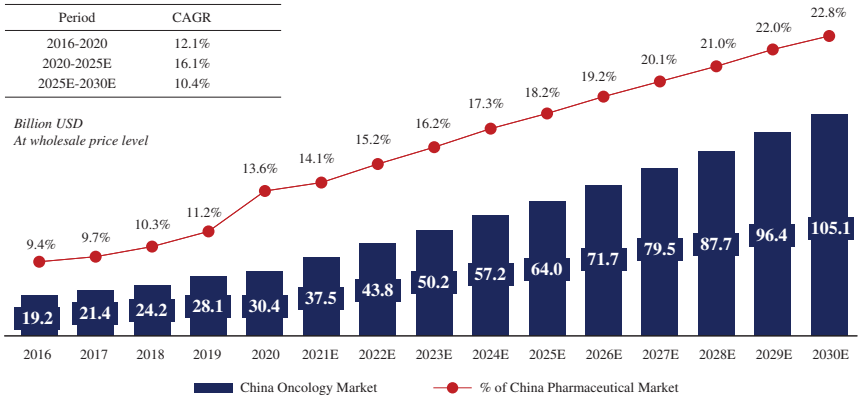
Use of combination therapies with novel therapies. The trend toward combination therapy is likely to continue to improve patient outcomes and drive growth in the U.S. market. Newly launched immuno-oncology drugs, which have dramatically impacted the treatment landscape, are supplements to be used in combination with, rather than as replacement of, existing targeted therapy treatments and are therefore expected to contribute to increased spending on drugs.

We anticipate that the foregoing factors will also contribute to revenue growth over time in the oncology market in China and elsewhere.

China Oncology Drug Market

The market for oncology drugs in China has grown rapidly in recent years and is expected to continue to maintain a high growth rate in the near future. In 2016, the market was US$19.2 billion, accounting for 9.4% of China's pharmaceutical market and increased to US$30.4 billion and 13.6% of China's pharmaceutical market in 2020. This represented a CAGR of 12.1%, and double-digit annual growth is expected to continue between 2020 and 2030, with the market expected to reach US$105.1 billion by 2030, accounting for 22.8% of China's pharmaceutical market, as shown in the following chart:

China Oncology Market 2016-2030E



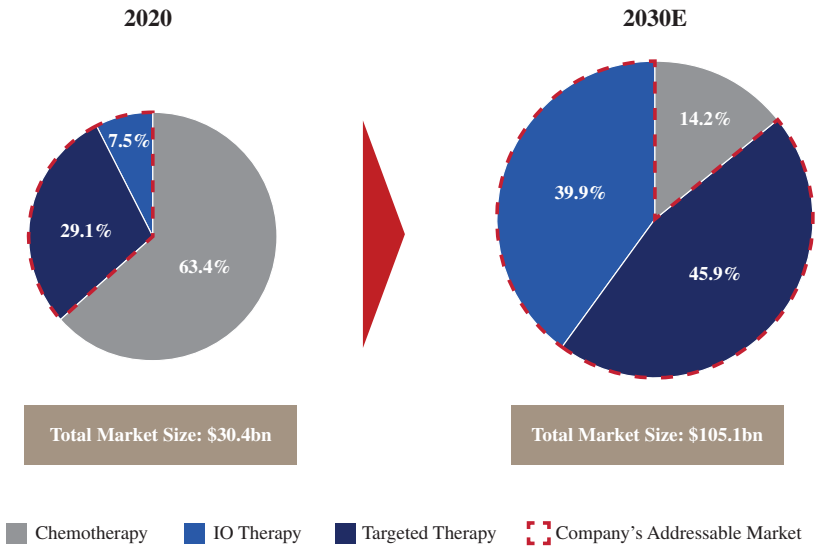
Notes: US$1 = RMB6.5; and E = estimated.

Source: Frost & Sullivan analysis.

China Market for Targeted Therapies and Immunotherapies

Unlike the global oncology market, China's oncology market is still dominated by traditional chemotherapies. The market for targeted therapies and immunotherapies in China was US$11.1 billion in 2020. With favorable policies, new drugs launched and increasing affordability for patients, this market is expected to grow to US$90.2 billion by 2030. By 2030, targeted therapies and immunotherapies are expected to comprise 85.8% of the market, as shown in the following chart:

Breakdown of the China Oncology Market by Therapy, 2020-2030E



Notes: At wholesale price level. bn = billion; IO Therapy = Immunotherapy; and E = estimated.

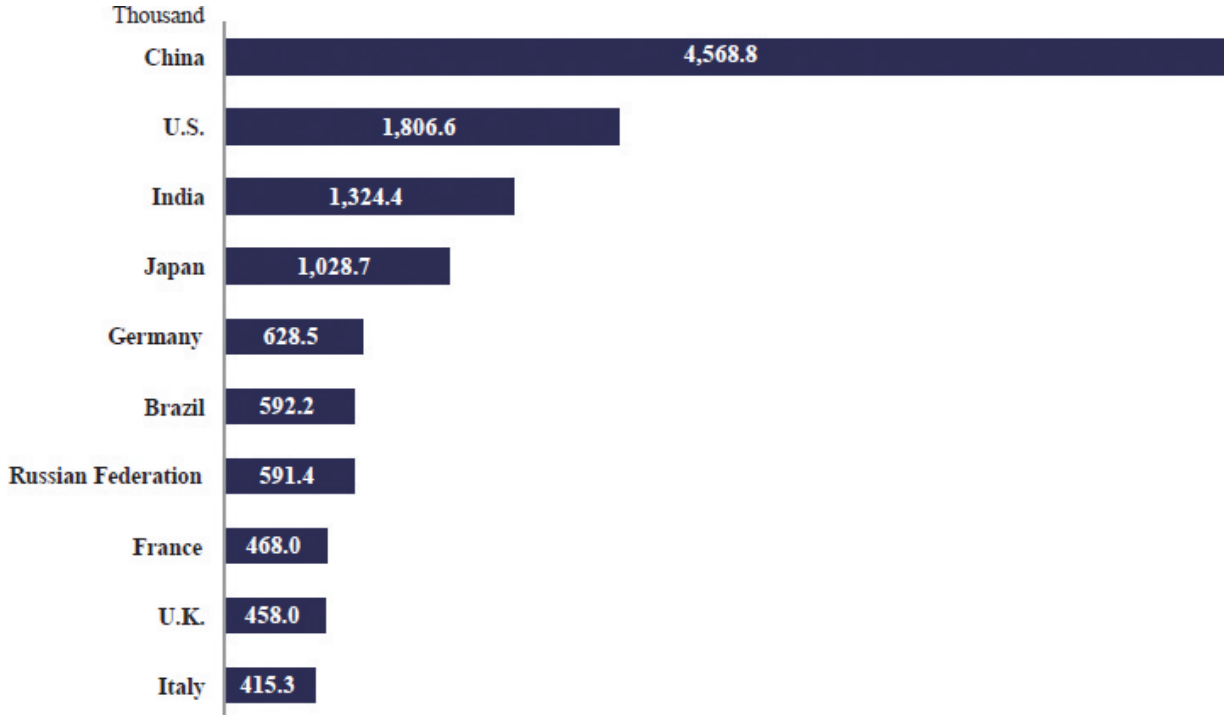
Source: Frost & Sullivan analysis.

Overall, the oncology drug market in China is growing at a faster pace than the global market, mostly attributable to China's large and growing cancer patient population with unmet medical needs, increasing patient access and affordability and favorable policies to support innovative drug development.

Large cancer patient population with unmet medical needs

Cancer incidence in China reached approximately 4.6 million new cases in 2020, accounting for approximately a quarter of global new cancer incidences. New cancer incidences in China are expected to grow to 5.2 million by 2025 and 5.8 million by 2030, respectively.

Cancer Incidences by Country, 2020



Sources: Global Cancer Observatory, WHO, ACS, NCCR, Frost & Sullivan analysis.

In 2019, the PRC government announced a Three-Year Plan for the Prevention and Treatment of Cancer which emphasizes policies to encourage the early detection of cancer. More new cancer cases are expected to be diagnosed through early detection.

The availability of oncology therapies in China has lagged behind other developed regions. Currently, there are only 43 oncology molecularly targeted drugs marketed in China, while there are as many as 107 options in the United States. Moreover, drugs approved in China have fewer approved indications compared with the same drugs approved by FDA. The market has demonstrated a rapid uptake of innovative oncology therapies when they were approved in China. For example, three new oncology drugs launched in China since 2010, Tagrisso, Herceptin and Avastin, have reached US$0.9 billion, US$0.8 billion and US$0.6 billion in sales in 2020, respectively.

Improving patient access and affordability

Both the increase in disposable income and the expansion of medical reimbursement coverage are expected to make oncology treatments more affordable in China, thereby increasing the market for oncology drugs.

Per capita disposable income of Chinese residents grew significantly from US$3,379.4 in 2015 to US$4,952 in 2020. However, the US$673.9 per capita health care spending in China still lags behind the US$11,559 recorded for the United States in 2019.

Moreover, the expansion of medical insurance coverage to reimburse more oncology drugs has presented a new opportunity for China's oncology market. From 2017 to 2020, a total of 53 new oncology drugs (excluding botanical oncology drugs) were included in the National Reimbursement Drug List released by the PRC Ministry of Human Resources and Social Security ("NRDL") as Part B drugs, including Elunate. Some oncology drugs, such as paclitaxel, were also moved from Part B to Part A, making them eligible for full reimbursement. Of the 53 new oncology drugs included in the NRDL, the following drugs are indicated for similar indications as our drugs that are approved or pending approval:

Stivarga targets third-line CRC in China, as does fruquintinib (approved for third-line CRC in China); Afinitor targets pancreatic NETs, as does surufatinib (an NDA under review for pancreatic NETs); and Sutent targets pancreatic NETs, as does surufatinib. The PRC government is expected to continue to expand the NRDL to include more innovative oncology drugs.

In 2018, China eliminated all import tariffs on oncology drugs. The zero-tariff policy reflects the Chinese government's dedication to catch up to the United States in the path to innovation by reducing market entry barriers. As more novel therapies enter the market, it is expected to increase Chinese patients' awareness and market acceptance of new cancer therapies and raise the bar for Chinese research and development.

There are a number of factors affecting the pricing of the same drug in different countries including but not limited to each company's business strategy, the current pricing of the standard of care, market demand, the structure of medical insurance coverage (public and private) available, the insurance and reimbursement coverage available, the distribution of pharmaceuticals, local and federal regulations on drugs and pricing and general economic conditions (including disposable income and GDP per capita).

Favorable policies to support innovative drug development

Historically, cumbersome pharmaceutical registration regulations led to limited availability of advanced therapies in China. Recently, the PRC government has enacted a series of policies to shorten the review and approval time for innovative drugs that address urgent medical needs. For example, the NMPA has reduced the timeline for new clinical trial application approvals to approximately 60 working days, which is similar to the United States.

The NMPA has also created a Priority Review approval system for drugs which meet urgent clinical needs or serious diseases. From 2016 and 2020, a total of 226 drugs have been approved under the Priority Review system, among which 7 and 4 were approved in 2016 and 2020, respectively. Our drug fruquintinib was approved through the Priority Review system. We will also look to receive Priority Review status for each of our other drug candidates at appropriate time.

In addition, a new market authorization holders system is being piloted which will allow for more flexibility in the use of contract manufacturing arrangements by biopharmaceutical companies. Furthermore, the PRC government has issued favorable tax policies, talent incentive programs and special public research and development subsidies to support innovative drug development by domestic companies.

With these reforms, more advanced cancer treatments are expected to enter the China market at an expedited pace. The increased availability of new and innovative therapies in China, combined with patients' heightened awareness of such treatments, are expected to foster the growth of China's oncology drug market.

In China and the United States, the time required for innovative drugs which are conducting global clinical trials to obtain the requisite approvals from the relevant local competent authorities to progress is approximately one year from the acceptance of NDA review by the relevant local competent authorities.

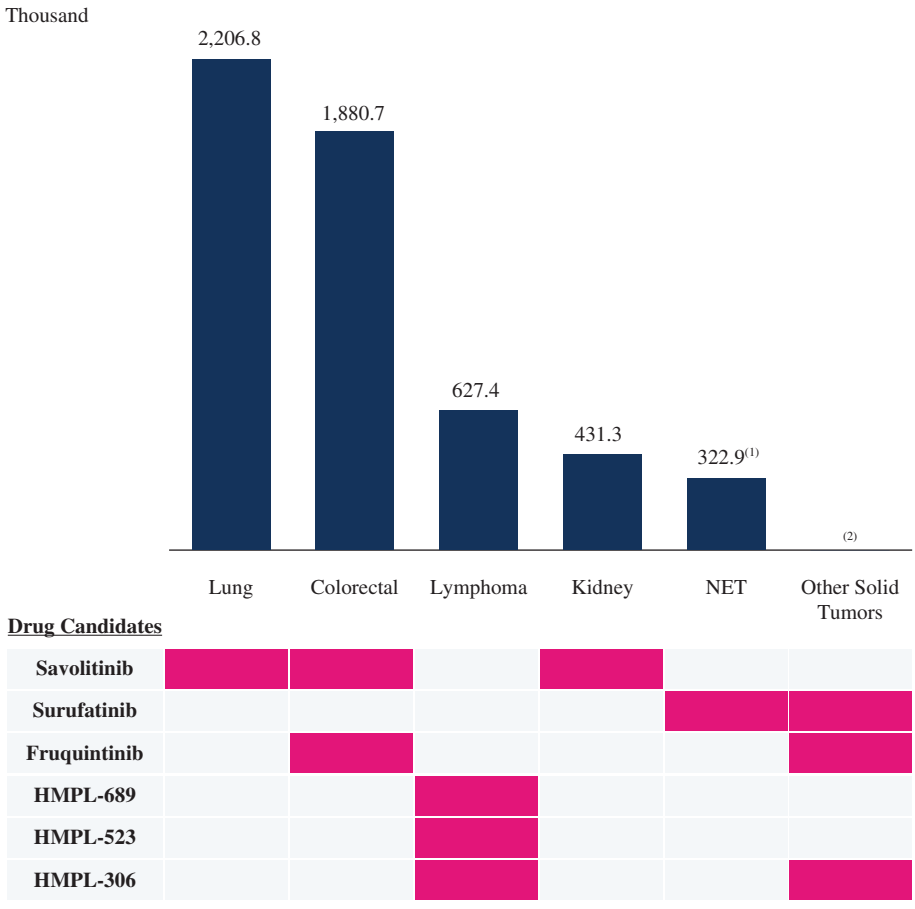
For further discussion of these regulatory reforms, see "– *China's Increasingly Favorable Regulatory Framework*."

OVERVIEW OF THERAPEUTIC AREAS OF INTEREST

Addressable Oncology Patient Populations Which are Targeted by Our Clinical-Stage Drug Candidates

Our drug candidates target oncology patient populations worldwide and in China. The two diagrams below illustrate the addressable cancer cases targeted by our clinical-stage product candidates, globally and in China, respectively:

New Cases of Addressable Cancers Globally, 2020

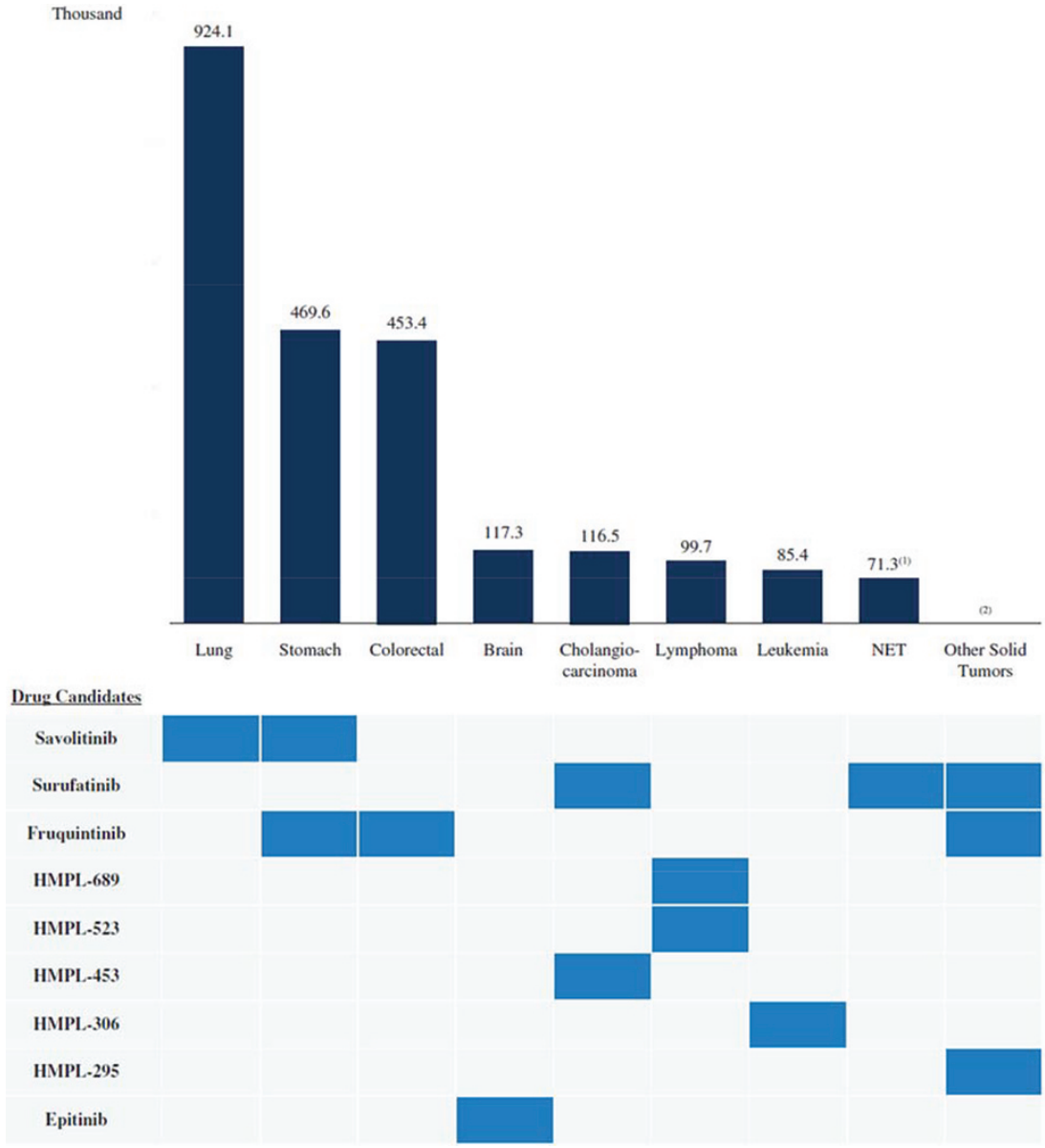


Notes: (1) NET = neuroendocrine tumors; NET patients' PFS is significantly longer than that of other cancer patients shown. See "– *Neuroendocrine Tumors*" for a further discussion; Only includes U.S. and China incidences.

(2) *Phase* Ib/II trials for fruquintinib in combination with checkpoint inhibitors in planning in solid tumors. We initiated a Phase Ib/II trial of surufatinib and tislelizumab in the U.S. and Europe in March 2021.

Source: Frost & Sullivan analysis; Company.

New Cases of Addressable Cancers in China, 2020



Notes: (1) NET = neuroendocrine tumors; NET patients' PFS is significantly longer than that of other cancer patients shown. See "– *Neuroendocrine Tumors*" for a further discussion.

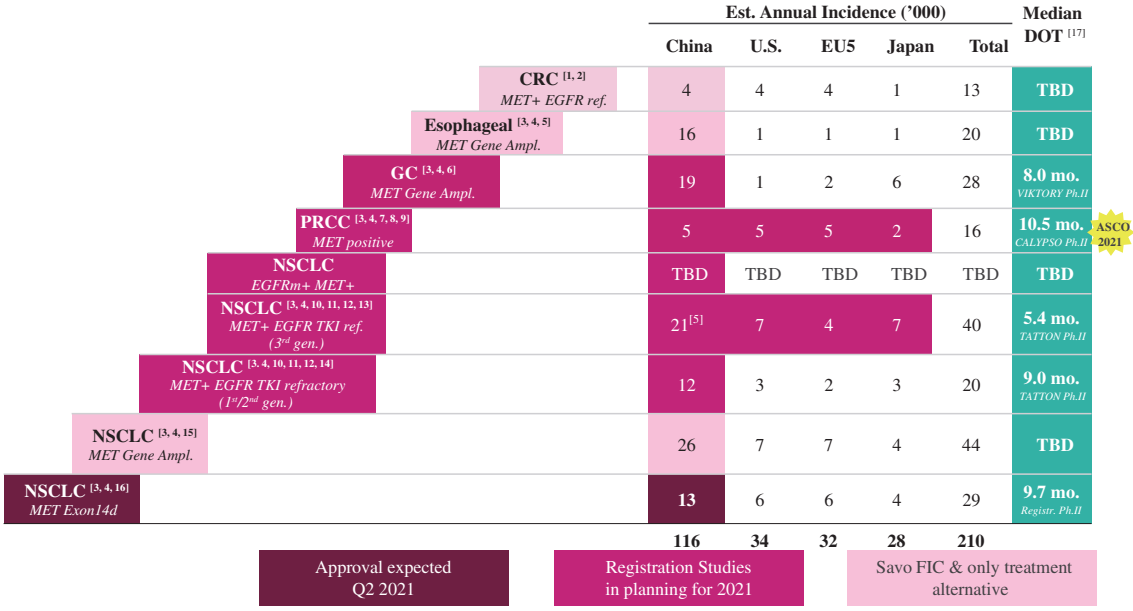
(2) Phase I studies of HMPL-295 in planning in solid tumors.

Source: Frost & Sullivan analysis; Company.

Market Potential of our Drug Candidates

The following tables illustrate the market potential for Savolitinib, Fruquintinib, Surufatinib, HMPL-689 and HMPL-523.

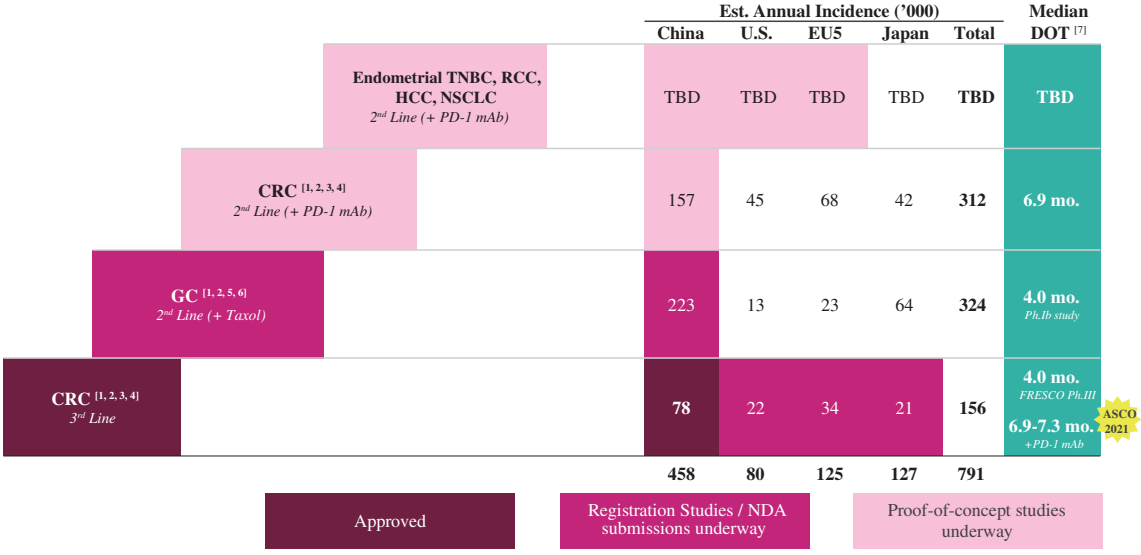
Market Potential for Savolitinib



Notes: All figures are estimates for preliminary illustrative purposes only.

[1] 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 Tagrisso; [14] Estimates 30% EGFR+ patients in U.S., EU5 and Japan are treated with 1st/2nd generation EGFRi; [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.

Market Potential for Fruquintinib



Notes: All figures are estimates for preliminary illustrative purposes only.

[1] Globocan; [2] SEER; [3] Markowitz, S. D., et al. NEJM 2009; [4] 3L estimated to be 50% of 1L and 2L estimated to

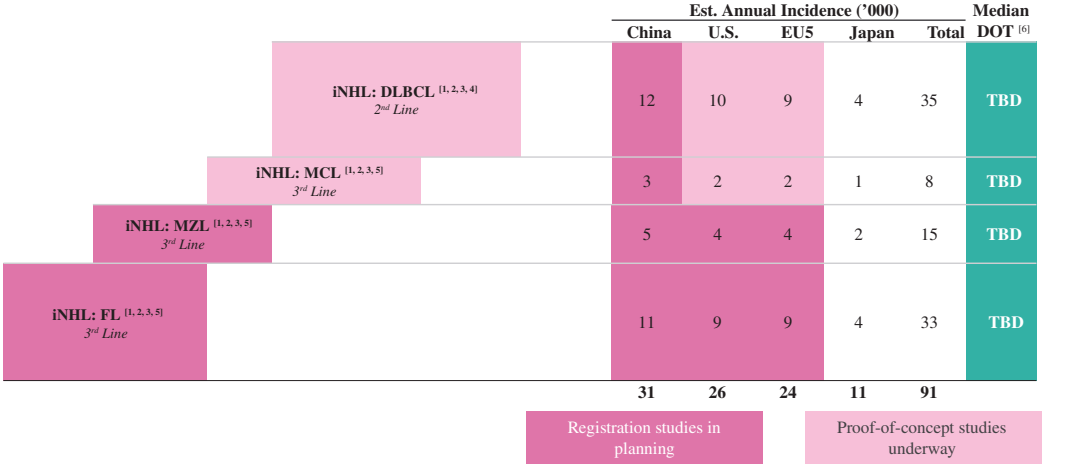
be 30% of all CRC patients; [5] de Mello RA, et al. World J Gastroenterol 2013; [6] 2L estimated to be 70% of 1L and 1L estimated to be 70% of all gastric cancer patients; [7] DOT = duration of treatment in latest study.

Market Potential for Surufatinib

Notes: All figures are estimates for preliminary illustrative purposes only.

[1] 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; [5] 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; [8] Supriya K. Saha, et a.l. The Oncologist 2016; Company estimates; [9] Estimates 40% BTC patients in 2L; [10] DOT = duration of treatment in latest study.

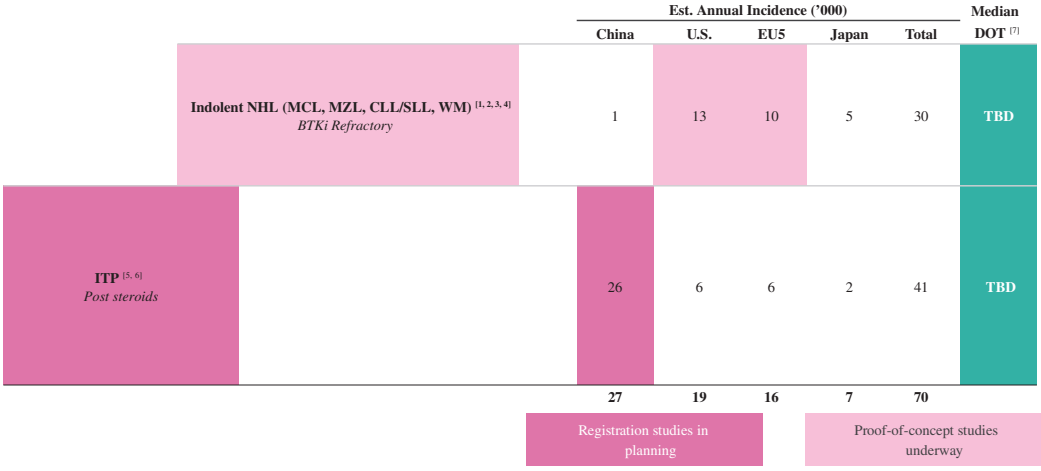
Market Potential for HMPL-689



Notes: All figures are estimates for preliminary illustrative purposes only

[1] 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.

Market Potential for HMPL-523



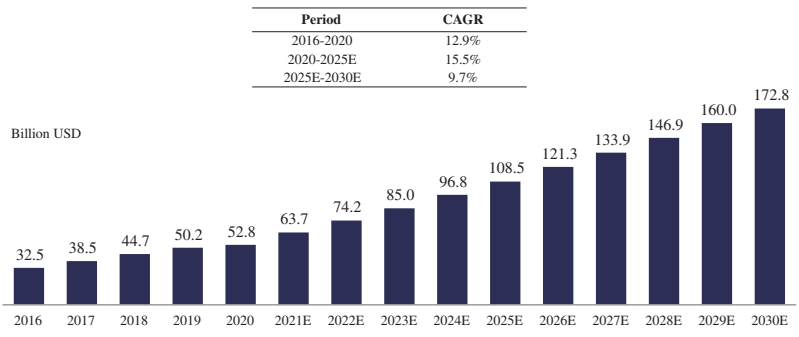
Notes: All figures are estimates for preliminary illustrative purposes only

[1] Globocan; [2] SEER; [3] IQVIA; Abbvie financial report; J&J financial report; AstraZeneca financial report; BeiGene financial report; [4] In China, number of BTKi refractory patients estimated at 20% of patients treated in 2020; ex-China, number of BTKi refractory patients estimated at 50% of patients treated in 2020; [5] Chinese guideline on the diagnosis and management of adult primary immune thrombocytopenia(version 2020); [6] Lee JY, Lee JH, Lee H, et al. Thrombosis Research, 2017, 155: 86-91; [7] DOT = duration of treatment in latest study.

Non-small Cell Lung Cancer

Lung cancer is the most common cancer in the world and the leading cause of cancer-related deaths. Nearly 1.8 million people die from lung cancer every year. The global market for NSCLC therapies was approximately US$52.8 billion in 2020 and is expected to grow to US$172.8 billion by 2030, as shown in the chart below:

Global NSCLC Market, 2016-2030E



Note: E =estimated.

Source: Frost & Sullivan analysis.

The five-year overall survival rates of all types of lung cancers are 21.7% and 19.7%, in the United States and China, respectively. NSCLC is a subtype of lung cancer which accounts for 85.0% of total lung cancer patients. Smoking is the leading risk factor for NSCLC. Other risk factors include exposure to radiation, air pollution and genetics.

In the United States, an estimated 194,500 new cases of NSCLC were diagnosed in 2020, and the number of incidences is expected to reach 238,100 by 2030. In the United States, approximately two-thirds of NSCLC patients are diagnosed at a late stage, with the five-year overall survival rate of only about 10.0%.

In China, there were an estimated 785,500 newly diagnosed NSCLC patients in 2020, and this number is expected to exceed one million by 2030. The majority of NSCLC patients are diagnosed when their disease is already at late stage, with approximately 17.0% patients at stage III and 50.0% at stage IV. The five-year overall survival rate of NSCLC patients in China is approximately the same as that in the United States, as a result of the availability of targeted therapies against EGFR mutations in China, which are prevalent in late-stage Chinese NSCLC patients.

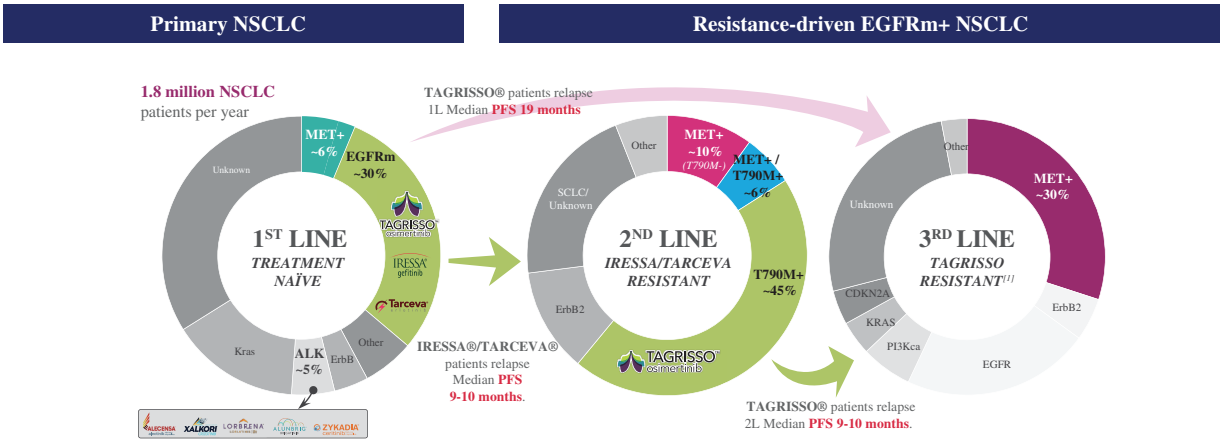
There have been significant breakthroughs in the development of effective immunotherapy and targeted therapies for NSCLC. A set of genetic abnormalities occurring in NSCLC have been identified as predictors for patients' responses to various targeted therapies, including EGFR and MET mutations as predictive biomarkers for advanced NSCLC. According to the guidelines of the National Comprehensive Cancer Network, a not-for-profit alliance of cancer centers devoted to patient care, research and education, targeted therapies are preferred over immunotherapies for patients whose tumors are positive for these genetic abnormalities.

EGFR mutations were the first biomarkers discovered to predict the response to targeted EGFR tyrosine kinase inhibitors. In the United States, approximately 46,500 persons, or 23.9% of NSCLC patients, are EGFRm+. For these patients, the National Comprehensive Cancer Network recommends Tagrisso as the preferred first-line treatment and as second-line treatment for patients who have progressed on a first-generation EGFR inhibitor. However, most of these patients eventually acquire resistance to this treatment, with median relapse occurring approximately 10 months after treatment with a first-generation EGFR inhibitor and 19 months after treatment with Tagrisso, a third-generation EGFR inhibitor, based on evidence in the Phase III FLAURA study. Eventually these patients develop resistance, indicating an unmet medical need in this setting. MET is a major driver for EGFR treatment resistance, and we believe that the savolitinib and Tagrisso combination that we are currently studying, if approved, could potentially be the first treatment option available for MET+ and patients with MET-driven resistance to first- second- or third-generation inhibitors.

In China, approximately 312,600 people, or 39.8% of NSCLC patients, are EGFRm+. The first-generation EGFR inhibitors, such as Iressa, Tarceva and Conmana are currently included on the NRDL for first-line treatment, and Tagrisso is currently included on the NRDL as a first-and second-line treatment. After the first-line treatment, these patients typically turn to Tagrisso or continue to use the first-generation EGFR inhibitors as their second-line treatment, and they have even fewer options for third-line treatment. As a result, there are market opportunities for next-generation targeted therapies with limited toxicity, as either monotherapies or as a combination with immunotherapies. Combinaton trials of savolitinib with Tagrisso are either in progress or in planning, which we believe positions us well to help address this unmet medical need.

The graph below shows the treatment paradigm for NSCLC patients who are EGFRm+ and have acquired resistance to first-generation EGFR inhibitors.

Treatment Paradigm for Patients Globally with Acquired Resistance in EGFRm+ NSCLC



Notes: (1) Primary drivers, based on aggregate rocelitinib/Tagrisso data published at 2016/2017 ASCO.

When initially diagnosed with advanced NSCLC, patients are recommended to undergo testing of their tumors to guide treatment. Patients whose tumors are found to be EGFRm+ are recommended for treatment with EGFR inhibitors, e.g. first generation EGFR inhibitors such as Iressa and Tarceva, or third-generation EGFR inhibitors, such as Tagrisso, which also inhibits the EGFR T790M mutation. Most of these patients' tumors eventually acquire resistance to such treatment through secondary aberrations. Approximately half of those treated with first generation EGFR inhibitors find their tumors develop the T790M mutation, and approximately a fifth of those develop additional aberrations, such as MET gene amplification. The former have the option to switch to Tagrisso, which blocks both the original EGFR mutation and the T790M mutation. However, approximately 30% of patients treated with Targrisso develop MET aberrations. Currently there are no targeted treatment options approved for patients that develop both EGFR and MET aberrations.

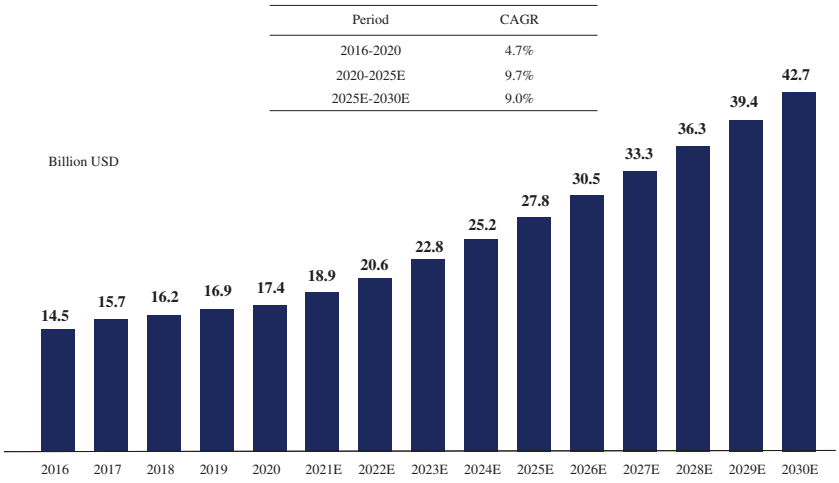
Source: Frost & Sullivan analysis.

Among EGFRm+ patients, the mutated driver gene MET can result in aberrant signaling through a number of mechanisms, including MET gene amplification and MET exon 14 skipping mutation. It is estimated that 4.0-6.0% of newly diagnosed NSCLC patients harbor genetic MET aberrations. Our drug candidate savolitinib, if approved, is expected to be the first therapy specifically targeting patients with these mutations in China.

Colorectal Cancer

CRC is the development of cancer in the colon or rectum. Globally, CRC is the third most commonly diagnosed cancer and the second leading cause of cancer-related deaths. The global market for CRC therapies was estimated to be approximately US$17.4 billion in 2020 and is expected to grow to US$42.7 billion by 2030, as shown in the chart below:

Global CRC Market, 2016-2030E



Note: E =estimated.

Source: Frost & Sullivan analysis.

It is estimated that approximately 1.9 million new cases of CRC occurred in 2020 globally. Factors that contribute to an increased risk for CRC include old age, a history of polyps, inflammatory intestinal conditions, a low-fiber/high-fat diet and a sedentary lifestyle.

In the United States, CRC is the fourth most commonly diagnosed cancer and the second leading cause of cancer-related deaths. In the United States, there were about 148,000 new CRC cases in 2020 with a five-year overall survival rate of 64.7%. However, mCRC accounts for approximately 23.2% of the newly diagnosed CRC patients in the U.S., and their prognosis is not favorable, with a five-year overall survival rate of approximately 14.7%, representing an unmet medical need. There are many options for late-stage or mCRC patients in the United States, among which chemotherapies in combination with anti-VEGF or anti-EGFR targeted therapies are the most commonly used.

In China, CRC has become increasingly prevalent. The incidence of new cases of CRC in China is estimated to range from 453,400 to 550,000 in 2020, compared to 400,700 in 2016. CRC incidence in China is expected to grow further to 606,300 by 2030. The five-year overall survival rate of CRC in China, which is estimated to be 56.9%, is lower than that in the United States. In addition, approximately 27.5% of new incidences of CRC in China are diagnosed at metastatic stage, which is higher than that of the mCRC in the United States. Chemotherapies in combination with anti-VEGFR or anti-EGFR targeted therapies are the common therapies for late-stage CRC patients in China. As more novel targeted therapies are receiving approvals and these therapies become more affordable in China, late-stage CRC patients have begun to receive increasing lines of therapies. It is estimated that among all CRC patients in China, there are approximately 15% who are receiving third-line treatment. These patients have a median five-year overall survival rate of only approximately 10.0%, which is significantly lower than the five-year overall survival rate of CRC patients diagnosed at an earlier stage.

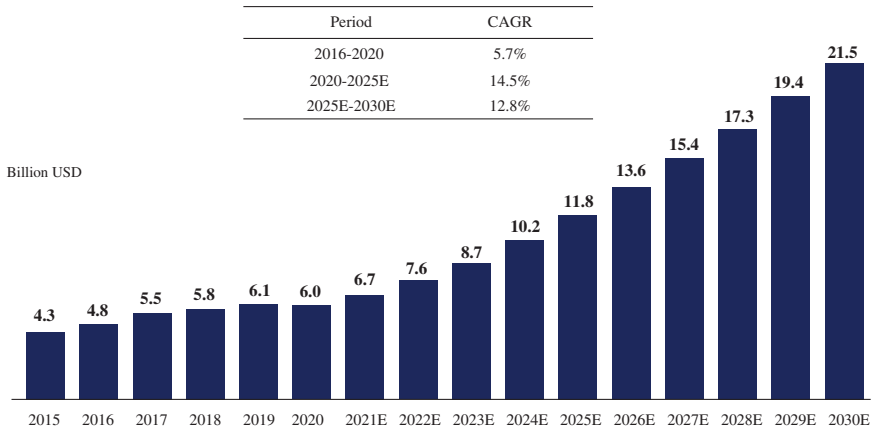
The Chinese guidelines for the management of colorectal liver metastases currently specifies the chemotherapeutic options when such disease progresses. It provides that drugs including fruquintinib, Stivarga and Erbitux can be considered for treatment of third- or fourth-line CRC. Among the available targeted therapies, fruquintinib has demonstrated numerically higher disease control rate, median PFS rate and median overall survival rate in a Phase III trial in Chinese third-line colorectal cancer patients. Due to its relatively benign effect on the liver, fruquintinib is the preferred treatment option over Stivarga in patients with liver metastasis. There were an estimated 22,000 new incidences of CRC with liver metastasis in China in 2020, most of which are in the late-stage third-line setting as demonstrated by the FRESCO study, which showed that approximately 70% of study evaluable patients had liver metastasis.

Neuroendocrine Tumors

NETs form in cells that interact with the nervous system or in glands that produce hormones. They can originate in various parts of the body, most often in the gut or the lungs and can be benign or malignant. NETs are typically classified as pancreatic NETs or other NETs.

The global market for NET therapies was estimated to be approximately US$6.0 billion in 2020 and is expected to grow to US$21.5 billion by 2030, as shown in the chart below:

Global NETs Market, 2016-2030E



Note: E = estimated.

Source: Frost & Sullivan analysis.

There were 19,700 newly diagnosed cases of NETs in the United States in 2020, compared to 71,300 diagnosed cases in China of which 62,200 were non-pancreatic cases and 9,100 were pancreatic cases. The U.S. incidence of diagnosed NETs is estimated to be seven in every 100,000 people, and this rate is increasing with the current estimate representing a six-fold increase since the 1970s.

Importantly, NETs are associated with a relatively long duration of survival compared to other tumors and as a result, while incidence rates are modest, there is a relatively large population of NETs patients. For example, in our Phase III trials of surufatinib in non-pancreatic and pancreatic NETs, median PFS was around 10 months. This is longer than that in our Phase III FRESCO study of fruquintinib in CRC, where fruquintinib-treated patients had a median PFS of 3.7 months. This leads to both a larger patient population and longer average time on treatment per patient.

NET Prevalence in the United States, 2020

Cancer Type	Survival (% Patients – 5 Years)	Prevalence (Est. Patients)
Pancreas	56%	9,070
Other GI	–	72,851
Total GI NET	**58%**	**81,921**
Lung	61%	38,409
Other	63%	21,402
All NET	**60%**	**141,732**

Note: GI = Gastrointestinal.

Sources: American Cancer Society, International Neuroendocrine Cancer Alliance, Frost & Sullivan analysis.

Although long-acting analogues of somatostatin have an established place in the medical treatment of patients with NETs, additional treatment options are needed. Chemotherapy is infrequently used in NET treatment as it has limited efficacy in these tumors. Prior to the registration of surufatinib in China, approved targeted therapies for NETs are limited to Sutent and Afinitor, each indicated for subsets of NETs patients. According to the Frost & Sullivan, no new indications are being developed for Sutent in China while Afinitor is being developed for breast cancer and diffuse large B cell lymphoma in China. The Phase III studies of surufatinib in NET patients demonstrated meaningful effect in Chinese patients across different types of NETs in respect of objective response rate (19% vs 2% placebo in the pancreatic NET study and 10% vs 0% placebo in the non-pancreatic NET study, both differences were statistically significant), PFS (10.9 months vs 3.7 months placebo in the pancreatic NET study and 9.2 months vs 3.8 months placebo in the non-pancreatic NET study, both differences were statistically significant) and tolerability. Surufatinib was approved by the NMPA in December 2020 for the treatment of non-pancreatic NETs and is now being marketed in China. In addition, surufatinib also demonstrated some anti-tumor activity in patients who had progressed following prior tyrosine kinase inhibitor treatment with Sutent, Afinitor and famitinib. See "*Business – Our Clinical Pipeline – 2. Surufatinib VEGFR 1, 2 and 3, FGFR1 and CSF-1R Inhibitor*" for more information.

Kidney Cancer

Kidney cancer is a type of cancer that starts in the cells in the kidney. Approximately 90.0% of kidney cancer patients have RCC. The three most common RCC subtypes are clear cell renal cell carcinoma, PRCC and chromophore renal cell carcinoma. Approximately 388,200 new cases of RCC were diagnosed globally in 2020. The global market for kidney cancer therapies was estimated to be approximately US$5.8 billion in 2020 and is expected to grow to US$16.4 billion by 2030.

No targeted therapies have been approved specifically for PRCC, although some efficacy was observed for cabozantinib in an investigator sponsored study, PAPMET, which reported ORR of 23% and median PFS of 9 months in 44 patients not selected for MET status and who mostly (95%) did not receive prior systemic therapy (Pal SK, et al. Lancet. 2021). Modest efficacy in non-clear cell renal cell carcinoma has been reported in sub-group analyses of broader RCC studies of VEGFR (e.g., Sutent) and mammalian target of rapamycin (e.g., Afinitor) tyrosine kinase inhibitors, with ORR of less than 10% and median PFS in first-line setting of four to six months and second-line setting of only one to three months (ESPN study, Tannir N. M. et al.).

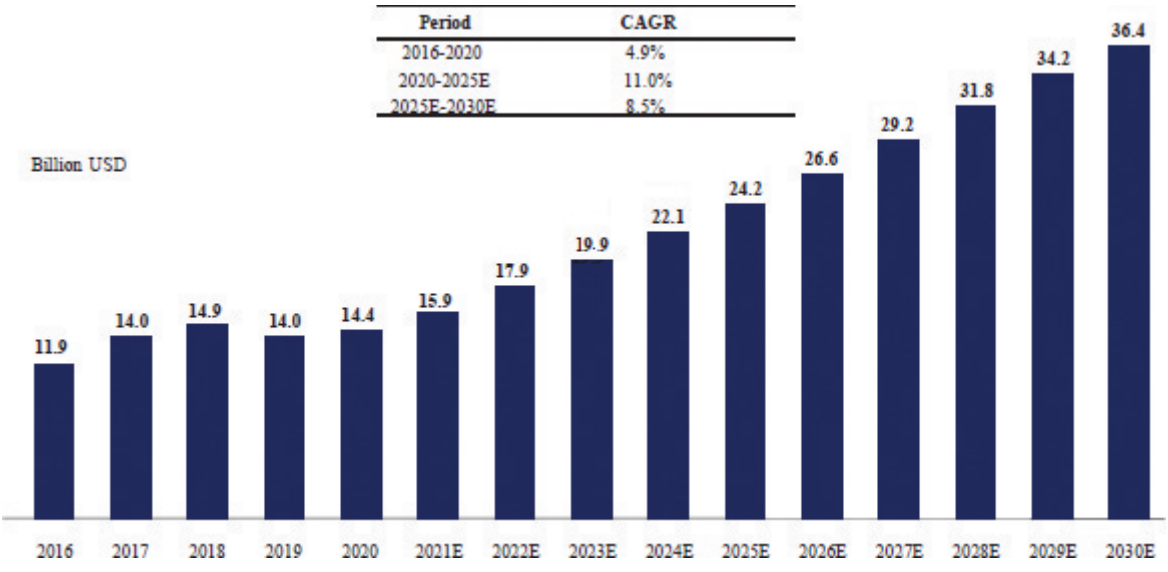
Anti-PD-1 and PD-L1 antibodies have been associated with clinical benefits in metastatic RCC, and MET dysregulation has been thought to play an important role in PRCC pathogenesis and is a mechanism of resistance against kinase inhibitors in clear cell renal cell carcinoma.

To address this market potential, we are developing savolitinib in combination with Imfinzi. Phase II data have shown that MET+ patients have a high response rate to monotherapy savolitinib treatment. Adding Imfinzi as a combination therapy may have added effectiveness, although the role of MET mutation in this setting remains to be better understood. In addition, in the broader kidney cancer setting, combinations of PD-1 or PD-L1 inhibitors with targeted therapies that have demonstrated positive single agent effect have shown incremental benefits. In first-line clear cell kidney cancer, for example, single agent treatment with the VEGFR inhibitor Inlyta showed an objective response rate of 34%, while single agent treatment with the PD-1 inhibitor Keytruda showed an objective response rate of 38%. However, treatment with both Keytruda and Inlyta showed an objective response rate of 59%.

Gastric Cancer

Gastric cancer is a cancer that develops in the lining of the stomach. Gastric cancer is the fifth most common cancer globally with an estimated 1,089,100 cases per year in 2020. The global market for gastric cancer therapies was estimated to be approximately US$14.4 billion in 2020 and is expected to grow to US$36.4 billion by 2030, as shown in the chart below:

Global Gastric Cancer Market, 2016-2030E



Note: E =estimated.

Source: Frost & Sullivan analysis.

Gastric cancer is especially prevalent in East Asian countries such as South Korea, Japan and China. There were an estimated 469,600 new incidences of gastric cancer in China in 2020. China's new incidences of gastric cancer are expected to grow to approximately 622,400 in 2030. The five-year overall survival rate of gastric cancer patients in China is 35.1%.

Advanced gastric cancer has a high unmet need, particularly in Asian populations, with limited treatment options for patients who have failed chemotherapy. As a result, we believe highly selective targeted therapies are critical to address a continued unmet need for this patient population. During the VIKTORY trial in Korea, approximately 3.5% of second-line patients were diagnosed with MET amplification. These patients with MET amplification generally have significantly poorer survival rates. We are developing fruquintinib in combination with Taxol for second-line gastric cancer treatment as well as savolitinib as a monotherapy for MET+ gastric cancer patients.

Hematological Cancer

Hematological cancer is a broad term used to describe cancers of the blood, which affect the production and function of blood cells. Most of these cancers start in the bone marrow where blood is produced. Hematological cancers are classified as leukemia (affecting blood and bone marrow), lymphoma (affecting the lymphatic system) and myeloma (affecting bone marrow). The two main categories of lymphoma are Hodgkin's lymphoma and non-Hodgkin lymphoma, and latter consists of B-cell type and T-cell or other types. Leukemia can be classified as acute leukemia and chronic leukemia according to different degrees of cell differentiation.

Conventional methods of treating hematologic cancers vary according to the specific disease or histology, but generally include chemotherapy, targeted therapy and, less frequently, radiation. Recently, chimeric antigen receptor T-cell (CAR-T) therapy has proven clinical efficacy in certain hematological cancers. The approval of CAR-T has enriched the therapy availability for hematological cancer patients. However, the therapy market is limited by numerous factors, including small volume of patients, complex logistics and high treatment cost.

The global market for hematological cancer therapies was estimated to be approximately US$52.5 billion in 2020 and is expected to grow to US$146.1 billion by 2030. The hematology drug market is still dominated by small molecular drugs and monoclonal antibodies. The top drugs in this

category, Revlimid and MabThera (also known as Rituxan), reached sales revenue of US$12.1 billion and US$4.5 billion in 2020, respectively. In comparison, the aggregate sales for Kymriah and Yescarta, the two of five approved CAR-T therapies, were US$1.0 billion in 2020. The other three are Tecartus, Breyanzi and Abecma, the sales numbers of which are not available yet. On March 26, 2021, FDA announced its most recent CAR-T drug approval for Abecma.

Lymphoma

Lymphoma is a cancer that begins in lymphocytes, infection-fighting cells of the immune system. Non-Hodgkin lymphoma accounts for approximately 90.0% of all lymphoma incidences.

In China, new incidences of non-Hodgkin lymphoma grew from 83,700 in 2016 to 92,800 in 2020, representing a CAGR of 2.6% during the period. China's new incidences of non-Hodgkin lymphoma are expected to grow to 117,400 in 2030.

In the United States, new incidences of non-Hodgkin lymphoma grew from 72,600 in 2016 to 77,200 in 2020, representing a CAGR of 1.6% during the period. New incidences of non-Hodgkin lymphoma in the United States are expected to grow to 95,500 in 2030.

Chemotherapy is the main treatment for lymphoma. Depending on the type and the stage of the lymphoma, chemotherapy may be used alone or combined with other treatments, such as immunotherapy drugs or radiation therapy. There is a wide gap between China and the United States in terms of the five-year overall survival rates of lymphoma patients. Lymphoma patients in China have a five-year overall survival rate of 37.2%, compared to 74.7% in the United States due to the adoption of biologics such as Rituxan.

The abnormal activation of B-cell receptor signaling is closely related to the development of B-cell type hematological cancers, which represent approximately 85% of all non-Hodgkin lymphoma cases (i.e., B-cell malignancies). Targeted B-cell receptor signaling therapies, including monoclonal antibodies and small molecules, have been proven to be clinically effective for the treatment of B-cell malignancies. Notable success has been achieved in B-cell malignancies in oncology, where small molecule inhibitors are now being used to target kinases down-stream from Syk in the B-cell signaling pathway, namely BTK and PI3Kδ.

Acute Myeloid Leukemia

Leukemia is a cancer that starts in cells that would normally develop into different types of blood cells, but instead mutate. Acute myeloid leukemia is a fast-growing type of leukemia.

There were an estimated 29,900 incidences of acute myeloid leukemia in China in 2020. It is estimated that there will be 34,700 new incidences of acute myeloid leukemia in China in 2030. Acute myeloid leukemia occurs in children and adults of all ages but is primarily a disease of older adults, with a median age at diagnosis of 68 years. Acute myeloid leukemia is universally fatal without treatment, with a median survival of approximately two months. The vast majority of patients do not respond to chemotherapy and progress to relapsed/refractory acute myeloid leukemia.

Combination chemotherapy regimens with or without stem cell transplantation are frontline therapy options for patients with newly diagnosed acute myeloid leukemia. Older patients with newly diagnosed acute myeloid leukemia who are ineligible for intensive chemotherapy typically have poor outcomes and few available treatment options. There is a clear need for new treatments for acute myeloid leukemia.

We see potential for our Syk and PI3Kδ inhibitors to be combined with targeted therapies in this arena.

Biliary Tract Cancer

Biliary tract cancer ("BTC") is a heterogeneous group of rare malignancies arising from the biliary tract epithelia. Cholangiocarcinomas are the most common biliary malignancies, which can be further

divided into intrahepatic and extrahepatic subcategories. Gemzar, a type of chemotherapy, is the major first-line therapy for BTC patients. Median survival is less than 12 months for patients with unresectable or metastatic disease at diagnosis.

There were an estimated 116,500 new incidences of cholangiocarcinoma in China in 2020. China's new incidences of cholangiocarcinoma are expected to grow to 157,100 in 2030. The five-year overall survival rate of cholangiocarcinoma patients after resection in China is approximately 11.7%.

There were an estimated 8,900 new incidences of cholangiocarcinoma in the United States in 2020. New incidences of cholangiocarcinoma in the United States are expected to grow to 12,500 in 2030. The five-year overall survival rate of cholangiocarcinoma patients in the United States is approximately 10% to 16% if the cancer has not yet spread to a distant part of the body.

There is currently no standard of care for cholangiocarcinoma patients who have progressed on chemotherapy. As a result, there is an unmet medical need for these patients. Our drug candidate surufatinib, given its unique angio-immuno profile, may offer a new targeted treatment option in this tumor type.

WHAT ARE IMMUNOLOGICAL DISEASES?

Immunological diseases, also known as autoimmune diseases, occur when a person's immune system mistakenly attacks its own body tissues. There are more than 100 types of autoimmune diseases, including, among others, rheumatoid arthritis and immune thrombocytopenia.

Overview of Treatment Options for Immunological Diseases

Immunological diseases in general cannot be cured, but the condition can be controlled in many cases. Traditional treatments include:

- anti-inflammatory drugs such as NSAIDS – to reduce inflammation and pain
- corticosteroids – to reduce inflammation
- disease-modifying antirheumatic drugs – to slow the progression of the disease
- pain-killing medication – such as paracetamol and codeine
- immunosuppressant drugs – to inhibit the activity of the immune system
- physical therapy – to encourage mobility

Targeted therapies, such as those targeting the B-cell signaling pathway, are now being used or studied for the treatment of a rapidly expanding number of immunological diseases. Janus tyrosine kinase, or JAK, inhibitors such as Xeljanz (JAK-3 inhibitor, marketed for rheumatoid arthritis and in development for ulcerative colitis, Crohn's disease and myelofibrosis), Jakafi (JAK-1/2 inhibitor, marketed for myelofibrosis and in development for acute myelogenous leukemia), Olumiant (JAK-1/2 inhibitor marketed for rheumatoid arthritis) and upadacitinib (JAK-1 inhibitor in development for rheumatoid arthritis, Crohn's disease, ulcerative colitis, atopic dermatitis, psoriatic arthritis and axial SpA); BTK inhibitors such as Imbruvica, Calquence, zanubrutinib and tirabrutinib marketed or in development for various hematological cancers; and TNFα inhibitors marketed for rheumatoid arthritis, such as Enbrel, Remicade, Humira and Cimzia.

Immune Thrombocytopenia

Immune thrombocytopenia, or ITP, is a clinical syndrome in which a decreased number of circulating platelets (thrombocytopenia) manifests as a bleeding tendency, easy bruising or extravasation of blood from capillaries into skin and mucous membranes.

The prevalence of ITP in China was 210,600 in 2020, and is expected to grow to 230,700 by 2030. In the United States, ITP is considered a rare disease with a prevalence of 37,400 in 2020.

Current treatments for ITP are inadequate since they do not reverse the disease progression and generally do not result in durable remissions. Novel agents that are currently in development target certain key steps in the disease process, including the interaction between T-cell and antigen presenting cells, the binding of the Fc portion of platelet autoantibodies to Fc-receptors on macrophages and the signaling pathways leading to platelet phagocytosis by macrophages (Syk inhibition).

Rheumatoid Arthritis

Rheumatoid arthritis is the most common autoimmune inflammatory arthritis in adults. It is a chronic inflammatory disease that can affect more than just joints and can cause systemic damage.

The global market for rheumatoid arthritis treatments is projected to be approximately US$65.7 billion by 2030. The prevalence of rheumatoid arthritis in China has steadily risen. The number of rheumatoid arthritis incidences in China was estimated to be 6.0 million as of 2020. In the future, risk factors associated with rheumatoid arthritis, including aging, environment and obesity, are expected to contribute to a larger number of rheumatoid arthritis cases.

Although China has one of the largest rheumatoid arthritis patient populations in the world, the current treatment options for rheumatoid arthritis patients in China are limited due to their high cost, poor efficacy and poor safety profile. Therefore, there is substantial market potential for new rheumatoid arthritis therapies. However, drugs which are biosimilar to TNFα inhibitors such as Enbrel and Humira are expected to become available in China which will significantly enhance the affordability of such drugs for patients.

CHINA'S INCREASINGLY FAVORABLE REGULATORY FRAMEWORK

China's regulatory framework is becoming increasingly favorable for the development and commercialization of innovative drugs that address unmet medical needs. The Chinese government has designated the pharmaceutical industry as one of China's "pillar industry sectors," aiming to transform China into an innovation-focused economy.

Expanded Reimbursement Coverage for Innovative Drugs

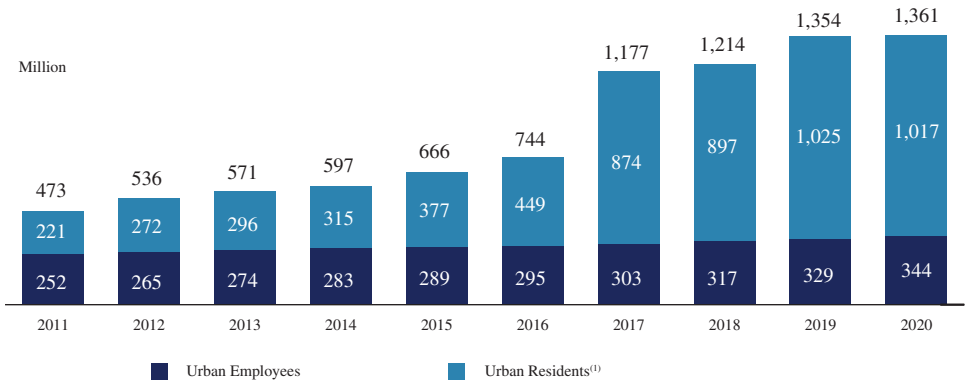
Overview of Medical Insurance in China

Historically, most of Chinese healthcare costs have been borne by patients out-of-pocket, which have limited the growth of more expensive pharmaceutical products like oncology drugs. However, in recent years the number of people covered by government and private insurance has increased. The National Medical Insurance Program was adopted pursuant to the Decision of the State Council on the Establishment of the Urban Employee Basic Medical Insurance Program issued by the State Council in December 1998, under which all employers in urban cities are required to enroll their employees in the basic medical insurance program under which the insurance premium is jointly contributed by the employers and employees. Program participants are eligible for full or partial reimbursement of the cost of medicines included in the NRDL.

The PRC Ministry of Labor and Social Security, together with other government authorities, has the power to determine the medicines included in the NRDL, which is divided into two parts, Part A and Part B. The Part A catalogue typically includes low-priced and clinically necessary drugs that are fully reimbursed and the Part B catalogue typically includes higher-priced or new drugs that generally require a 10% to 30% co-payment from patients. The Ministry of Human Resources and Social Security or MoHRSS, sets the drug reimbursement price for all drugs included in the NRDL.

The Chinese basic medical insurance scheme consists of the Urban and Rural Residents Basic Medical Insurance Scheme (URBMIS) and the Urban Employee Basic Medical Insurance Scheme (UEBMIS). According to MoRHSS, URBMIS and UEBMIS covered 1,017 million and 344 million people in China, respectively, as of December 31, 2020.

Urban Population Enrollment in National Basic Medical Insurance, 2011 – 2020



Note: (1) Includes rural residents since 2017.

Sources: National Medical Insurance Bureau ; MoHRSS; Frost & Sullivan Analysis.

Expansion of National Reimbursement Drug List to Include Innovative Drugs

Since 2000, the MoHRSS has published six versions of the NRDL, with each update adding a large number of drugs. In December 2020, NHSA and MoHRSS released the official work plan for the adjustment of the 2020 NDRL: 162 drugs were involved in price negotiations and 119 were successfully negotiated. Drug prices fell the most during the 2020 round of negotiations. The average decline of drug prices was 50.64%. In 2020, 17 new oncology drugs (including 3 types of generic drugs) entered Part B of the 2020 NDRL.

Inclusion into the NRDL typically results in a much higher sales volume and significant sales growth despite a reduction in the price. For example, after being included in the NRDL in July 2017, Avastin's sales revenue increased by 86% from 2017 to 2018. Tagrisso, which was approved in March 2017, was included in the NRDL in October 2018, and its 2018 sales revenue increased by approximately 325% in comparison with 2017 market performance. Herceptin was included in the NRDL in July 2017, and its 2018 sales revenue increased by approximately 50% in comparison with its 2017 market performance. Recent publicly available data have shown that other drugs have experienced a similar pattern, with sales volume increases more than compensating for price reductions from inclusion on the NRDL, such as Stivarga, Aitan, Focus V, Sutent, Afinitor and Sandostain LAR.

Regulatory Reform in Relation to New Drug Registration

In October 2017, the General Office of the State Council released Opinions on Reform of the Drug and Medical Device Review and Approval (關於深化審評審批制度改革鼓勵藥品醫療器械創新的意見). The opinions aim to encourage innovation, accelerate drug development and approval, and reform clinical trial and life-cycle management.

	Content	Potential Benefits
Reforming clinical trial management	▪ Implementing record-filing system instead of qualification for clinical trial sites ▪ Accepting clinical trial data generated abroad ▪ Improving the efficiency of ethics review, optimizing the approval procedure for clinical trials	✓ Increasing availability of clinical trial sites ✓ Making simultaneous marketing in domestic and overseas markets possible ✓ Shortening the approval time of IND applications
Accelerating review and approval	▪ Accelerating the review and approval of drugs with urgent clinical needs	✓ Shortening the approval time of NDA applications
Encouraging innovation	▪ Enhancing protection of patents and clinical trial data ▪ Developing pilot pharmaceutical patent term compensation system ▪ Making dynamic adjustment to National Reimbursement Drug List	✓ Extending the patent term of innovative drugs ✓ Raising the affordability and availability of innovative drugs
Lifecycle management	▪ Implementing the Marketing Authorization Holder (MAH) system	✓ In favor of innovative small and medium-sized enterprises and start-ups who can benefit from a wider range of R&D and manufacturing options

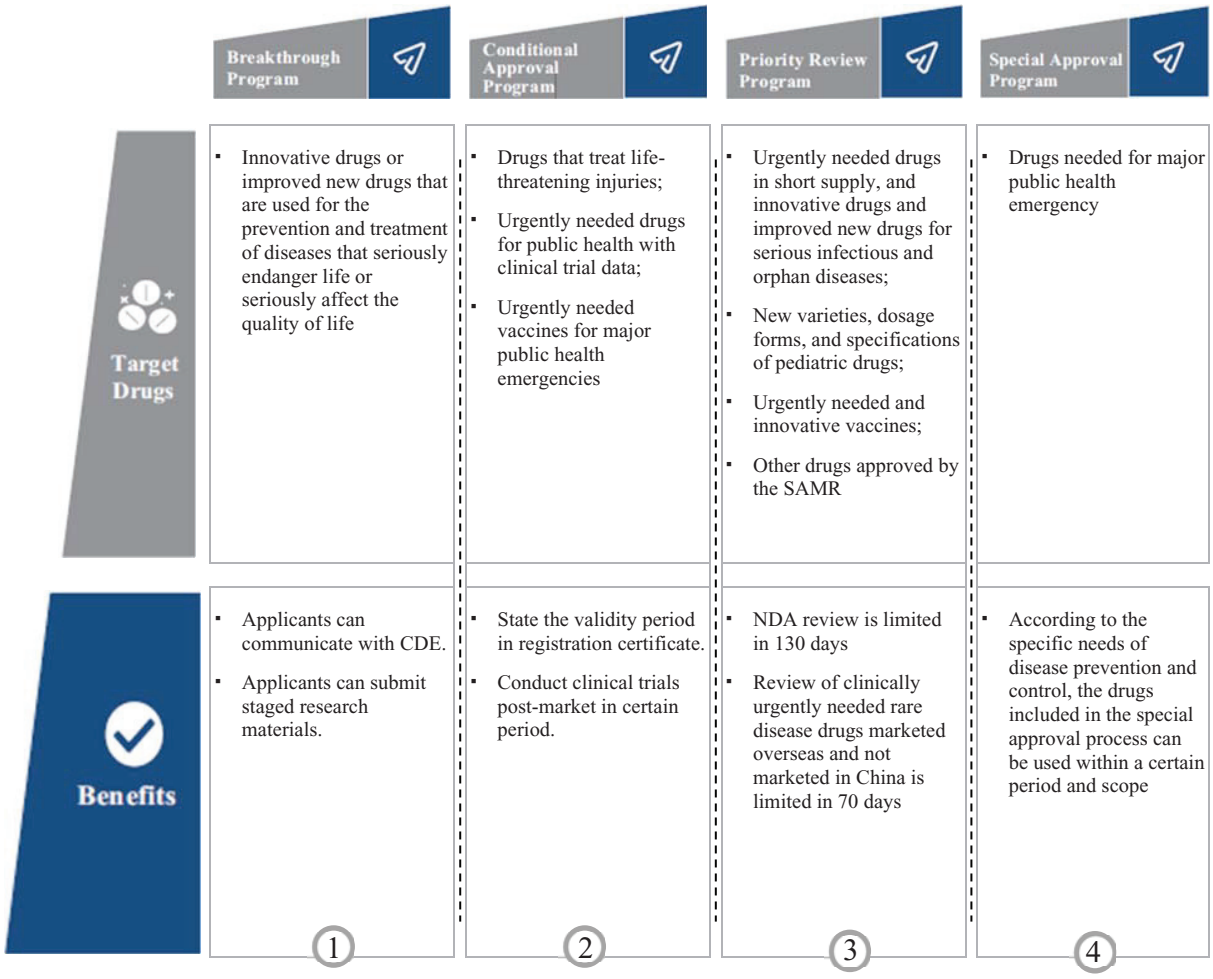
Sources: NMPA; Frost & Sullivan analysis.

In December 2017, the NMPA released the Opinions on Priority Review and Approval for Encouraging Drug Innovation (國家食品藥品監督管理總局關於鼓勵藥品創新實行優先審評審批的意見), which further clarified that a Priority Review system for clinical trial applications and drug registration is available to the following categories of drugs, among others, which we believe will benefit our drug candidates:

- drugs with significant clinical value which will be manufactured locally in China;
- drugs with significant clinical value using advanced technologies, innovative treatment methods or having distinctive treatment advantages; and
- drugs with distinctive clinical advantages for the prevention and treatment of malignant tumors.

The NMPA also specified that concurrent applications for new drug clinical trials which are already approved in the United States or European Union are also eligible for Priority Review.

On March 30, 2020, the State Administration for Market Regulation, released a revised Drug Registration Regulation ("Revised DRR") as part of its efforts to strengthen and streamline its regulation of the pharmaceutical industry, effective July 1, 2020. The Revised DRR established the below four accelerated approval pathways:



Sources: PRC government websites, Frost & Sullivan analysis.

Regulatory Reform in Relation to Data Protection in the Pharmaceutical Industry

On April 25, 2018, the NMPA issued the Implementation Measures for Data Protection of Drug Tests (Interim) (藥品試驗數據保護實施辦法(暫行)) ("Implementation Measures") which narrow the scope of protected data for certain drugs to independently generated and undisclosed non-clinical and clinical study data related to product efficacy that is submitted for marketing authorization purposes. The Implementation Measures cover innovative drugs, innovative therapeutic biologics, orphan drugs, pediatric drugs, and generic drugs to which pertinent patents have been invalidated. Self-obtained clinical data relating to innovative therapeutic biologics approved and marketed in China is protected for 12 years from the date of marketing authorization in China. Data for innovative drugs approved and marketed in China is protected for 6 years from the date of marketing authorization in China. Data for orphan drugs and pediatric drugs is protected for six years from the date of the first approval of the relevant indication in China.

Three-Year Plan for the Prevention and Treatment of Cancer

In March 2019, the PRC government announced a Three-Year Plan for the Prevention and Treatment of Cancer (癌症防治工作三年計劃), which emphasized increasing early screening and improving access to oncology medications through the NRDL. These policies are expected to further grow the oncology market in China.

Three-Year Plan for the Prevention and Treatment of Cancer

Requirement	Content
Establish Cancer Registration and Reporting System	• Establish the registration and reporting system for cancer in the health care institutions above the county level
Promote '3-early Steps' for Cancer	• Promote early screening and detection, early diagnosis and early treatment of cancer
Focus on Prevention of Cancer	• Spread knowledge of health and cancer
Establish Prevention and Treatment System for Cancer	• Establish prevention and treatment system for cancer at four levels (country, province, city and county) and provide technical support
Guarantee Medicine Supply	• Make sure that oncology drugs are not only listed in the NRDL at a reduced price but also accessible to people in hospitals
Improve Technology	• Improve the level of science and technology and overcome the technological bottleneck of prevention and treatment of cancer
Cover More Drugs for Unmet Clinical Needs	• Guarantee people can use oncology drugs in the NRDL as soon as possible

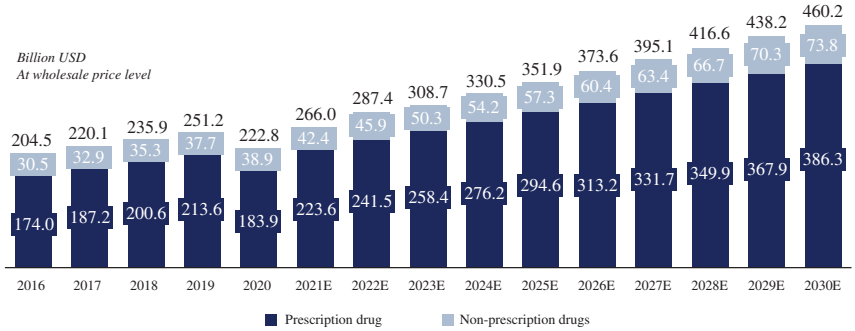
Sources: PRC government websites, Frost & Sullivan analysis.

OVERVIEW OF MARKET LANDSCAPE FOR OUR OTHER VENTURES

The joint ventures comprising our Other Ventures primarily sell prescription and over-the-counter proprietary and licensed drugs in China. China was the world's second-largest pharmaceutical market, including both prescription drugs and over-the-counter pharmaceutical products, estimated at US$222.8 billion in 2020. It is expected to further grow to US$460.2 billion by 2030, with a CAGR of 9.6% between 2020 and 2025 and 5.5% between 2025 and 2030, as shown in the chart below:

China Pharmaceutical Market, 2016-2030E

CAGR	Prescription	Non-prescription	Total
2016 – 2020	1.4%	6.3%	2.2%
2020 – 2025E	9.9%	8.0%	9.6%
2025E – 2030E	5.6%	5.2%	5.5%



Notes: US$1 = RMB6.5; and E = estimated.

Source: Frost & Sullivan analysis.

Rising per capita incomes, an aging population, and, with respect to prescription drugs, regulatory reforms and greater access to health care through improved medical insurance programs are expected to be the key drivers of growth in this market.

The prescription drug market in China is highly competitive and is characterized by a number of established, large pharmaceutical companies, as well as some smaller emerging pharmaceutical companies. Prescription drugs sold in China compete primarily on the basis of brand recognition, pricing, sales network, promotion activities, product efficacy, safety and reliability.

Over-the-counter pharmaceutical products are the main component of the consumer health business of Other Ventures. Over-the-counter pharmaceutical products sold in China compete primarily on the basis of brand recognition, pricing, sales network, promotion activities, product safety and reliability.

SOURCES OF INFORMATION

We have engaged Frost & Sullivan to conduct a detailed analysis and to prepare an industry report on the worldwide and China oncology and pharmaceutical markets. Frost & Sullivan is an independent global market research and consulting company founded in 1961 and is based in the United States. Services provided by Frost & Sullivan include market assessments, competitive benchmarking, and strategic and market planning for a variety of industries.

We have included certain information from the F&S Report in this document because we believe such information facilitates an understanding of the pharmaceutical markets, including the oncology and immunology drug markets, for potential investors. In compiling and preparing the F&S Report, Frost & Sullivan has adopted the following assumptions: (i) the overall social, economic and political environment in China, the United States and globally is expected to remain stable during the forecast period; (ii) the economic and industrial development in China, the United States and globally is likely to maintain a steady growth trend over the next decade; (iii) related key industry drivers are likely to continue driving the growth of the relevant global inhibitor market and oncology drugs market during the forecast period, such as the increasing number of new cancer incidences, increasing number of oncology drugs, supportive government programs and policies, increasing amount of research & development expenditures and improved affordability of drugs; (iv) the negative impact caused by the COVID-19 outbreak in 2020 on the industry was limited and taking into account the impact of the COVID-19 outbreak and estimating market growth for 2021 and beyond in a conservative manner based on the industry and economic recovery in China, the United States and globally since the second quarter of 2020; and (v) there is no extreme force majeure or industry regulation by which the market may be affected dramatically or fundamentally. Frost & Sullivan prepared the F&S Report based on public and proprietary sources. Public sources utilized include news articles, marketing materials and filings by other industry participants as well as information from trade associations. Proprietary sources consist of Frost & Sullivan's own research database, survey data, industry analyst reports and exclusive interviews with industry participants, customers and other industry experts. Frost & Sullivan utilized its proprietary forecasting models to cross-check and synthesize the data to produce both qualitative and quantitative analyses and projections included in this document Frost & Sullivan believes that the basic assumptions used in preparing the F&S Report, including those used to make future projections, are factual, correct and not misleading. Frost & Sullivan has independently analyzed the information, but the accuracy of the conclusions of its review largely relies on the accuracy of the information collected. Frost & Sullivan research may be affected by the accuracy of these assumptions and the choice of these primary and secondary sources.

We have agreed to pay Frost & Sullivan a fee of RMB550,000 (HK$654,961) for the preparation of the F&S Report which was not contingent upon our successful listing or on the content of the F&S Report.

The following section sets updated and supplemental information relating to selected aspects of our business and operations to reflect changes subsequent to the filing of our 2020 Annual Report.

OVERVIEW

We are a global commercial-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted therapies and immunotherapies for the treatment of patients with cancer and immunological diseases.

Founded in 2000, our Company was one of the first companies to establish an in-house drug discovery engine in China aimed at creating novel therapies for the global market, according to Frost & Sullivan. As these innovations have progressed, we have added extensive clinical and regulatory, manufacturing and commercial operations resulting in a fully-integrated biopharmaceutical company of over 1,300 personnel as of June 8, 2021 (the "Latest Practicable Date"). This allows us to retain complete operational control of our assets, in order to realize their full economic value in our two focus markets of China and the United States, which represented nearly 60% of the global pharmaceutical market in 2020.

Over the past fifteen years, our in-house discovery engine has created a broad pipeline of ten clinical stage drug candidates with a further seven oncology and immunology drug candidates in preclinical testing. Our success in discovery has also led to development collaborations with leading global pharmaceutical companies such as AstraZeneca and Eli Lilly.

In 2018, we became the first ever biotech company to bring a novel oncology drug, fruquintinib for third-line mCRC patients, from discovery through to unconditional approval and launch in China. Since then, we have built an oncology commercial team of about 520 persons in China to market fruquintinib as well as our other products as they are approved. Our commercial team launched our second in-house discovered oncology drug, surufatinib for advanced non-pancreatic NET, in early 2021. Our third in-house discovered drug, savolitinib for lung cancer, is now undergoing final regulatory review with a potential launch in China as early as mid-2021. A further seven oncology drug candidates are in an earlier stage of clinical development in China (Phase I/Ib and Phase Ib/II proof of concept studies), with one having transitioned into a Phase II registration-intent study in April 2021 and one targeted to transition into a Phase II registration-intent study in 2021.

In the United States, our three lead assets are also entering final regulatory review or have started Phase III registration or Phase II registration-intent studies, and a further three oncology drug candidates are in an earlier stage of clinical development (Phase I/Ib and Phase Ib/II proof of concept studies). Supporting all international clinical and regulatory activities is a rapidly expanding organization of about 80 personnel based primarily in New Jersey as of the Latest Practicable Date. We are also now building our own U.S. commercial team in preparation for a potential surufatinib U.S. launch in late 2021 or early 2022. If approved, surufatinib will become only the second ever novel oncology drug discovered by a biotech company in China to be launched in the United States, according to Frost & Sullivan.

Our portfolio of in-house discovered drug candidates are being developed both as monotherapies and in novel drug combinations to treat a wide spectrum of diseases which we believe may address unmet medical needs and represent large commercial opportunities globally. Beyond our core markets of China and the United States, we intend to pursue opportunities for additional geographical partnerships to fully realize the value of our assets.

We started operations in 2000 as a wholly owned subsidiary of CK Hutchison. Our Shares have been admitted to trading on the AIM since 2006, and our ADSs have been listed on Nasdaq since 2016. Immediately following the completion of the Global Offering, CK Hutchison will continue to be indirectly interested in approximately 39.19% of our Shares in issue (assuming the Over-allotment Option is not exercised) or approximately 38.48% of our Shares in issue (assuming the Over-allotment Option is exercised in full).

Our operational achievements and capabilities to date include:

Broad pipeline of differentiated targeted therapies and immunotherapies built for the global market. We have a pipeline of differentiated drug candidates covering both novel and validated targets, including MET, VEGFR, FGFR, CSF-1R, PI3K8, Syk, IDH, ERK and EGFR. The aim of our research is to develop drugs with high selectivity and superior safety profiles, a key benefit of which is that our drug candidates have the potential to be effectively paired with other oncology and immunology therapies at effective dosages with fewer side effects (although drugs with high selectivity may also be associated with target-related adverse events and drug tolerance issues).

Commercially launching products while continuing to discover new assets. In China, we have launched two of our internally developed drugs, fruquintinib (Elunate in China) and surufatinib (Sulanda in China), to patients, and we have filed for marketing authorization for savolitinib. All three drugs are in late-stage development outside of China, with the most advanced being surufatinib for which we completed a rolling NDA submission in the United States in April 2021. In addition, we have seven additional drug candidates in earlier stage clinical development (Phase I/Ib and Phase Ib/II proof of concept studies) and several advanced preclinical drug candidates.

Comprehensive global in-house discovery and development capabilities. We have a comprehensive drug discovery and development operation covering chemistry, biology, pharmacology, toxicology, chemistry and manufacturing controls for clinical and commercial supply, clinical and regulatory and other functions. It is led by a team of approximately 680 scientists and staff as of the Latest Practicable Date, who have created one of the broadest global clinical pipelines among our peer oncology and immunology focused biotechnology companies according to Frost & Sullivan. Currently, we are conducting and planning over 40 different clinical studies in oncology patients globally, including plans for over ten Phase III registration and Phase II registration-intent studies underway by the end of 2021.

Fast expanding and productive international organization. Our U.S. and European teams of approximately 80 mainly clinical and regulatory staff as of the Latest Practicable Date have significantly broadened our international operations, particularly in the United States, Europe, Japan and Australia. Our international clinical team has established a productive track record since it was established in 2018, including the submission of a rolling U.S. NDA filing for surufatinib, initiation of a large global randomized controlled study for fruquintinib, and ongoing U.S. and European Phase I/II trials for our drug candidates HMPL-689, HMPL-523 and HMPL-306. The FDA granted surufatinib Fast Track Designations for non-pancreatic and pancreatic NETs as well as an orphan drug designation for pancreatic NETs. Fruquintinib has also received FDA Fast Track Designation for late-stage CRC. We are now also building a commercial team in the United States, having completed the recruitment of a senior leadership team based in New Jersey, to support the potential upcoming launch of surufatinib in the United States.

Long-standing drug marketing and distribution experience to support the realization of in-house oncology innovations in China. We have built large-scale and profitable drug marketing and distribution capabilities through our Other Ventures operations, which primarily manufacture, market and distribute prescription drugs in China. Our 20-year track record and deep institutional knowledge of the drug marketing and distribution process are being leveraged to bring our in-house oncology innovations to patients. We have built and continue to expand our in-house oncology drug sales team of about 520 persons (compared to 90 at the end of 2019) to support the commercialization of recently launched Elunate and Sulanda and our other innovative drugs, if approved, throughout China. Our oncology drug sales team has the capability to cover over 2,500 oncology hospitals and over 20,000 oncology physicians in China, a network that we estimate represents over 90% of oncology drug sales in China.

Oncology Commercial Operations

Surufatinib – Sulanda in China

We received approval from the NMPA for Sulanda as a treatment for patients with advanced non-pancreatic NET in December 2020 and commercially launched it in mid-January 2021, within three

weeks of approval. By the end of January 2021, Sulanda prescriptions had been written in 30 provinces in China. Further commercialization activities are underway. Most notably, we are working to improve patient access to Sulanda. We have implemented a broad-scale, need-based patient access program which could materially reduce patients' out-of-pocket costs, while aiming to have Sulanda be included on the 2022 NRDL. According to Frost & Sullivan, there were potentially over 300,000 patients living with NET in China in 2019. See "*Recent Developments – Summary of First Quarter 2021 Highlights*" for details on the sales of Sulanda for the three months ended March 31, 2021.

Fruquintinib – Elunate in China

At the end of 2018, our collaboration partner Eli Lilly commenced commercial sales of Elunate targeting the more than 80,000 mCRC third-line patients in China each year. In January 2020, Elunate was included on China's NRDL and is therefore now available in public hospitals throughout China, paving the way to significantly broaden access for advanced CRC patients and rapidly build penetration in China over the coming years. In October 2020, we took over the development and execution of all on-the-ground medical detailing, promotion and local and regional marketing responsibilities in China through an amendment to our collaboration terms with Eli Lilly. Since taking on these commercial responsibilities, we have deployed our oncology drug sales force to market Elunate. We are now quickly expanding hospital pharmacy listings, one of the most important factors affecting broad-scale adoption of Elunate in China. We increased hospital listings to approximately 380, an approximately 95% increase since our assumption of responsibility.

Driven in part by the inclusion of Elunate on the 2020 NRDL and our assumption of responsibility for detailing, promoting and marketing the drug in China in October 2020, total in-market sales of Elunate by Eli Lilly, as provided to us by Eli Lilly, increased by 91.5% to US$33.7 million for the year ended December 31, 2020 compared to US$17.6 million for the year ended December 31, 2019. We recognize revenue for royalties and manufacturing costs and, since October 1, 2020, additional service payments in association with our expanded role in the commercialization of Elunate paid to us by Eli Lilly. Subject to meeting pre-agreed sales targets, Eli Lilly will pay us an estimated total of 70% to 80% of Elunate sales in the form of royalties, manufacturing costs and service payments. See "*Recent Developments – Summary of First Quarter 2021 Highlights*" for details on the sales of Elunate for the three months ended March 31, 2021.

Savolitinib – to be marketed by AstraZeneca, if approved, in China

We have submitted an NDA to the NMPA for the treatment of patients with MET exon 14 skipping alteration NSCLC. The NDA was accepted in May 2020, priority review status was granted in July 2020 and review is underway. If the NDA is approved, we will be responsible for manufacturing and all other marketing authorization holder responsibilities, and our commercial collaboration partner AstraZeneca is expected to launch savolitinib in China through the same large-scale oncology commercial organization that markets Tagrisso, Imfinzi and Iressa, among others. In return for these commercial rights, AstraZeneca will pay us a 30% royalty on all sales, various development and commercial milestones and manufacturing fees.

Additional potential indications are being developed for each of surufatinib, fruquintinib and savolitinib, as described below.

International Clinical Drug Development (Outside China)

Six of our oncology drug candidates are in development outside China, including savolitinib. Our fast expanding international organization, led mainly from the United States, is developing these candidates. We completed the rolling submission of our first U.S. NDA, for surufatinib, in April 2021. We are on track to complete recruitment of a global Phase III study for fruquintinib in late 2021. Further, the organization is progressing three oncology drug candidates (HMPL-689, HMPL-523 and HMPL-306) toward Phase I, I/Ib and II proof-of-concept or registration enabling studies later in 2021.

Savolitinib, via a global collaboration with AstraZeneca, is in a registration-intent Phase II study with additional global registration studies set to start in 2021.

The following table summarizes the status of our international clinical drug portfolio's development as of the Latest Practicable Date:

Our International Clinical Development Pipeline

Program	Treatment	Indication	Target patient	Study name	Sites	Phase	Dose finding/ safety run-in	Proof-of-concept	Registration
Savolitinib MET	**Savolitinib** + Tagrisso	NSCLC	2L/3L EGFRm; Tagrisso ref.; MET+	SAVANNAH	Global	II (Reg)	*		
	Savolitinib + Imfinzi (PD-L1)	Papillary RCC	MET+	SAMETA	Global	III	**		
	Savolitinib + Imfinzi (PD-L1)	Papillary RCC	All	CALYPSO	UK/Spain	II	***		
	Savolitinib + Imfinzi (PD-L1)	Clear cell RCC	VEGFR TKI refractory	CALYPSO	UK/Spain	II	***		
	Savolitinib	Gastric cancer	MET+	VIKTORY	S Korea	Ib/II	***		
	Savolitinib	Colorectal cancer	MET+		US	II	***		
Surufatinib VEGFR 1/2/3; FGFR1; CSF-1R	**Surufatinib**	NET	Refractory		US	Ib (NDA)			NDA Submitted
	Surufatinib	NET	Refractory		EU	Ib (MAA)			MAA Planned
	Surufatinib	Biliary tract cancer			US	Ib			
	Surufatinib	Soft tissue sarcoma			US	Ib			
	Suru. + tislelizumab (PD-1)	Solid tumors			US/EU	Ib/II			
Fruquintinib VEGFR 1/2/3	**Fruquintinib**	Colorectal cancer	Refractory	FRESCO-2	US/EU/JP	III			
	Fruquintinib	Breast cancer			US	Ib			
	Fruq. + tislelizumab (PD-1)	TN breast cancer			US	Ib/II	**		
	Fruq. + tislelizumab (PD-1)	Solid tumors			TBD	Ib/II	**		
HMPL-689 PI3Kδ	**HMPL-689**	****			Australia	I			
	HMPL-689	Indolent NHL			US/EU	I/Ib			
HMPL-523 Syk	**HMPL-523**	Indolent NHL			Australia	Ib			
	HMPL-523	Indolent NHL			US/EU	I/Ib			
HMPL-306 IDH 1/2	**HMPL-306**	Solid tumors			US/EU	I			
	HMPL-306	Hem. malignancies			US/EU	I			

* Phase II registration-intent study subject to regulatory discussion; ** In planning; *** Investigator-initiated trials (IIT); and **** Conducted in healthy volunteers. (Reg) = Registration Intent; (NDA) = NDA submitted for review; (MAA) = MAA submission planned; and (Mkt) = NDA approved and product is on the market.

Notes: MET = mesenchymal epithelial transition receptor; VEGFR = vascular endothelial growth factor receptor; TKI = tyrosine kinase inhibitor; EGFRm = epidermal growth factor receptor mutation; NET = neuroendocrine tumors; FGFR1 = fibroblast growth factor receptor 1; CSF-1R = colony stimulating factor-1 receptor; PI3Kδ = Phosphatidylinositol-3-Kinase delta; Syk = spleen tyrosine kinase; NSCLC = non-small cell lung cancer; RCC = renal cell carcinoma; NHL = non-Hodgkin's Lymphoma; TN = triple negative; and IDH 1/2 = isocitrate dehydrogenase 1/2.

Savolitinib – selective MET inhibitor in late-stage clinical development as a monotherapy and in combination therapies in global partnership with AstraZeneca

Savolitinib is a potent and selective small molecule inhibitor of the MET receptor tyrosine kinase, an enzyme which has been shown to function abnormally in many types of solid tumors. We designed savolitinib through chemical structure modification to specifically address kidney toxicity, the primary issue that halted development of several other selective MET inhibitors. In clinical trials to date in over 1,100 patients globally, savolitinib has shown promising signs of clinical efficacy in patients with multiple types of MET gene alterations in lung cancer, kidney cancer and gastric cancer with an acceptable safety profile.

We are currently testing savolitinib in global partnership with AstraZeneca, both as a monotherapy and in combination with immunotherapy and targeted therapy. Most notably, we are currently progressing the SAVANNAH study on savolitinib in combination with Tagrisso for treating EGFRm+, NSCLC patients who have progressed following first or second-line Tagrisso therapy due to MET amplification. The study has fully enrolled one of the three dose cohorts and is expected to complete enrollment in mid-2021, with planning for the global Phase III study now underway.

Proof-of-concept studies of savolitinib in kidney cancer (as a monotherapy as well as in combination with a PD-L1 inhibitor) and gastric cancer (as a monotherapy as well as in combinations with

chemotherapy) have demonstrated positive results, with subsequent clinical development in planning. For example, we are initiating a global Phase III pivotal trial (SAMETA) for savolitinib in combination with Imfinzi, AstraZeneca's anti-PD-L1 antibody durvalumab, in MET positive patients with PRCC, a form of kidney cancer. Savolitinib opportunities are also continuing to be explored in multiple other MET-driven tumor settings via investigator-initiated studies including CRC.

Surufatinib – unique angio-immuno kinase inhibitor with NDA submission completed in the United States; potential first VEGFR/FGFR/CSF-1R inhibitor for all advanced NETs

Surufatinib, which has been approved in China for the treatment of advanced non-pancreatic NETs, is a novel, oral angio-immuno kinase, small molecule inhibitor that selectively inhibits the tyrosine kinase activity associated with VEGFR and FGFR, which both inhibit angiogenesis, and CSF-1R, which regulates tumor-associated macrophages, promoting the body's immune response against tumor cells. Its unique dual mechanism of action may be very suitable for possible combinations with other immunotherapies. We believe surufatinib is potentially the first VEGFR/FGFR/CSF-1R inhibitor for all advanced NETs.

In the United States, the FDA granted orphan drug designation to surufatinib for the treatment of pancreatic NETs in November 2019 and granted Fast Track Designations for the treatment of both pancreatic NETs and non-pancreatic NETs in April 2020. In May 2020, we reached an agreement with the FDA that the completed SANET-ep and SANET-p studies in China, along with existing data from surufatinib in U.S. non-pancreatic and pancreatic NET patients, could form the basis to support an NDA submission. Pharmacokinetic and safety data from U.S. Phase Ib NET cohorts demonstrated similar profiles of surufatinib between Chinese and U.S. patients.

We completed a U.S. NDA submission in April 2021 for surufatinib for the treatment of pancreatic and non-pancreatic NETs. This is our first NDA in the United States. Filing acceptance of the NDA is subject to FDA review of the complete application. The data package will also be used to file an MAA to the EMA, based on scientific advice from the CHMP.

We have various additional clinical trials of surufatinib ongoing as a single agent, as well as in combination with checkpoint inhibitors. In March 2021, we dosed the first patient in a combination study of surufatinib with tislelizumab, an anti-PD-1 antibody being developed by BeiGene, in the United States and Europe. In addition, we believe surufatinib has potential in a number of other tumor types such as NETs, CRC, small cell lung cancer, gastric cancer and soft tissue sarcoma.

Surufatinib is the first oncology medicine that we have launched in China and expanded development globally without the support of a development partner. We own all rights to surufatinib globally.

Fruquintinib – potential selective VEGFR 1, 2 and 3 inhibitor with the best selectivity for its targets in global Phase III development

Fruquintinib, which has been approved in China for the treatment of advanced mCRC, is a highly selective and potent oral inhibitor of vascular endothelial growth factor receptors, known as VEGFR 1, 2 and 3. We believe that fruquintinib has the potential to become a global small molecule VEGFR 1, 2 and 3 inhibitor for many types of solid tumors on the basis of it having the highest selectivity, and we are currently studying fruquintinib in CRC, gastric cancer, breast cancer and other solid tumor types. Fruquintinib was designed to improve kinase selectivity to minimize off-target toxicities, improve tolerability and provide more consistent target coverage. The tolerability in patients to date, along with fruquintinib's low potential for drug-drug interaction based on preclinical assessment, suggests that it may be highly suitable for combinations with other anti-cancer therapies.

Building on the data collected from our successful Phase III trial in China, known as the FRESCO study, which supported fruquintinib's approval in China, we initiated FRESCO-2, a large randomized controlled study of fruquintinib in the United States, Europe and Japan. The first patient was dosed in September 2020, and the study is enrolling over 680 patients in approximately 165 sites in 14 countries.

The FDA granted Fast Track Designation for the development of fruquintinib for the treatment of patients with mCRC in June 2020. The FDA has acknowledged the totality of the fruquintinib clinical data, including the FRESCO-2 study, if positive, the prior positive Phase III FRESCO study demonstrating improvement in OS that led to fruquintinib approval for mCRC in China in 2018 and additional completed and ongoing supporting studies in mCRC, could support a future NDA for the treatment of patients with third-line and above mCRC. The EMA and PMDA have reviewed and endorsed the FRESCO-2 study design. Preliminary data of U.S. Phase I/Ib CRC cohorts demonstrated encouraging efficacy in patients refractory or intolerant to Stivarga and Lonsurf.

We are planning global combination studies of fruquintinib with BeiGene's anti-PD-1 antibody tislelizumab for the treatment of various solid tumor cancers, including a Phase Ib/II study in advanced, refractory triple negative breast cancer.

Fruquintinib is being commercialized and developed in partnership with Eli Lilly in China, where we are responsible for development, manufacturing, on-the-ground medical detailing, promotion and local and regional marketing activities.

We own all rights to fruquintinib outside of China.

HMPL-689 – PI3Kδ inhibitor with the best selectivity with potential in hematological cancer

HMPL-689 is a novel, highly selective and potent small molecule inhibitor targeting the isoform PI3Kδ. In preclinical pharmacokinetic studies, HMPL-689's pharmacokinetic properties have been found to be favorable with good oral absorption, moderate tissue distribution and low clearance. HMPL-689 is also expected to have low risk of drug accumulation and drug-drug interaction and is highly potent, particularly at the whole blood level.

We have early-stage clinical trials of HMPL-689 ongoing, and preliminary evidence suggests that HMPL-689 may perform in the clinic as designed. Based on extensive Phase I/Ib proof-of-concept clinical data in China and Australia on HMPL-689, we have opened 18 U.S. and European sites for a Phase I/Ib study with patient enrollment underway, focusing on advanced relapsed or refractory lymphoma. In the second half of 2021, we plan to complete FDA regulatory discussions, followed by the initiation of Phase II registration-intent studies.

We own all rights to HMPL-689 globally.

HMPL-523 – potentially the first selective Syk inhibitor for hematological cancer

HMPL-523 is a novel, highly selective, oral, small molecule inhibitor targeting the Syk for the treatment of hematological cancers and certain chronic immune diseases. Syk is a major component in B-cell receptor signaling and is an established therapeutic target in multiple subtypes of B-cell lymphomas. Because B-cell malignancies are heterogeneous and patients commonly experience relapse despite current therapies, there is a need for new therapies.

We have various clinical trials of HMPL-523 ongoing. We have 22 U.S. and European sites for a Phase I/Ib study with patient enrollment underway, focusing on advanced relapsed or refractory lymphoma and are close to establishing our Phase II dose.

We own all rights to HMPL-523 globally.

HMPL-306 – potentially the first dual inhibitor of IDH1 and IDH2 with applications in hematological malignancies, gliomas and solid tumors

HMPL-306 is a novel small molecule dual-inhibitor of isocitrate dehydrogenase 1 and 2, or IDH1 and IDH2, enzymes. IDH1 and IDH2 mutations have been implicated as drivers of certain hematological malignancies, gliomas and solid tumors, particularly among acute myeloid leukemia patients. We initiated an international Phase I study with the first patient dosed in the United States in March 2021.

We own all rights to HMPL-306 globally.

China Clinical Drug Development

We are the marketing authorization holder of two internally discovered and developed innovative oncology medicines (Elunate and Sulanda) and may have a third drug (savolitinib), potentially the first selective MET inhibitor in China, if the NDA currently under review is approved. We have seven additional drug candidates in earlier stage clinical development (Phase I/Ib and Phase Ib/II proof-of-concept studies) and several advanced preclinical drug candidates. Our four submitted China NDAs were classified by the NMPA as Category 1. If submitted for approval, all of our drug candidates are expected to be classified as Category 1, as they are innovative drugs that have not been marketed inside or outside of China.

The following table summarizes the status of our China clinical programs as of the Latest Practicable Date:

Our China Clinical Development Pipeline

Program	Treatment	Indication	Target patient	Study name	Phase	Dose finding/ safety run-in	Proof-of-concept	Registration
Savolitinib MET	**Savolitinib**	NSCLC	MET exon 14 skipping		II (NDA)			NDA accepted
	Savolitinib + Tagrisso	NSCLC	2L EGFR TKI ref. NSCLC; MET+	SACHI	III	*		
	Savolitinib + Tagrisso	NSCLC	Naïve MET+ & EGFRm NSCL	SANOVO	III	*		
	Savolitinib	Gastric cancer	2L; MET+		II (Reg)	*		
Surufatinib VEGFR 1/2/3; FGFR1; CSF-1R	**Surufatinib**	Pancreatic NET	All	SANET-p	NDA			NDA accepted
	Surufatinib	Non-Pancreatic NET	All	SANET-ep	III (Mkt)			Marketed
	Surufatinib	Biliary tract cancer	2L; chemotherapy refractory		IIb/III			
	Surufatinib + Tuoyi (PD-1)	NEN, ESCC, BTC			II			
	Surufatinib + Tuoyi (PD-1)	SCLC, GC, Sarcoma			II			
	Surufatinib + Tuoyi (PD-1)	TC, EMC, NSCLC			II			
	Surufatinib + Tyvyt (PD-1)	Solid tumors			I			
Fruquintinib VEGFR 1/2/3	**Fruquintinib**	Colorectal cancer	≥3L; chemotherapy refractory	FRESCO	III (Mkt)			Marketed
	Fruquintinib + Taxol	Gastric cancer	2L	FRUTIGA	III			
	Fruquintinib + Tyvyt (PD-1)	CRC, EMC, RCC, HCC			Ib/II			
	Fruquintinib + Tyvyt (PD-1)	GI tumors			Ib/II			
	Fruq. + geptanolimab (PD-1)	CRC			Ib			
	Fruq. + geptanolimab (PD-1)	NSCLC			Ib			
HMPL-689 PI3Kδ	**HMPL-689**	FL, MZL			II (Reg)			
	HMPL-689	MCL, DLBCL			Ib			
	HMPL-689	CLL/SLL, HL			Ib			
HMPL-523 Syk	**HMPL-523**	B-cell malignancies	All		I/Ib			
	HMPL-523	ITP	All		I/Ib			
HMPL-453 FGFR 1/2/3	**HMPL-453**	IHCC			II			
HMPL-306 IDH 1/2	**HMPL-306**	Hem. malignancies			I			
HMPL-295 (ERK, MAPK pathway)	**HMPL-295**	Solid tumors			I	*		
Epitinib EGFR	**Epitinib**	Glioblastoma	EGFR gene amplified		Ib/II			
Theliatinib EGFR wt	**Theliatinib**	Esophageal cancer	EGFR over-expression			**		

* In planning; and ** Discontinued. (Reg) = Registration Intent; (NDA) = NDA submitted for review; (MAA) = MAA submission planned; and (Mkt) = NDA approved and product is on the market.

Notes: MET = mesenchymal epithelial transition receptor; VEGFR = vascular endothelial growth factor receptor; TKI = tyrosine kinase inhibitor; EGFRm = epidermal growth factor receptor mutation; FGFR1 = fibroblast growth factor receptor 1; CSF-1R = colony stimulating factor-1 receptor; NET = neuroendocrine tumors; NEN = neuroendocrine neoplasms; ESCC =esophageal squamous-cell carcinoma; BTC = biliary tract cancer; SCLC = small cell lung cancer; GC = gastric cancer; TC = thyroid cancer; EMC = endometrial cancer; CRC = colorectal cancer; HCC = hepatocellular carcinoma; GI = gastrointestinal; PI3Kδ = Phosphatidylinositol-3-Kinase delta; Syk = spleen tyrosine kinase; NSCLC = non-small cell lung cancer; RCC = renal cell carcinoma; NHL = Non-Hodgkin's Lymphoma; FL = follicular lymphoma; MZL = marginal zone lymphoma; MCL = mantle cell lymphoma; DLBCL = diffuse large B cell lymphoma; CLL/SLL = chronic lymphocytic leukemia/small lymphocytic lymphoma; HL = Hodgkin's lymphoma; ITP = immune thrombocytopenic purpura; IHCC = Intrahepatic cholangiocarcinoma; IDH 1/2 = isocitrate dehydrogenase 1/2; ERK = extracellular-signal-regulated kinase; and MAPK = RAS-RAF-MEK-ERK signaling cascade.

Savolitinib – NDA filed for potentially the first selective MET inhibitor in China

In May 2020, an NDA for savolitinib for the treatment of NSCLC with MET exon 14 skipping alterations was accepted for review by the NMPA, supported by a Phase II registration study, and the NMPA subsequently granted it priority review status. This is the first NDA filing for savolitinib globally and first for a selective MET inhibitor in China. Data from this study were most recently presented at the American Society of Clinical Oncology ("ASCO") 2020 Virtual Scientific Program.

We intend to initiate several studies in China in 2021, including two further pivotal Phase III studies in combination with Tagrisso in NSCLC patients in the second half of 2021 and a potential registrational Phase II study in metastatic gastric cancer in mid-2021.

Surufatinib – commercially launched as Sulanda in China in non-pancreatic NETs in January 2021; first VEGFR/FGFR/CSF-1R inhibitor for all advanced NETs (if also approved for advanced pancreatic NETs)

Surufatinib was approved by the NMPA in December 2020 for the treatment of non-pancreatic NETs and is now being marketed by us in China under the brand name Sulanda. The NMPA approval of surufatinib was based on results from the SANET-ep study, a Phase III trial in patients with advanced non-pancreatic NETs conducted in China. The positive results of this trial were highlighted in an oral presentation at the 2019 ESMO Congress and published in *The Lancet Oncology* in September 2020. Our in-house oncology drug sales team is now responsible for the marketing and commercialization of surufatinib throughout China for this indication.

We have submitted a second NDA in China for surufatinib in advanced pancreatic NETs supported by our SANET-p study, a Phase III trial in patients with advanced pancreatic NETs conducted in China. The NDA was accepted in September 2020, and review is underway. If approved, we believe surufatinib would be the only approved targeted therapy able to address and treat all subtypes of NETs.

We have commenced combination studies of surufatinib with Tuoyi, a PD-1 monoclonal antibody being developed by Junshi in China, where we are currently conducting Phase II studies in nine solid tumor indications, including NENs, BTC, gastric cancer, thyroid cancer, small cell lung cancer, soft tissue sarcoma, endometrial cancer, esophageal cancer and NSCLC. During ASCO 2021, encouraging preliminary Phase I/Ib results were presented for surufatinib in combination with Tuoyi in neuroendocrine carcinoma and gastric cancer.

In addition, we have expanded our collaboration with Innovent and, in July 2020, started a Phase I study in China to evaluate the safety and efficacy of Tyvyt in combination with surufatinib.

Fruquintinib – commercially launched as Elunate in China in CRC in November 2018; potential VEGFR 1, 2 and 3 inhibitor with the best selectivity for many solid tumors

Fruquintinib was first commercially launched in China, marketed by our partner Eli Lilly, in November 2018 for the treatment of advanced CRC. In January 2020, fruquintinib was included on the NRDL thereby broadening access by advanced CRC patients in China. Since launch, Eli Lilly has deployed a dedicated team of over 140 oncology commercial personnel to market fruquintinib in China. Since October 1, 2020, we have taken over development and execution of all on-the-ground medical detailing, promotion and local and regional marketing activities for fruquintinib in China, using our in-house oncology drug sales team supported by our long-standing drug marketing and distribution platforms. Subject to meeting pre-agreed sales targets, Eli Lilly will pay us an estimated total of 70% to 80% of Elunate sales in the form of royalties, manufacturing costs and service payments.

We believe that fruquintinib is a VEGFR 1, 2 and 3 inhibitor with the best selectivity and could be considered for development in China in many solid tumor indications in which VEGFR inhibitors have been approved globally. To this end, since 2018, we have assumed all planning, execution and decision-making responsibilities for life cycle indication development of fruquintinib in China.

In addition to its commercial launch in CRC in China, we have made progress with fruquintinib in various other cancer indications, including the FRUTIGA study in China, a pivotal Phase III study in

approximately 700 patients to evaluate the efficacy and safety of fruquintinib in combination with Taxol, a chemotherapy medication, compared with Taxol monotherapy for second-line treatment of advanced gastric cancer in patients who had failed first-line chemotherapy. We expect to complete enrollment of the study around the end of 2021.

We are conducting Phase Ib/II dose expansion studies in China of fruquintinib with Tyvyt, a PD-1 monoclonal antibody being developed by Innovent, in different tumor types, including HCC, endometrial cancer, RCC and CRC. Furthermore, we intend to conduct studies of fruquintinib in combination with BeiGene's tislelizumab for the treatment of various solid tumor cancers in China. During ASCO 2021, encouraging preliminary Phase I/Ib results were presented for fruquintinib in combination with two different PD-1 inhibitors: Tyvyt and geptanolimab.

HMPL-689 – PI3Kδ inhibitor with the best selectivity and with potential in hematological cancer

Our Phase I dose escalation study on HMPL-689 in China has been completed, and a recommended Phase II dose was selected. HMPL-689 was well tolerated, exhibiting dose-proportional pharmacokinetics, a manageable toxicity profile and single-agent clinical activity in relapsed/refractory B-cell lymphoma patients. Our Phase Ib expansion study in China is ongoing in multiple sub-categories of indolent non-Hodgkin's lymphoma. In April 2021, we commenced a registration-intent Phase II trial of HMPL-689, a highly selective and potent PI3Kδ inhibitor, in China in patients with relapsed or refractory follicular lymphoma and marginal zone lymphoma, two subtypes of non-Hodgkin's lymphoma.

HMPL-523 – potentially the first selective Syk inhibitor for hematological cancer

Data from an extensive Phase I/Ib dose escalation and expansion study (covering more than 200 patients) on HMPL-523 has encouraged us to initiate exploratory studies in China on multiple indolent non-Hodgkin's lymphoma sub-categories, including chronic lymphocytic leukemia/small lymphocytic lymphoma, follicular lymphoma, marginal zone lymphoma, Waldenstrom's macroglobulinemia and mantle cell lymphoma.

Furthermore, in August 2019 we commenced a Phase I study of HMPL-523 in China for the treatment of immune thrombocytopenia, an autoimmune disorder characterized by low platelet count and an increased bleeding risk. Dose escalation is near completion with planning and preparation for a Phase III trial in China now underway.

HMPL-453 – highly selective FGFR 1/2/3 inhibitor with potential in solid tumors

HMPL-453 is a highly selective and potent FGFR 1/2/3 inhibitor. Aberrant FGFR signaling is associated with tumor growth, promotion of angiogenesis, as well as resistance to anti-tumor therapies. A Phase II study is ongoing in patients with advanced IHCC with FGFR2 fusion that had failed at least one line of systemic therapy. IHCC is a cancer that develops within the bile ducts, the second most common primary hepatic malignancy after hepatocellular carcinoma. Approximately 10-15% of IHCC patients have tumors that harbor FGFR2 fusion.

HMPL-306 – potentially the first dual inhibitor of IDH1 and IDH2 with applications in hematological malignancies, gliomas and solid tumors

A Phase I trial in China was initiated in July 2020 in patients of relapsed or refractory hematological malignancies with an IDH1 and/or IDH2 mutation. Multiple sites have been initiated, and we aim to establish the Phase II dose in 2021.

HMPL-295 – an investigative and highly selective small molecule inhibitor of ERK in the MAPK pathway with the potential to address intrinsic or acquired resistance from upstream mechanisms such as RAS-RAF-MEK

HMPL-295, a novel ERK inhibitor, is our tenth in-house discovered small molecule oncology drug candidate. ERK is a downstream component of the RAS-RAF-MEK-ERK signaling cascade (MAPK pathway). This is our first of multiple candidates in discovery targeting the MAPK pathway.

We own all rights to HMPL-295 globally.

Epitinib – clinical-stage EGFR inhibitor

We have completed Phase I/Ib studies of epitinib, a small molecule EGFR inhibitor with demonstrated ability to penetrate the blood-brain barrier.

We are evaluating further development strategies for epitinib.

Discovery Research & Preclinical Development

We have built a drug discovery engine based in China, which has already produced a pipeline of 17 differentiated clinical and late pre-clinical stage drug candidates covering both novel and validated targets of which two are now marketed and one is under review for approval. We strive to create differentiated novel oncology and immunology treatments with global potential. These include furthering both small molecule and biologic therapies which address aberrant genetic drivers and cancer cell metabolism, modulate tumor immune microenvironment and target immune cell checkpoints. We design drug candidates with profiles that enable them to be used in innovative combinations with other therapies, such as chemotherapy, immunotherapy and other targeted therapies in order to attack disease simultaneously through multiple modalities and pathways. We believe that this approach can significantly improve treatment outcomes for patients.

In addition to our ten clinical-stage assets, we have three more novel oncology drug candidates in preclinical stage, including HMPL-653 (targeting solid tumors), HMPL-A83 (targeting hematological malignancies and solid tumors) and HMPL-760 (targeting hematological malignancies). We retain all global rights to these three drug candidates and are targeting dual U.S. and China IND submissions for some of them during 2021. We have also partnered with Inmagene to develop a further four novel immunological disease drug candidates that we created and are in preclinical stage.

Beyond these clinical and preclinical stage candidates, we continue to conduct research into discovering new types of drug candidates, including among others, small molecules addressing cancer-related apoptosis, cell signaling, epigenetics and protein translation; biologic drug candidates including bispecific antibodies; and novel technologies including antibody-drug conjugates and heterobifunctional small molecules.

Manufacturing

Our manufacturing site in Suzhou is a GMP-certified production facility, providing supplies of our drug candidates for clinical trials and Elunate and Sulanda for commercial sale. We plan to continue to invest resources in the Suzhou facility, expanding the production team in phases. At the end of 2020, we commenced construction of a large-scale manufacturing plant for innovative drugs in Shanghai. The Shanghai factory will be our largest manufacturing facility, with a production capacity estimated to be five times that of our manufacturing plant in Suzhou. The first phase will be primarily for small molecule production, while the second phase is expected to include expansion into large molecule production.

Other Ventures

In addition to our Oncology/Immunology operations, our Other Ventures include large-scale drug marketing and distribution platforms covering about 320 cities and towns in China with approximately 4,800 manufacturing and commercial personnel as of December 31, 2020. Built over the past 20 years, it primarily focuses on prescription drug and consumer health products mainly through: (i) Shanghai Hutchison Pharmaceuticals, a non-consolidated joint venture with a commercial team of about 2,200 staff managing the medical detailing and marketing of a range of own-brand prescription drug products; (ii) Hutchison Sinopharm, a consolidated joint venture focused on providing commercial services for our own marketed drugs, as well as marketing third-party prescription drug products and our science-based infant nutrition products; and (iii) Hutchison Baiyunshan, a non-consolidated joint venture focused on

the manufacturing, marketing and distribution of primarily own-brand over-the-counter drugs. See "*Recent Developments – Recent Disposal*" for more information on Hutchison Baiyunshan.

Net income attributable to our Company from our Other Ventures totaled US$41.4 million, US$41.5 million and US$72.8 million for the years ended December 31, 2018, 2019 and 2020, respectively, and are remitted to our Group through dividend payments primarily from our non-consolidated joint ventures mentioned above. In 2020, dividends of US$86.7 million were paid from these joint ventures to our Group, with aggregate dividends received since inception of over US$300 million.

OUR STRENGTHS

We believe the following strengths have contributed to our success and differentiate us from our competitors:

Fully-integrated biopharmaceutical company with capability to support development and launch of our products in our core markets

Our fully integrated drug discovery and development operation encompasses all aspects of research and development, clinical and regulatory capabilities, commercialization and manufacturing, all of which work seamlessly together. With the NMPA's approval of fruquintinib, in 2018, we became the first Chinese biopharmaceutical company to bring a targeted oncology therapy from discovery through unconditional approval and commercialization in China. In addition, we received approval from the NMPA for surufatinib as a treatment for patients with advanced non-pancreatic NET in December 2020 and commercially launched it in mid-January 2021, within three weeks of approval.

In-house discovery. We have built a drug discovery engine based in China, which has been engaged in innovative drug research and development for almost two decades, making us one of the first globally-facing novel drug discovery companies in China, according to Frost & Sullivan. With highly integrated chemistry, biology, pharmacology, toxicology, chemistry and manufacturing control functions, this team is responsible for de novo in-house discovery and development of two marketed drugs, eight (including one undergoing marketing authorization review) potential new drugs in various stages of human testing and three potential new drugs nearing clinical testing.

Clinical and regulatory capabilities. Our dedicated research and development team comprises approximately 680 scientists and staff with offices in Shanghai, Suzhou and New Jersey as of the Latest Practicable Date. Together, the global organization has achieved approval of two NDAs in China, is managing two further applications currently under review in China and is in the process of submitting an NDA in the United States. Currently, we are conducting and planning over 40 different clinical studies in oncology patients globally, including plans for over ten Phase III registration and Phase II registration-intent studies underway by the end of 2021.

Commercialization. We have built, and continue to expand, our in-house oncology drug sales team of about 520 persons to support the commercialization of Elunate, Sulanda and our other innovative drugs, if approved, throughout China as of the Latest Practicable Date. Our oncology drug sales team has the capability to cover most of the top oncology hospitals and oncology physicians in China which we estimate represents over 90% of oncology drug sales in China, and we are rapidly expanding our U.S.-based international commercial capabilities. The scale, experience and deep understanding of the Chinese healthcare system of our commercial team, including in particular how drugs are approved and ordered by hospitals and doctors and the drug distribution system in China, represent a significant barrier to entry for newer entrants into the oncology drug sector in China.

Manufacturing. Our in-house manufacturing capabilities include a GMP-certified formulation facility in Suzhou which produces supplies of our drug candidates for clinical trials and commercial supplies of Elunate and Sulanda and a large-scale manufacturing plant for innovative drugs in Shanghai, which is currently under construction. The first phase of our Shanghai plan will focus on small molecule production and the second phase is expected to include an expansion into large molecule production.

Commercialized drugs and late-stage clinical drug candidates with significant commercial potential

We have two approved and launched assets, one asset under NMPA priority review and seven drug candidates in clinical development. We believe the success of our commercialized drugs and late-stage clinical drug assets will be driven by their uniquely selective clinical profiles, high level of efficacy in patients and their ability to provide clinical benefits as compared to that of treatment alternatives, if any are available. We retain majority control and therefore the economics for most of our assets.

- *Fruquintinib*. Fruquintinib, self-discovered and developed by our Company and sold under the brand name Elunate, was approved for marketing in China by the NMPA in September 2018 and commercially launched with Eli Lilly in late November 2018 for third-line treatment of mCRC. In January 2020, Elunate was included in China's NRDL and is therefore now available in public hospitals throughout China at a reduced price, paving the way to significantly broaden access for advanced CRC patients and rapidly build penetration in China over the coming years.

  In China, CRC has become increasingly prevalent. The incidence of CRC in China is estimated to range from 453,400 to 550,000 new cases in 2020, compared to 400,700 in 2016. It is estimated that among all CRC patients in China, there are approximately 15% who are receiving third-line treatment. Among the available targeted therapies, fruquintinib has demonstrated numerically higher disease control rate, median PFS rate and median overall survival rate in a Phase III trial in Chinese third-line colorectal cancer patients, compared to Phase III results for other therapies in the same patient population. As the first mover to bring a self-discovered and developed innovative targeted cancer treatment to market in China with the launch of Elunate, we believe we are well positioned to take advantage of this market opportunity. According to Frost & Sullivan, the global market for CRC therapies was approximately US$17.4 billion in 2020 and is expected to grow to US$42.7 billion by 2030.

  In October 2020, we took over the development and execution of all on-the-ground medical detailing, promotion and local and regional marketing activities in China through an amendment to our collaboration terms with Eli Lilly. Subject to meeting pre-agreed sales targets, we are entitled to 70% to 80% of the economics in China. In addition, as we retain all global rights, we are entitled to 100% of the economics outside of China, where we are conducting a Phase III registration study in the United States, Europe and Japan.

  We believe that fruquintinib has the potential to become a global small molecule VEGFR 1, 2 and 3 inhibitor with the best selectivity for many types of solid tumors, and we are currently studying fruquintinib in CRC, gastric cancer, lung cancer and other solid tumor types.

- *Surufatinib*. Surufatinib, self-discovered and developed by our Company and sold under the brand name Sulanda, was approved for marketing in China by the NMPA in December 2020 and commercially launched by us in January 2021 for the treatment of advanced non-pancreatic NETs. By the end of January 2021, Sulanda prescriptions had been written in 30 provinces in China.

  In China, there were about 71,300 newly diagnosed NET patients in 2020. Among all newly diagnosed NET patients, at least 55% are suitable for drug therapy or drug adjuvant therapy. While no China prevalence data exists, according to Frost & Sullivan, there could be over 300,000 patients living with the disease. Importantly, NETs are associated with a relatively long duration of survival compared to other tumors and as a result, while incidence rates are modest, there is a relatively large population of NETs patients. We believe the benefit of surufatinib as a monotherapy to patients with non-pancreatic NETs in China could be significant as compared to the minimal treatment alternatives currently available to them. According to Frost & Sullivan, the global market for NET therapies was approximately US$6.0 billion in 2020 and is expected to grow to US$21.5 billion by 2030.

  We have implemented a broad-scale, need-based patient access program which could materially reduce patient out-of-pocket costs and are applying for Sulanda to be included in the 2022

NRDL. We have also completed a rolling NDA submission to the FDA. We retain the global economics for surufatinib.

We believe surufatinib is potentially the first VEGFR/FGFR/CSF-1R inhibitor for all advanced NETs. We currently have various clinical trials of surufatinib ongoing as a single agent in patients with NETs, BTC and soft tissue sarcoma and in combination with checkpoint inhibitors. We believe surufatinib has potential in a number of other tumor types such as breast cancer with FGFR 1 activation.

- *Savolitinib*. Savolitinib was granted priority review status by the NMPA in May 2020 and review is currently underway for its treatment of MET exon 14 skipping alteration NSCLC.

  In China, there were an estimated 785,500 newly diagnosed NSCLC patients in 2020, and this number is expected to exceed one million by 2030. It is estimated that 4.0-6.0% of newly diagnosed NSCLC patients harbor genetic MET aberrations. There are currently no approved selective MET inhibitors on the market in China. Thus savolitinib, if approved, is expected to be the first therapy in China specifically targeting patients with these mutations. According to Frost & Sullivan, the China market for small molecule MET inhibitors is expected to grow to US$4.8 billion by 2030.

If the NDA is approved, we will be the marketing authorization holder, earning a risk-free royalty of 30% of sales, and our collaboration partner AstraZeneca is expected to launch savolitinib in China through the same oncology commercial organization that markets Tagrisso, Imfinzi and Iressa, among others. Outside of China, AstraZeneca has more control and pays us a tiered royalty rate from 14% to 18% on product revenues, subject to certain potential adjustments.

We believe savolitinib is potentially the first selective MET inhibitor for the treatment of kidney cancer and gastric cancer in China.

Our other late-stage clinical assets include HMPL-523, HMPL-689 and HMPL-453, which we believe have the potential to be first-in-class and/or best-in-class oncology therapies.

Globally-facing research and development approach to discovering and developing next-generation therapies for the treatment of cancer and immunological diseases

Leveraging our fully integrated platform, our research and development strategy has focused on developing differentiated drug candidates to treat unmet medical needs such as CRC, NET, lung cancer, gastric cancer and hematological malignancies. We have assembled a broad and highly differentiated portfolio of assets in various stages of development and have advanced ten self-discovered drug candidates into the clinic in the past ten years.

We focus on both more novel targets, including MET, CSF-1R, Syk and ERK, and more validated targets, including VEGFR, PI3Kδ and IDH. A primary objective of our research efforts has been to develop drug candidates with unique selectivity to limit off-target toxicity, high potency to optimize the dose selection with the objective to lower the required dose and thereby limit compound-based toxicity, chemical structures deliberately engineered to improve drug absorption and exposure in the targeted tissue, and the ability to be combined with other therapeutic agents, including targeted therapies, immunotherapies and chemotherapies. Such combination therapies can be more efficacious than a single treatment as they can treat the cancer from multiple angles at the same time and potentially decrease the likelihood that the cancer will develop a resistance to the treatment which can be a significant problem for monotherapies. We believe that this approach can significantly improve treatment options for patients, and it has led to favorable clinical outcomes in clinical trials to date.

Moreover, our highly-focused, globally-facing research and development approach, combined with the depth and breadth of our drug discovery organization, enables us to expand our pipeline of new drug candidates designed to offer differentiated novel oncology and immunology treatments in various mechanisms and technologies. These include, among others, small molecules addressing cancer-related

apoptosis, cell signaling, epigenetics and protein translation; biologic drug candidates including monoclonal and bispecific monoclonal antibodies; and novel technologies including antibody – drug conjugates and heterobifunctional small molecules. We believe our research and development team has the potential to discover candidates that are global first-in-class or best-in-class therapies in their respective categories and are well suited for combination therapies.

Successful track record of drug marketing and distribution execution

We have leveraged and will continue to leverage our deep institutional knowledge of the drug marketing and distribution process to bring our in-house oncology innovations to patients in China.

With future sales of our self-discovered oncology drugs in mind, we began building a large-scale national oncology commercial infrastructure in China over 18 months ago. We accelerated the growth of this dedicated oncology drug sales team to about 520 staff to support our assumption of all on-the-ground medical detailing, promotion and local and regional marketing activities for Elunate in October 2020 and the launch of Sulanda in mid-January 2021 in China. We expect this team will continue to grow steadily as a result of our commitment to executing the commercialization of these and our other drugs which may be approved in China. In addition, we are continuing to expand our U.S.-based international commercial capabilities.

A key to our ability to rapidly build our commercial organization in China has been the deep know-how in marketing and selling drugs within the complex medical system in China developed over the last two decades by our profitable Other Ventures operations. The joint ventures and subsidiaries in Other Ventures primarily manufacture, market and distribute prescription drugs in China and serve a dual purpose as both an extensive prescription drug sales network with significant expertise in commercial sales and distribution in China and an ongoing source of cash to partially fund our research and development activities. Many of the drugs sold by our Other Ventures are household-name brands and/or have significant or leading market shares.

Our Other Ventures operations have advanced to a significant scale, with our prescription drugs business operating a network of about 2,300 medical sales representatives covering hospitals in about 320 cities and towns in China as of December 31, 2020. Net income attributable to our Company from Other Ventures totaled US$41.4 million, US$41.5 million and US$72.8 million for the years ended December 31, 2018, 2019 and 2020, respectively. As of December 31, 2020, we have received dividends from Other Ventures totaling over US$300 million since inception, which have been reinvested into our Oncology/Immunology operations.

Global partnerships and strategic collaborations, with a growing portfolio of unpartnered drug candidates over which we own all global rights

We have been successful in entering into and effectively managing partnerships and strategic collaborations with leading pharmaceutical companies. For example, our partnerships with AstraZeneca with respect to savolitinib, and Eli Lilly with respect to fruquintinib, have brought us clinical, regulatory and manufacturing support, which have accelerated the development of our drug candidates and have been a source of funding. We also believe that AstraZeneca's portfolio of proprietary targeted therapies is well suited to be used in combinations with savolitinib, and we are studying combinations of savolitinib with AstraZeneca's Tagrisso (T790M+) and Imfinzi (PD-L1). These combinations of multiple global first-in-class compounds are difficult to replicate, and we believe represent a significant opportunity for us and AstraZeneca.

As our drug candidate pipeline has further developed, we have amended the terms of these collaborations several times to take more control over drug development and/or improve the potential economics of the arrangements for us. Specifically, we amended our collaboration agreement with Eli Lilly with respect to fruquintinib (Elunate), which gives us, among other things, all planning, execution and decision making responsibilities for life cycle indication development of fruquintinib in China. With the added flexibility in our Eli Lilly agreement, we entered into clinical collaboration agreements on a

cost-sharing basis with Innovent globally to evaluate combination therapies of fruquintinib with their PD-1 inhibitor, as well as a global collaboration with BeiGene to study fruquintinib in combination with its anti-PD-1 antibody. A subsequent amendment to the Eli Lilly agreement in 2020 gave us an expanded role in the development and execution of all on-the-ground medical detailing, promotion and local and regional marketing activities for fruquintinib in China. In return, subject to meeting pre-agreed sales targets, we will receive an estimated total of 70% to 80% of Elunate sales from Eli Lilly in the form of royalties, manufacturing costs and service payments. Furthermore, we and AstraZeneca amended the terms of our collaboration to increase the royalties on sales potentially payable to us in exchange for our contribution of certain clinical development costs for savolitinib.

In addition, we own all global rights with respect to our other eight clinical-stage drug candidates which enables us to selectively enter into collaborations with respect to these drugs to further their development. For example, we entered into global collaboration agreements with Innovent and Junshi to evaluate surufatinib in combination with their PD-1 inhibitors. The agreement with Innovent was subsequently expanded to include the evaluation of fruquintinib in combination with its PD-1 inhibitor. In 2020, we entered into a global collaboration agreement with BeiGene to evaluate surufatinib, as well as fruquintinib as noted above, in combination with its anti-PD-1 antibody. More recently, we recognized that our drug discovery organization was developing more new preclinical drug candidates than we could bring through clinical trials concurrently with our numerous other ongoing trials. To address this, we entered into a strategic partnership with Inmagene to further develop four of our novel preclinical drug candidates discovered by us for the potential treatment of multiple immunological diseases. Funded by Inmagene, the companies will work together to move the drug candidates towards IND submission. Flexibility in the development of our unpartnered drug candidates is important in providing us with multiple paths to advance such drugs to maximize their commercial potential.

Experienced and stable management team with proven track record in drug discovery, development and commercialization

We are led by an experienced and stable management team of seasoned industry executives, including many with senior-level experience at leading pharmaceutical companies such as Pfizer, Bristol-Myers Squibb, Sanofi, Eli Lilly, Roche and Gilead. Christian Hogg, our Chief Executive Officer, joined our Company in 2000 as our first employee. Mr. Hogg has since led all aspects of the creation, implementation and management of our strategy, business and listings, including the establishment of both our Oncology/Immunology and Other Ventures operations.

Led by our Chief Scientific Officer, Dr. Wei-guo Su, our research and development management team has extensive relevant experience. All team members have worked at multinational pharmaceutical and biotechnology companies and have participated in the discovery or development of a number of well-known drugs sold globally, including Alimta, Erbitux, Gemzar, Incivek, Sutent, Verzenio and Zithromax. Together, they have systematically built a productive research and development team of approximately 680 scientists and staff, of which over 350 had advanced technical degrees including 32 M.D.s and 82 doctorate degrees as of the Latest Practicable Date. This team has a proven track record in internal discovery, with our current ten self-discovered drug candidates having all advanced into the clinic in the past ten years.

We have also been successful in recruiting senior management teams for our Oncology/Immunology commercial organizations in China and, more recently, in the United States in preparation for a potential surufatinib U.S. launch in late 2021 or early 2022.

OUR STRATEGIES

Our vision is to be a global leader in the discovery, development and commercialization of targeted therapies and immunotherapies for the treatment of patients with cancer and immunological diseases. Key elements of our strategy are to:

Realize the global potential of our oncology drug candidates

Our first wave of innovation, surufatinib (unpartnered), fruquintinib (partnered in China with Eli Lilly) and savolitinib (partnered globally with AstraZeneca), are either commercialized, under review for marketing authorization, in the process of being filed for marketing authorization or in registrational studies in multiple jurisdictions. In the last several years, we have significantly expanded both the number of indications being studied in clinical trials for these drugs to cover a wide range of cancer types and the scale of the clinical trials for these drugs and the geographies in which they are conducted. In tandem with our ongoing progression of such drugs, we will continue to invest in the future with our deep pipeline of unpartnered next wave of oncology assets for which we own all rights globally and have significant flexibility in driving their development. Over the next 12 months, we plan to initiate late stage global development of HMPL-689 (PI3Kδ) and HMPL-523 (Syk) and progress early development of HMPL-453 (selective FGFR 1/2/3 inhibitor) and HMPL-306 (IDH1 and IDH2 inhibitors). Progressing the clinical trials of our drug candidates in combination with other drug therapies, such as PD-1/L1 inhibitors, will also remain a priority as we explore the most effective ways to treat cancers from multiple angles. We plan to continue to add to our pipeline as novel drug candidates progress through IND-enabling studies.

We intend to accelerate our global drug development by leveraging our advanced clinical trial data from China. We may also selectively conduct clinical trials concurrently in China and other jurisdictions so that the programs progress in parallel globally. To broaden and scale our international operations and support the increasing clinical activities in the United States and Europe, we also plan to continue significantly expanding our clinical teams in those geographies.

Continue designing and creating molecules to develop into medicines with specific and differentiated characteristics for the benefit of patients

We believe our world-class drug discovery engine is our key competitive advantage. We aim to retain and grow our team of skilled scientists and provide them a stable and well-funded platform, with a clear strategic focus and long-term purpose to deliver global first-in-class and best-in-class medicines to patients.

We strive to create differentiated novel oncology and immunology treatments with global potential. These include furthering both small molecule and monoclonal antibody therapies which address aberrant genetic drivers, inactivated T-cell response and insufficient T-cell response. Our drug discovery team has utilized our expertise in advanced medicinal chemistry to develop next-generation tyrosine kinase inhibitors that have both high selectivity and superior pharmacokinetic properties. We believe these characteristics are crucial to maximizing effectiveness, such as in inhibiting targeted genetic drivers of cancer cell proliferation and angiogenesis. Equally importantly, we will continue to design chemical and biologic drug candidates with profiles that allow them to be used in innovative combinations with other selective inhibitors, chemotherapy agents and immunotherapies. Such combination therapies enable treatment of cancer via multiple pathways and modalities simultaneously, which has the potential to significantly improve treatment outcomes.

We plan to continue to build out our global pipeline of self-discovered drug candidates by advancing a rich pipeline of early-stage drug candidates, which include biologics addressing novel targets designed for use in combination with our small molecules as well as potentially a broad range of third-party therapies. We will also focus on developing drug candidates targeting new pathways that represent unmet medical needs such as our investigational new ERK 1/2 inhibitor, HMPL-295, which would be our tenth in-house discovered small molecule oncology drug candidate to enter into the clinic and the first of multiple candidates in discovery targeting the MAPK pathway.

Build and scale our marketing and commercialization capabilities globally

We plan to leverage our long-standing drug marketing and distribution know-how and infrastructure to support our innovative oncology product launches, focusing in particular on the Chinese and U.S.

markets. We have a 20-year track record of marketing and selling products in China. We aim to grow our in-house oncology drug sales team in China of about 520 persons to over 900 persons by the end of 2023.

Outside of China, we intend to commercialize our products, if approved, in the United States where we have already begun to build our own sales team and are preparing to be ready to launch surufatinib, if approved, in late 2021 or early 2022. In Europe, Japan and other major markets, we intend to form collaborations with leading biopharmaceutical companies and/or contract sales organizations to fully realize the value of our assets. We are also focused on building out our commercial infrastructure to support our existing products and potential launches.

We will also continue to scale our manufacturing capacity to support the sales of our approved drugs, including expanding our existing Suzhou facility production team in phases, as well as our new plant in Shanghai, which we recently started constructing. This new plant represents a five-fold expansion of our existing production capacity, and we will look to maintain appropriate capacity in the future in line with the development of our pipeline of drug candidates and approved drugs.

Identify global business development and strategic acquisition opportunities to complement our internal research and development activities

We plan to explore opportunities to access complementary drug candidates and/or acquire interests in other biopharmaceutical companies to supplement our in-house research and development capabilities and to enhance our current drug candidate pipeline. We will also evaluate assets for in-licensing opportunities in China, with a focus on drug candidates with the potential to both complement our existing drug pipeline and have synergistic effects with each other.

In addition, we expect to progress some of our drug candidates by pursuing business development opportunities with other biopharmaceutical companies both in China and globally. For instance, in 2020 we began collaborating with BeiGene to evaluate combining surufatinib and fruquintinib with its anti-PD-1 antibody tislelizumab for the treatment of various solid tumor cancers in the United States, Europe, China and Australia. In 2021, we partnered with Inmagene to develop four of our self-discovered preclinical drug candidates for the potential treatment of various immunological diseases.

We will also continue to work with our partners, AstraZeneca and Eli Lilly, to optimize the potential of our drug candidates savolitinib (globally with AstraZeneca) and fruquintinib (in China with Eli Lilly). For example, in May 2020, we received acceptance for review of the savolitinib NDA in China for the treatment of NSCLC harboring MET exon 14 skipping alteration. If approved, this would be the first marketing authorization for savolitinib anywhere in the world. In July 2020, we amended our collaboration with Eli Lilly to assume responsibility for all on-the-ground medical detailing, promotion and local and regional marketing activities in China for Elunate, thereby expanding its potential economic value to our Company.

Capitalize on regulatory reforms currently underway in China aimed at addressing existing unmet medical needs and improving the health of its people

We believe the Chinese oncology market, which comprises approximately a quarter of the global oncology patient population, represents a substantial and fast-growing market opportunity. The oncology drug market in China is growing rapidly as a result of important government reforms that are underway, including the expansion of the NRDL to improve access to innovative drugs. We intend to capitalize on this market opportunity by leveraging and expanding our large and well-established drug discovery and commercial sales operations in China.

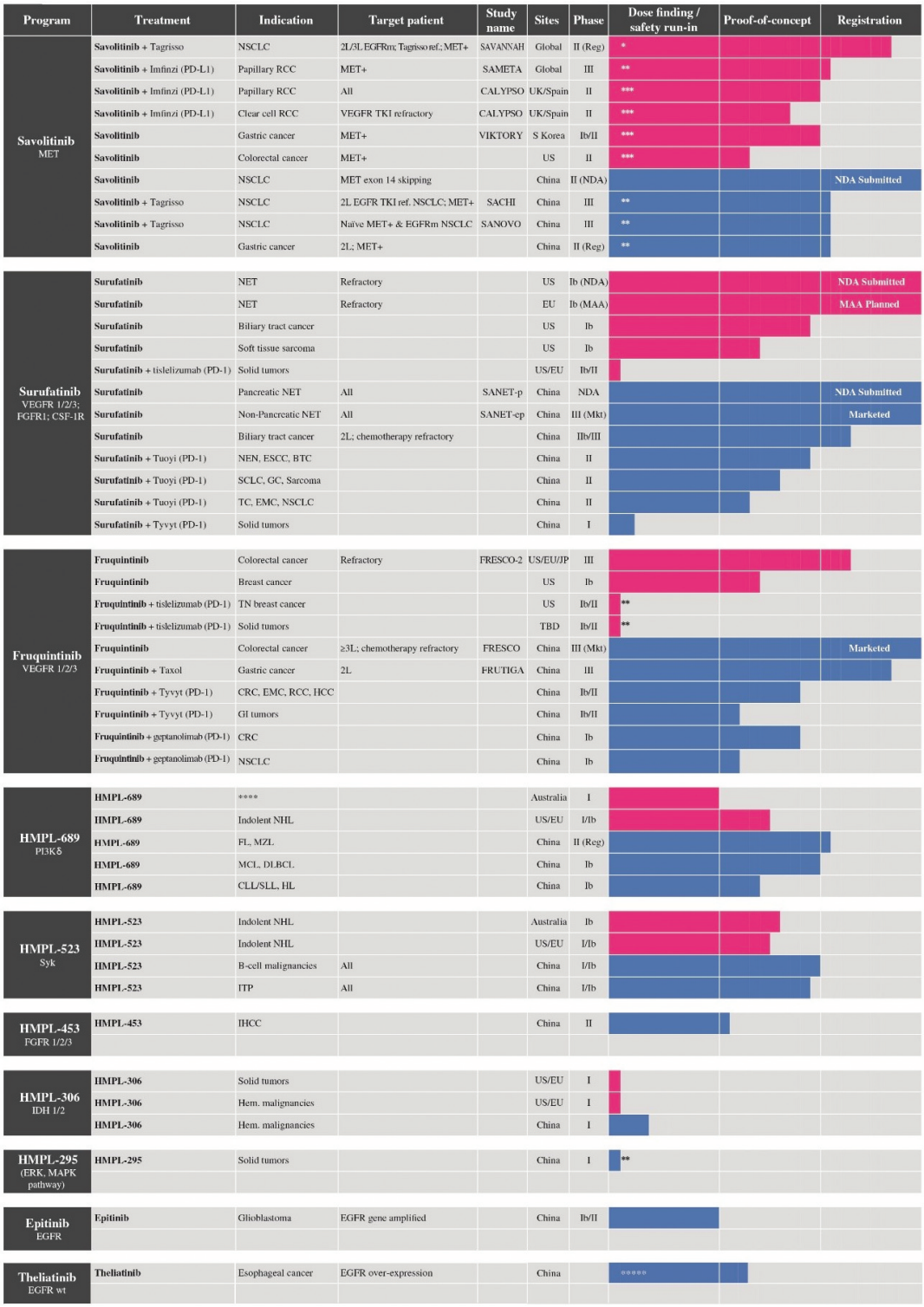
Historically, cumbersome pharmaceutical registration regulations led to limited availability of advanced therapies in China and high prices for those that were available. This led to surgery and chemotherapy being the standard of care for most patients in China. Over the past decade, the PRC government has endeavored to foster an innovative biopharmaceutical ecosystem, and in the last

few years, the pace of reforms has accelerated with a clear focus on providing Chinese patients access to world-class oncology therapies through expanded insurance reimbursement and reduced time for clinical trials and drug approvals.

Having invested in drug innovation in China for about 20 years, beginning at a time when almost no other domestic companies were involved in innovative oncology research, we believe we are well positioned to capture this market opportunity. Supported by China's improving regulatory environment, we intend to rapidly advance our drug candidates to meet the country's unmet medical needs in oncology.

OUR CLINICAL PIPELINE

The following table summarizes the status of our clinical programs as of the Latest Practicable Date:



* Phase II registration-intent study subject to regulatory discussion; ** In planning; *** Investigator-initiated trials(IIT); **** Healthy volunteers; and ***** Discontinued. (Reg) = Registration Intent; (NDA) = NDA submitted for review; (MAA) = MAA submission planned; and (Mkt) = NDA approved and product is on the market.

Notes: MET = mesenchymal epithelial transition receptor, VEGFR = vascular endothelial growth factor receptor, TKI = tyrosine kinase inhibitor, EGFRm = epidermal growth factor receptor mutation, FGFR1 = fibroblast growth factor receptor 1, CSF-1R = colony stimulating factor-1 receptor, NET = neuroendocrine tumors, NEN = neuroendocrine neoplasms, ESCC = esophageal squamous-cell carcinoma, BTC = biliary tract cancer, SCLC = small cell lung cancer,

GC = gastric cancer, TC = thyroid cancer, EMC = endometrial cancer, CRC = colorectal cancer, HCC = hepatocellular carcinoma, GI = gastrointestinal, Syk = spleen tyrosine kinase, PI3Kδ = Phosphatidylinositol-3-Kinase delta, NSCLC = non-small cell lung cancer, RCC = renal cell carcinoma, NHL = Non-Hodgkin's Lymphoma, FL = follicular lymphoma, MZL = marginal zone lymphoma, MCL = mantle cell lymphoma, DLBCL = diffuse large B cell lymphoma, CLL/SLL = chronic lymphocytic leukemia/small lymphocytic lymphoma, HL = Hodgkin's lymphoma, ITP = immune thrombocytopenic purpura, IHCC = Intrahepatic cholangiocarcinoma, IDH 1/2 = isocitrate dehydrogenase 1/2, ERK = extracellular-signal-regulated kinase, MAPK pathway = RAS-RAF-MEK-ERK signaling cascade.

The following is a summary of the clinical pipeline for our drug candidates, many of which are being investigated against multiple indications. All of our marketed drugs and pipeline candidates are small molecule.

1. Savolitinib MET Inhibitor

Savolitinib is a potent and selective inhibitor of MET, an enzyme which has been shown to function abnormally in many types of solid tumors. We designed savolitinib to address human metabolite-related renal toxicity, the primary issue that halted development of several other selective MET inhibitors. In clinical studies to date, savolitinib has shown promising signs of clinical efficacy in patients with MET gene alterations in NSCLC, PRCC, CRC, gastric cancer and prostate cancer with an acceptable safety profile. In global partnership with AstraZeneca, savolitinib has been studied in over 1,100 patients to date, both as a monotherapy and in combinations. For more information regarding our partnership with AstraZeneca, see "*– Overview of Our Collaborations – AstraZeneca.*"

Mechanism of Action

MET is a signaling pathway that has specific roles in normal mammalian growth and development. However, the MET pathway has also been shown to function abnormally in a range of different cancers, primarily through MET gene amplification, overexpression and gene mutations.

The aberrant activation of MET has been demonstrated to be highly correlated in many cancer indications, including kidney, lung, gastric, colorectal, esophageal and brain cancer. It plays a major role in cancer pathogenesis (i.e., the development of the cancer), including tumor growth, survival, invasion, metastasis, the suppression of cell death as well as tumor angiogenesis.

MET also plays a role in drug resistance in many tumor types. For instance, MET gene amplification has been found in NSCLC and CRC following anti-EGFR treatment, leading to drug resistance. Furthermore, MET dysregulation is considered to play a role in the immunosuppression and pathogenesis of kidney cancer.

See "*Industry Overview – Overview of Molecular Targets and Market Landscape – MET Pathway-Overview of MET Inhibitors*" for more details.

Savolitinib Research Background

First-generation selective MET inhibitors previously discovered by multinational pharmaceutical companies had positive pre-clinical data that supported their high MET selectivity and pharmacokinetic and toxicity profiles, but did not progress very far due to kidney toxicity. The issue appeared to be that certain metabolites of earlier compounds had dramatically reduced solubility and appeared to crystalize in the kidney, resulting in obstructive toxicity. With this understanding, we designed our compound, savolitinib (also known as AZD6094 and HMPL-504, formerly known as volitinib), differently while preserving high MET inhibition properties across multiple types of MET aberrations. Savolitinib has not shown any renal toxicity to date and does not appear to carry the same metabolite problems as the earlier selective MET compounds based on studies in over 1,100 patients conducted by AstraZeneca in global partnership with the Company.

Savolitinib Pre-clinical Evidence

In pre-clinical trials, savolitinib demonstrated strong in vitro activity against MET, affecting its downstream signaling targets and thus blocking the related cellular functions effectively, including proliferation, migration, invasion, scattering and the secretion of VEGF, that plays a pivotal role in tumor angiogenesis.

One of our key areas of focus in our pre-clinical trials is to achieve superior selectivity on a number of kinases. A commonly used quantitative measure of selectivity is through comparing enzyme IC_{50}, which represents the concentration of a drug that is required for 50% inhibition of the target kinase in vitro and the plasma concentration required for obtaining 50% of a maximum effect in vivo. High selectivity is achieved with a very low IC_{50} for the target cells, and a very high IC_{50} for the healthy cells (approximately 100 times higher than for the target cells). IC_{50} is measured in nM (nano-mole, a microscopic unit of measurement for the number of small molecules required to deliver the desired inhibitory effect).

In the MET enzymatic assay, savolitinib showed potent activity with IC_{50} of 5 nM. In a kinase selectivity screening with 274 kinases, savolitinib had potent activity against the MET Y1268T mutant (comparable to the wild-type), weaker activity against other MET mutants and almost no activity against all other kinases. Savolitinib was found to be approximately 1,000 times more potent to MET than the next non-MET kinase. Similarly, in cell-based assays measuring activity against MET phosphorylation, savolitinib demonstrated potent activity in both ligand-independent (gene amplified) and ligand-dependent (overexpressed) cells with IC_{50} at low nanomolar levels. In target related tumor cell function assays, savolitinib showed high potency with IC_{50} of less than 10 nM. Furthermore, savolitinib demonstrated cytotoxicity only on tumor cells that were MET gene amplified or MET overexpressed. In other cells, inhibition measurements demonstrated that IC_{50} amounts were over 30,000 nM, which is thousands of times higher than the IC_{50} on MET tumor cells.

The data above suggest that (i) savolitinib has potent activity against tumor cell lines with MET gene amplification in the absence of HGF, indicating that there is HGF-independent MET activation in these cells; (ii) savolitinib has potent activity in tumor cell lines with MET overexpressed, but only in the presence of HGF, indicating HGF-dependent MET activation; and (iii) savolitinib has no activity in tumor cell lines with low MET overexpression/gene amplification, suggesting that savolitinib has strong kinase selectivity.

Savolitinib Clinical Development

As discussed below, we have tested, and are currently testing, savolitinib in partnership with AstraZeneca in multiple indications, both as a monotherapy and in combination with other targeted therapies.

Non-small Cell Lung Cancer

We have two ongoing studies, which subject to positive clinical outcome, are designed to support NDA submission in NSCLC. The table below shows a summary of the clinical trials that we have recently completed and underway for savolitinib in NSCLC patients.

Current and Recent Clinical Trials of Savolitinib in NSCLC

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
Savolitinib monotherapy	HUTCHMED	NSCLC with MET exon 14 skipping alteration	China (32)	II Registration	NDA accepted (May 2020)	NCT02897479
Savolitinib + Tagrisso	AstraZeneca and HUTCHMED	SAVANNAH: 2L/3L EGFRm+; Tagrisso refractory; MET+	Global (104)	II Registration-intent	Ongoing. Data to support progressing into Phase III, expected in 2H 2021	NCT03778229
Savolitinib + Tagrisso	AstraZeneca and HUTCHMED	2L/3L EGFRm+; Tagrisso refractory; MET+	Global (N/A)	III	In planning. Intend to initiate in 2H 2021	N/A
Savolitinib + Tagrisso	AstraZeneca and HUTCHMED	SACHI: 2L EGFR TKI refractory NSCLC; MET+	China (45)	III	In planning. Intend to initiate in 2H 2021	N/A
Savolitinib + Tagrisso	AstraZeneca and HUTCHMED	SANOVO: Naïve patients with EGFRm & MET+	China (45)	III	In planning. Intend to initiate in 2H 2021	N/A
Savolitinib + Tagrisso	AstraZeneca and HUTCHMED	NSCLC EGFRm+; Tagrisso refractory	Global (43)	I/Ib	Final data presented at WCLC in January 2021. Supported initiation of SAVANNAH	NCT02143466

Notes:

(1) Expected maximum number of sites.

Global = more than two countries; 2L = second line; 3L = third line; and refractory = resistant to prior treatment.

Savolitinib Monotherapy

It is estimated that 2-3% of newly diagnosed NSCLC patients have a specific genetic mutation, known as MET exon 14 skipping alterations which leads to poor prognosis. This equates to over 10,000 new patients per year in China. Current chemotherapies and immunotherapies provide limited efficacy in MET exon 14 skipping NSCLC patients.

Phase II study of savolitinib monotherapy in NSCLC patients with MET exon 14 alteration (Status: NDA accepted; NCT02897479)

We have completed enrollment of a 70-patient Phase II registration-intent study in China of savolitinib as a monotherapy for MET exon 14 skipping NSCLC patients who have progressed following prior systemic therapy, or unable to receive chemotherapy.

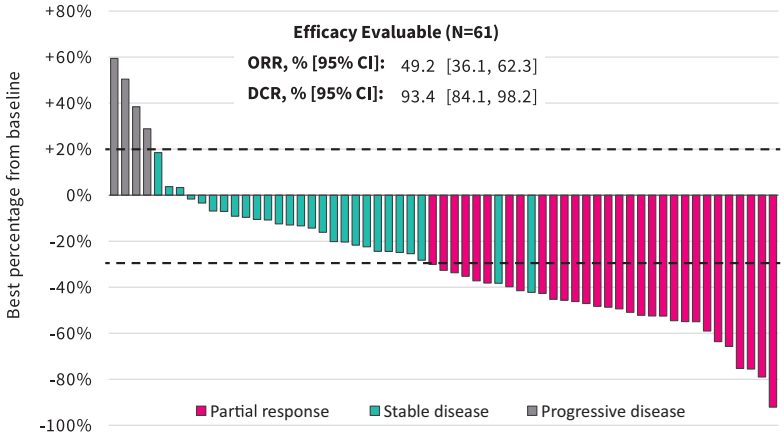
At the ASCO Annual Meeting in June 2020, we presented interim data on 70 treated patients, of which 61 patients were efficacy evaluable at the data cut-off date of March 31, 2020. The overall data were encouraging, with efficacy in line with other selective MET inhibitors, despite the inclusion of patients with a more aggressive subtype (36% with pulmonary sarcomatoid carcinoma) and with tolerable safety. Efficacy measurements included the ORR (the percentage of patients in the study who show either partial response (tumor measurement reduction of greater than 30%) or complete response), disease control rate, median PFS and median OS.

At subsequent data cut-off date of August 3, 2020, in the 61 evaluable patients, ORR was 49.2% and disease control rate was 93.4%. Median duration of response was 8.3 months (95% confidence interval: 5.3-16.6). In the full analysis set of 70 patients, median PFS was 6.8 months (95% confidence interval: 4.2-9.6). Median OS was 12.5 months (95% confidence interval: 10.5-23.6). A 95% confidence interval means that there is a 95% chance that the results will be within the stated range. CTC grade 3 or above TEAEs, with greater than 5% incidence related to savolitinib treatment were peripheral edema (9%),

increased aspartate aminotransferase (13%) and increased alanine aminotransferase (10%). Clinical data demonstrated an acceptable safety profile with an adverse events-related discontinuations rate of 14.3%.

Results from this study formed the basis for an NDA filing which was accepted by the NMPA in May 2020. Priority review status was granted in July 2020 and, subject to approval, launch is expected as early as mid-2021.

Phase II Study of Savolitinib Monotherapy Showing Effect in MET Exon 14 Alteration NSCLC Patients



Notes: N = number of patients; ORR = objective response rate; DCR = disease control rate; and CI = confidence interval.

Source: Lu S, Fang J et al. Phase II study of savolitinib in patients (pts) with pulmonary sarcomatoid carcinoma (PSC) and other types of non-small cell lung cancer (NSCLC) harboring MET exon 14 skipping mutations (METex14+). Journal of Clinical Oncology 2020 38:15_suppl, 9519-9519.

Savolitinib and Tagrisso Combination

In 2015, AstraZeneca received FDA approval for Tagrisso, its drug for the treatment of T790M+ EGFRm+, tyrosine kinase inhibitor-resistant NSCLC. A drug with this type of activity is known as a third-generation EGFR inhibitor. In 2018, Tagrisso's label was expanded to include previously untreated patients with EGFRm+ NSCLC. In December 2020, Tagrisso's label was further expanded to include adjuvant therapy after tumor resection in EGFRm+ NSCLC patients. Tagrisso has been established as a new standard of care in the treatment of EGFRm+ NSCLC and has now been approved in over 80 countries. Understanding the mechanism of acquired resistance following Tagrisso treatment is a key clinical question to inform the next treatment choice. A portion of EGFRm+ tyrosine kinase inhibitor-resistant patients and a portion of T790M+ EGFRm+ tyrosine kinase inhibitor-resistant patients progress because of MET gene amplification.

At the European Society of Medical Oncology Congress in 2018, AstraZeneca presented the first results on the acquired resistance spectrum detected in patient plasma samples after progression in the first-line (FLAURA) and second-line T790M (AURA3) Phase III studies. MET amplification was among the most frequent mechanisms of acquired resistance to Tagrisso, with 15% of patients in the FLAURA study and 19% of patients in the AURA3 study exhibiting MET amplification after treatment with Tagrisso. Ongoing research with tissue (biopsy) samples will further elucidate the incidence of MET and other mechanisms in the development of resistance to EGFR inhibitors.

Data presented in June 2017 at the ASCO by Harvard Medical School and Massachusetts General Hospital Cancer Center showed that about 30% (7/23 patients) of Tagrisso-resistant third-line NSCLC patients harbored MET gene amplification based on analysis of tissue samples. This third-line patient population was generally heavily pre-treated and highly complex from a molecular analysis standpoint, with the study showing that more than half of the MET gene amplification patients also harbored additional genetic alterations, including EGFR gene amplification and K-Ras mutations.

As discussed in more detail below, we and AstraZeneca are studying savolitinib in combination with Tagrisso as a treatment choice for patients who have developed a resistance to tyrosine kinase inhibitors (primarily Tagrisso). The acceptance and uptake of Tagrisso indicates that the market potential for savolitinib in Tagrisso-resistant, NSCLC could be material.

TATTON study: Phase Ib/II expansion studies of savolitinib in combination with Tagrisso in NSCLC EGFRm+ inhibitor refractory patients (Status: complete; NCT02143466)

The TATTON study is a global exploratory Phase I/Ib study in NSCLC aiming to recruit patients with MET gene amplification who had progressed after prior treatment with EGFR inhibitors to support a decision on global Phase II/III registration strategy. This followed the completion of TATTON Part A, a Phase I study that established that a savolitinib and Tagrisso combination could be safe and well tolerated and also demonstrated preliminary signs of efficacy. In 11 evaluable patients who were MET positive, the ORR was 55% with a disease control rate of 100%.

As of data cut-off on March 4, 2020, a total of over 220 patients had received the savolitinib plus the Tagrisso combination treatment across six TATTON treatment arms, Parts A, B1, B2, B3, C and D. Final analysis for the B and D parts of the study were most recently presented at the 2020 World Conference on Lung Cancer Worldwide Virtual Event held in January 2021, and interim data (data cut-off on March 29, 2019) were previously published in *The Lancet Oncology* in February 2020. As summarized below, the combination demonstrated an encouraging anti-tumor activity and an acceptable risk-benefit profile, regardless of dose.

First and second-generation EGFRm+ inhibitor refractory patients with acquired resistance driven by MET amplification

TATTON Part B2 tested patients who were T790M negative with no prior third-generation EGFR tyrosine kinase inhibitor treatment. Of the 51 patients who received treatment (48 efficacy evaluable), 33 patients had confirmed responses (65% of treated patients; 69% of evaluable patients) with 45 patients experiencing disease control (88% of treated patients; 94% of evaluable patients). The median PFS was 9.1 months (95% confidence interval: 5.5-12.8 months). Pooled CTC grade 3 or above TEAEs in Part B of the study with greater than 5% incidence independent of causality were decreased neutrophil count (7%), increased aspartate aminotransferase (6%), increased alanine aminotransferase (5%), and pneumonia (5%).

TATTON Part B3 tested patients who were T790M positive with no prior third-generation EGFR tyrosine kinase inhibitor treatment. Of the 18 patients who received treatment, 12 patients had confirmed responses (67%) with 18 patients experiencing disease control (100%). The median PFS was 11.1 months (95% confidence interval: 4.1 months – 22.1 months).

In late 2017, the TATTON Part D study was initiated to study Tagrisso combined with a lower savolitinib dose (300 mg once daily) in the context of maximizing long-term tolerability of the combination for patients who could be in poor condition and/or on the combination for long periods of time. Of the 42 patients who received treatment (40 efficacy evaluable), 26 patients had confirmed responses (62% of all patients; 65% of evaluable patients) with 39 patients experiencing disease control (93% of all patients; 98% of evaluable patients). The median PFS was 9.0 months (95% confidence interval: 5.6-12.7 months). CTC grade 3 or above TEAEs in Part D of the study with greater than 5% incidence independent of causality were pneumonia (10%), drug hypersensitivity (7%), pulmonary embolism (5%), diarrhea (5%), myalgia (5%) and generalized edema (5%). Overall the combination regimen of savolitinib 300 mg and Tagrisso was tolerable. In Part D of the study, there was lower incidence of grade ≥3 AEs and SAEs as compared to Part B. The TATTON Part D study demonstrated that a lower dose did not impair clinical efficacy, while maintaining a better tolerability profile. The results led to the selection of the 300 mg savolitinib plus 80 mg Tagrisso combination dose for the SAVANNAH study, and two additional cohorts of savolitinib 300 mg twice daily dose (BID) and 600 mg once daily dose (QD) plus 80 mg Tagrisso combination doses are recruiting, as discussed below.

Tagrisso or another experimental third-generation EGFRm tyrosine kinase inhibitor refractory patients with acquired resistance driven by MET amplification

The TATTON Part B1 study also enrolled NSCLC patients that had progressed after treatment with a third-generation EGFR inhibitor as a result of MET gene amplification acquired resistance. These patients were recruited prior to the April 2018 FDA approval of Tagrisso as a first-line treatment and the January 2019 update to the National Comprehensive Cancer Network guidelines that state that Tagrisso is the preferred first-line treatment for patients with EGFR mutation regardless of pre-treatment T790M mutation status.

Savolitinib in combination with Tagrisso from the TATTON Part B1 study showed promising data. Of the 69 patients that had progressed on Tagrisso monotherapy and harbored MET amplification (60 patients were efficacy evaluable), there were 23 patients with confirmed responses (33% of all patients; 38% of evaluable patients) with 52 patients experiencing disease control (75% of all patients; 87% of evaluable patients). The median PFS was 5.5 months (95% confidence interval: 4.1-7.7 months).

Savolitinib Plus Tagrisso Combination Showing Effect in EGFR Refractory Patients Who Are Either Tagrisso Refractory (Part B1) or Tagrisso Naïve (Parts B2, B3, D)

	TATTON Part B Osimertinib 80mg +Savolitinib 600mg[1]			**TATTON Part D Osimertinib 80mg +Savolitinib 300mg**
	Part B1 (n=69) Prior third-generation EGFR-TKI	**Part B2 (n=51)** No prior third-generation EGFR-TKI (T790M negative)	**Part B3 (n=18)** No prior third-generation EGFR-TKI (T790M positive)	**Part D (n=42)** No prior third-generation EGFR-TKI (T790M negative)
ORR, % [95%CI] . . .	33% [22, 46]	65% [50, 78]	67% [41, 87]	62% [46, 76]
Complete response, % . . .	0	0	0	0
Partial response, %	33%	65%	67%	62%
Non-response, % . . .				
Stable disease (≥ 6 weeks)	42%	24%	33%	31%
Progressive disease	12%	6%	0	2%
Not evaluable . . .	13%	6%	0	5%
Disease control rate, % [95% CI]	75% [64, 85]	88% [76, 96]	100% [81, 100]	93% [81, 99]
Median DoR, months [95% CI]	9.5 [4.2, 14.7]	10.7 [6.1, 14.8]	11.0 [2.8, NR]	9.7 [4.5, 14.3]
Median PFS, months [95% CI]	5.5 [4.1, 7.7]	9.1 [5.5, 12.8]	11.1 [4.1, 22.1]	9.0 [5.6, 12.7]

Notes: [1] Most patients were enrolled to Part B1, B2, B3 on 600 mg savolitinib, prior to weight-based dosing implementation, but following a protocol amendment in response to a safety signal of hypersensitivity, the final 21 patients enrolled in Part B were dosed with savolitinib by body weight as follows: patients who weighed ≤ 55 kg (n=8) received 300 mg daily and those weighing >55 kg (n=13) received 600 mg daily; Best response data are for patients who had an opportunity to have two follow-up scans; CI = confidence interval; n = number of patients; NR = not reached; ORR = objective response rate; DoR = duration of response; PFS = progression free survival; and EGFR-TKI = epidermal growth factor receptor tyrosine kinase.

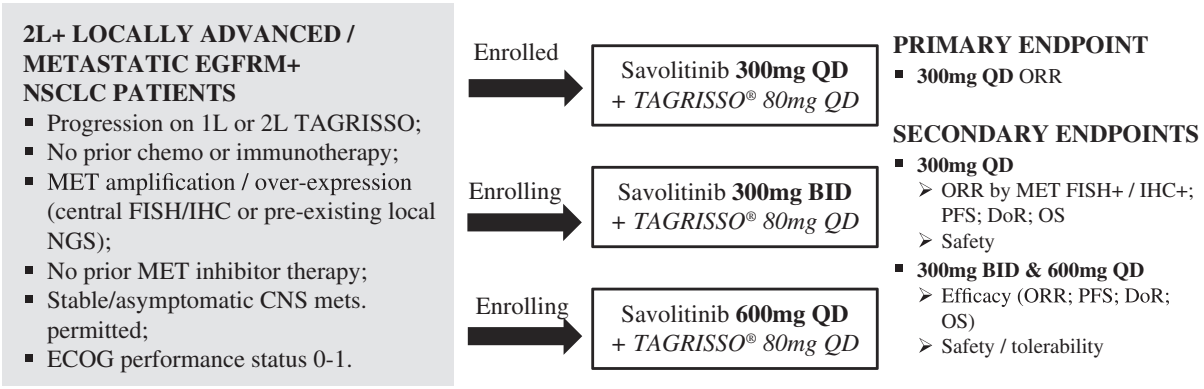
Source: Han JY, Sequist LV, Ahn MJ, et al. Osimertinib + savolitinib in patients with EGFRm MET-amplified/overexpressed NSCLC: Phase Ib TATTON Parts B and D final analysis. Poster presented at: 2021 World Conference on Lung Cancer Singapore; January 28-21, 2021; Virtual. https://bit.ly/3cl7QRE

SAVANNAH study: Phase II study of savolitinib in combination with Tagrisso in NSCLC Tagrisso-refractory EGFRm+ patients (Status: enrolling; NCT03778229)

Based on the encouraging results of the multiple TATTON studies, we and AstraZeneca have initiated a global Phase II study of savolitinib in combination with Tagrisso in EGFRm+ NSCLC patients with MET gene amplification who have progressed following first or second-line Tagrisso therapy. The SAVANNAH study is a single-arm study in North and South America, Europe and Asia. Subject to positive clinical outcomes and regulatory interactions, the SAVANNAH study is designed to support potential NDA submission for savolitinib.

The SAVANNAH study has now fully enrolled the savolitinib 300mg QD and Tagrisso cohort, and is currently enrolling two additional cohorts of savolitinib 300mg BID and 600mg QD. The SAVANNAH study will also determine optimal design of the planned global Phase III study regarding optimal biomarker strategy and dosage regimen. Enrollment is expected to complete in mid-2021 and planning for the global Phase III study is now underway.

The SAVANNAH Study Design: Addressing Tagrisso Resistance Through Combination Therapies



Notes: 1L = first line; 2L = second line; 2L+ = second line and above; EGFRM+ = epidermal growth factor receptor mutation positive; ECOG = Eastern Cooperative Oncology Group; BID = twice daily; QD = once daily; FISH (+) = fluorescence in situ hybridization (positive); IHC (+) = immunohistochemistry (positive); ORR = objective response rate; PFS = progression free survival; DoR = duration of response; OS = overall survival; and MET = mesenchymal epithelial transition receptor.

Source: Company.

In-Planning – SACHI study: China Phase III study of combination with Targrisso in 2L EGFR TKI refractory, MET amplified NSCLC patients

We intend to initiate a Phase III study in China targeting EGFR TKI refractory second-line NSCLC patients in the second half of 2021.

In-Planning – SANOVO study: China Phase III study of combination with Targrisso in EGFR mutant and MET positive NSCLC patients

We intend to initiate a Phase III study in China targeting treatment naïve patients who are both EGFR mutation and MET positive in the second half of 2021.

Kidney Cancer

The table below shows a summary of the clinical trials that we have recently completed or are underway for savolitinib in kidney cancer patients.

Current and Recent Clinical Trials of Savolitinib in Kidney Cancer

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
Savolitinib + Imfinzi	AstraZeneca and HUTCHMED	SAMETA: MET-driven, unresectable and locally advanced or metastatic PRCC	Global (N/A)	III	In planning Expected to begin enrollment in the second half of 2021	N/A
Savolitinib + Imfinzi	Queen Mary University of London, Vall d'Hebron Institute of Oncology, AstraZeneca	CALYPSO: PRCC	U.K./ Spain (18)	II	Data update in ASCO. Interim analysis supports progressing into Phase III.	NCT02819596
Savolitinib + Imfinzi	Queen Mary University of London, Vall d'Hebron Institute of Oncology, AstraZeneca	CALYPSO: Clear cell RCC; VEGFR TKI refractory	U.K./ Spain (18)	II	Ongoing	NCT02819596
Savolitinib monotherapy	AstraZeneca and HUTCHMED	SAVOIR: PRCC	Global (58)	III	Completed. Support decision to progress into Phase III.	NCT03091192

Notes:

(1) Expected maximum number of sites.

PRCC = papillary renal cell carcinoma; RCC = renal cell carcinoma; ASCO GU 2020 = the American Society of Clinical Oncology's 2020 Genitourinary Cancers Symposium; VEGFR TKI refractory = resistant to prior VEGFR tyrosine kinase inhibitor treatment; Global = more than two countries; PFS = progression free survival; and MET = mesenchymal epithelial transition receptor.

PRCC is the most common of the non-clear cell renal cell carcinomas representing about 14% of kidney cancer, with approximately half of patients estimated to harbor MET-driven disease. No targeted therapies have been approved specifically for PRCC, although some efficacy was observed for cabozantinib in an investigator sponsored study, PAPMET, which reported ORR of 23% and median PFS of 9 months in 44 patients not selected for MET status and who mostly (95%) did not receive prior systemic therapy (Pal SK, et al. Lancet. 2021). Modest efficacy in non-clear cell renal cell carcinoma has been reported in sub-group analyses of broader RCC studies of VEGFR (e.g., Sutent) and mammalian target of rapamycin (e.g., Afinitor) TKI, with ORR of <10% and median PFS in first-line setting of four to six months and second-line setting of only one to three months (ESPN study, Tannir N. M. et al.).

During an Australian Phase I study, our investigators noted positive outcomes among PRCC patients with a strong correlation to MET gene amplification status. Out of a total of eight PRCC patients in our Australia Phase I study who were treated with various doses of savolitinib, three achieved confirmed partial responses. A further three of these eight PRCC patients achieved stable disease, which means patients without partial response but with a tumor measurement increase of less than 20%. This aggregate ORR of 38% was very encouraging for PRCC, which has no effective approved treatments. These responses were also durable as demonstrated by a patient who has been on the therapy for over 30 months and had tumor measurement reduction of greater than 85%. Importantly, the level of tumor response among these PRCC patients correlated closely with the level of MET gene amplification. The patients with consistent MET gene amplification across the whole tumor responded most to savolitinib, and with those patients with the highest level of MET gene amplification responding most to the treatment.

Recent data have emerged to show that PRCC responds to immunotherapy such as inhibitors of an immune checkpoint known as PD-1 used by cancer cells to avoid being attacked by the immune system. Preliminary data from the KEYNOTE-427 study (Cohort B) as presented by Merck & Co at the ASCO's 2019 Genitourinary Cancers Symposium showed objective response in treatment naïve PRCC patients

treated with the PD-1 inhibitor Keytruda was 25%. In the broader kidney cancer setting, combinations of PD-1 or PD-L1 drugs with targeted therapies that demonstrated single agent effect have demonstrated additive benefits.

Savolitinib and Immunotherapy Combinations

Immunotherapy combinations are rapidly changing the treatment landscape in kidney cancer. Immune checkpoints such as PD-L1 are sometimes used by cancer cells to avoid being attacked by the immune system. As such, drugs that target these checkpoints are being developed or marketed as cancer treatments. Imfinzi is an anti-PD-L1 antibody owned by AstraZeneca. Anti-PD-L1 antibodies have been associated with clinical benefits in metastatic RCC, and MET dysregulation has been considered to play an important role in PRCC pathogenesis (including in our savolitinib Phase I and Phase II monotherapy studies) and is a mechanism of resistance against kinase inhibitors in clear cell renal cell carcinoma. Moreover, it is believed that the MET signaling pathway has a complex interplay with the immune system, including correlation with PD-L1 expression, immune suppression through angiogenesis and many other facets of the immune system. Our CALYPSO study discussed below aims to explore and potentially confirm this interplay.

CALYPSO study: Phase II study of savolitinib in combination with Imfinzi in both PRCC and clear cell renal cell carcinoma patients (Status: dose expansion ongoing; NCT02819596)

The CALYPSO study is an investigator-initiated open-label Phase II study of savolitinib in combination with Imfinzi. The study is evaluating the safety and efficacy of the savolitinib and Imfinzi combination in both PRCC and clear cell renal cell carcinoma patients at sites in the U.K. and Spain.

Interim results of the PRCC cohort of the CALYPSO study were most recently presented at the ASCO 2021 and showed encouraging efficacy across all patients, both MET+ and MET-. In the 41 patients who were selected regardless of PD-L1 or MET status, ORR was 29% (12/41), while median PFS was 4.9 months (95% confidence interval: 2.5-10.0 months). Median OS was 14.1 months (95% confidence interval: 7.3-30.7 months). For the 14 patients whose tumors are MET-driven, ORR was 57% (8/14), median PFS was 10.5 months (95% confidence interval: 2.9-15.7), and median OS was 27.4 months (95% confidence interval: 7.3-NR). Tolerability was consistent with established single agent safety profiles. In the analysis previously presented at ASCO's Genitourinary Cancers Symposium in 2020, there were 13 treatment related CTC grade 3 or above TEAEs that occurred in more than three patients, with edema (10%), nausea (5%) and transaminitis (5%) being most frequent. We and AstraZeneca continue to explore development of the savolitinib-Imfinzi combination in PRCC patients.

In-Planning – SAMETA: Phase III in combination with Imfinzi PD-L1 inhibitor in MET-driven, unresectable and locally advanced or metastatic PRCC

Based on the encouraging results of the SAVOIR and CALYPSO studies, we intend to initiate a global Phase III, open-label, randomized, controlled study of savolitinib plus Imfinzi versus sunitinib monotherapy versus Imfinzi monotherapy in patients with MET-driven, unresectable and locally advanced or metastatic PRCC. The study is expected to begin enrollment by the second half of 2021.

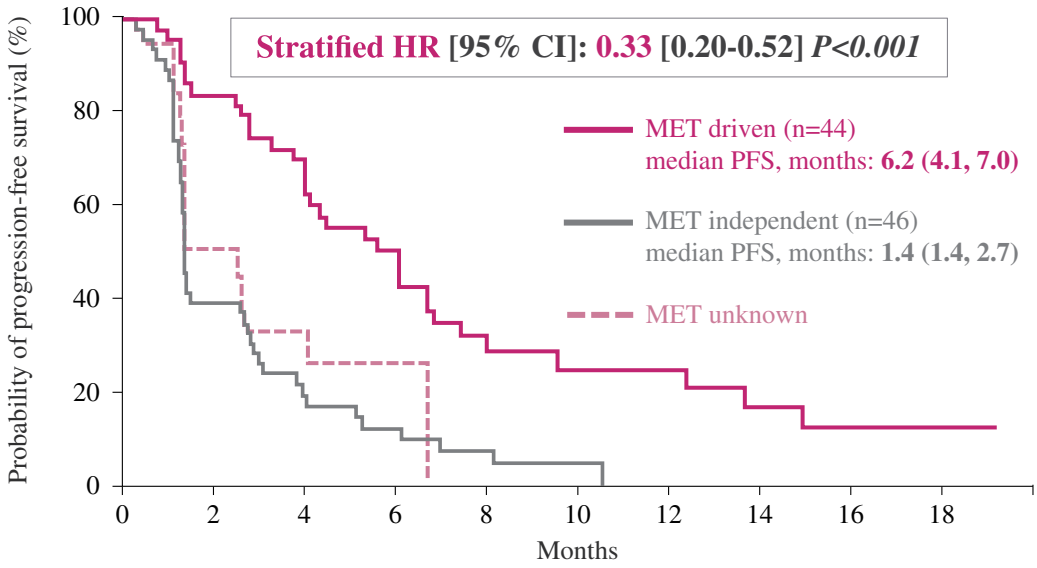
Savolitinib Monotherapy

Phase II study of savolitinib monotherapy in PRCC (Status: completed; NCT02127710)

In early 2017, we presented the results of our global Phase II study in PRCC at the ASCO's Genitourinary Cancers Symposium and subsequently published these results in the Journal of Clinical Oncology. Of 109 patients treated with savolitinib, PRCC was MET driven in 44 patients (40%), MET independent in 46 patients (42%) and MET status unknown in 19 patients (17%). The ORR based on confirmed partial responses in all patients was 7% (8/109). MET-driven PRCC was strongly associated with encouragingly durable response to savolitinib with an ORR in the MET-driven group of 18% (8/44) as compared to 0% (0/46) in the MET independent group (p=0.002). Of the eight patients exhibiting a partial response, six were still responding to treatment at data cutoff, with a duration of response of 2.4

to 16.4 months. Two patients who achieved a partial response subsequently experienced progressive disease after 1.8 and 2.8 months. P-value is a measure of the probability of obtaining the observed sample results, with a lower value indicating a higher degree of statistical confidence in these studies. Median PFS for patients with MET-driven and MET-independent PRCC patients was 6.2 months (95% confidence interval: 4.1-7.0) and 1.4 months (95% confidence interval: 1.4-2.7), respectively (hazard ratio=0.33; 95% confidence interval: 0.20-0.52; p<0.001). Hazard ratio is the probability of an event (such as disease progression or death) occurring in the treatment arm divided by the probability of the event occurring in the control arm of a study, with a ratio of less than one indicating a lower probability of an event occurring for patients in the treatment arm. Savolitinib had a disease control rate of 73% in the MET-driven group and 28% in the MET independent group for efficacy evaluable patients. Savolitinib was well tolerated, with no reported CTC grade 3 or above TEAEs with greater than 5% incidence. Total aggregate savolitinib CTC grade 3 or above TEAEs occurred in just 19% of patients.

Phase II Study of Savolitinib Monotherapy in PRCC in the United States, Canada and Europe. This Study Clearly Demonstrated MET-Driven Patients had Better PFS Compared to MET Independent Patients.



Notes: n = number of patients; CI = confidence interval; and HR = hazard ratio.

Disease progression occurred in 33 (75%), 44 (96%), and 14 patients (74%) with MET-driven, MET-independent, and MET-unknown papillary renal cell carcinoma, respectively.

Source: Choueiri TK, Plimack E, Arkenau HT, et al. Biomarker-Based Phase II Trial of Savolitinib in Patients With Advanced Papillary Renal Cell Cancer. J Clin Oncol. 2017;35(26):2993-3001. doi:10.1200/JCO.2017.72.2967.

SAVOIR study: Phase III study of savolitinib monotherapy in PRCC (Status: enrollment suspended; NCT03091192)

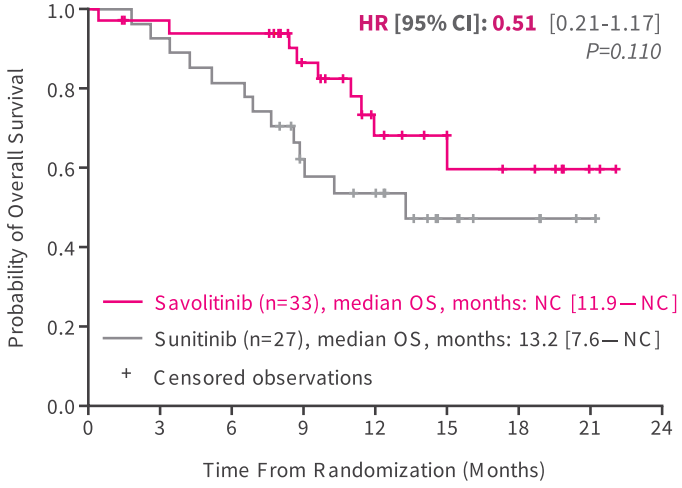
We initiated the SAVOIR study in June 2017. The SAVOIR study was designed to be a global Phase III, open-label, randomized, controlled trial evaluating the efficacy and safety of savolitinib (600 mg once daily) compared with Sutent in patients with MET-driven, unresectable, locally advanced or metastatic PRCC. MET status was confirmed by the novel targeted next-generation sequencing assay developed for savolitinib. Patients were randomized in a 1:1 ratio to receive either treatment with savolitinib or treatment with Sutent. The primary endpoint for efficacy in the SAVOIR study was median PFS, with secondary endpoints of OS, ORR, duration of response, best percentage change in tumor size, disease control rate, and safety and tolerability.

To further understand the role of MET-driven disease in PRCC, we conducted a global molecular epidemiology study, which screened, using our companion diagnostic, archived tissue samples from

PRCC patients to identify MET-driven disease. Historical medical records from these patients were then used to determine if MET-driven disease is predictive of worse outcome, in terms of PFS and OS, in PRCC patients. Confounding results from this external study led to the early termination of SAVOIR in December 2018, with 60 patients randomized at the time.

Results from the 60 randomized patients (33 savolitinib, 27 Sutent) were promising and data were presented at ASCO and published simultaneously in *JAMA Oncology* in May 2020. In terms of OS, savolitinib patients had not reached median OS at data cut-off, compared to 13.2 months for Sutent patients (HR 0.51; 95% CI: 0.21-1.17; p=0.110). Median PFS was 7.0 months for savolitinib patients, compared to 5.6 for Sutent patients (HR 0.71; 95% CI: 0.37-1.36; p=0.313). Responses were observed in 27% and 7% of savolitinib and Sutent patients, respectively. This difference did not reach statistical significance due to the small sample size. In terms of safety, Grade ≥3 AEs were reported in 42% of savolitinib patients versus 81% of Sutent patients, with AEs leading to dose modification in 30% and 74% of savolitinib and Sutent patients, respectively. CTC grade 3 or above adverse events with greater than 5% incidence related to savolitinib treatment were increased aspartate aminotransferase (15%) and increased alanine aminotransferase (12%). Those related to Sutent were anemia (15%), hypertension (15%), thrombocytopenia (7%), increased aspartate aminotransferase (7%), and increased alanine aminotransferase (7%).

SAVOIR 60-Patient Study of Savolitinib Monotherapy in MET-Driven PRCC Patients. This Study Demonstrated a Strong Signal of Response and Potential Survival Benefit Compared to Sutent Monotherapy



	Savolitinib (N=33)	Sutent (sunitinib, N=27)
Objective response rate, % [95% CI]	27.3% [13.3, 45.5]	7.4% [0.9, 24.3]
PFS, months [95% CI]	7.0 [2.8, NC]	5.6 [4.1, 6.9]
		Hazard Ratio: 0.71 [0.37, 1.36]
Disease control rate @ 6 months, % [95% CI]	48.4% [30.8, 66.5]	37.0% [19.4, 57.6]
Disease control rate @ 12 months, % [95% CI]	30.3% [15.6, 48.7]	22.2% [8.6, 42.3]

Notes: At data cut-off, all nine savolitinib responders remained in response, while one of two sunitinib responders remained in response. n = number of patients; CI = confidence interval; NC = not calculated; OS = overall survival; PFS = progression-free survival; and HR = hazard ratio.

Source: 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.

Based on these data, we and AstraZeneca are actively evaluating the opportunity to restart clinical trials of savolitinib in combination with Imfinzi versus Sutent monotherapy and versus Imfinzi

monotherapy in patients with MET-driven, unresectable and locally advanced or metastatic PRCC. The study is expected to begin enrollment in the second half of 2021.

Gastric Cancer

The table below shows a summary of our clinical trial for savolitinib in gastric cancer patients.

Clinical Trials of Savolitinib in Gastric Cancer

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
Savolitinib monotherapy	HUTCHMED and Samsung Medical Center	VIKTORY: Gastric cancer (MET amplification)	China & South Korea (21)	Ib/II	Completed. Support decision to progress into Phase II registration intent study	NCT01985555/ NCT02449551
Savolitinib monotherapy	HUTCHMED	2L+ gastric cancer with MET amplification	China (30)	II registration intent	In-planning. Intend to initiate in mid-2021	N/A

Note:

(1) Expected maximum number of sites.

Phase II gastric cancer studies have been completed in China and in South Korea. A total of over 1,000 gastric cancer patients have been screened in these studies and those patients with confirmed MET-driven disease were treated with savolitinib.

Phase Ib/II study of savolitinib monotherapy in MET amplified gastric cancer in China (Status: completed; NCT01985555)

Preliminary results of the China study were presented at the 2017 Chinese Society of Clinical Oncology for the efficacy evaluable MET gene amplified patients. Based on confirmed and unconfirmed partial responses, the ORR was 43% (3/7) and disease control rate was 86% (6/7), with ORR of 14% (3/22) and disease control rate of 41% (9/22) among the overall efficacy evaluable aberrant MET set of patients with MET amplification (n=7) and MET overexpression (n=15). As of data cut-off, the longest duration of treatment was in excess of two years. Savolitinib monotherapy was determined to be safe and well tolerated in patients with advanced gastric cancer. CTC grade 3 or above TEAEs with greater than 5% incidence included abnormal hepatic function in 13% (4/31), gastrointestinal bleeding or decreased appetite in 10% (3/31 each), and diarrhea or gastrointestinal perforation in 6% (2/31 each). This China study concluded that savolitinib monotherapy demonstrated promising anti-tumor efficacy in gastric cancer patients with MET gene amplification, and that the potential benefit to these patients warranted further exploration, with enrollment continuing.

VIKTORY Phase II study of savolitinib in MET amplified gastric cancer in South Korea (Status: completed; NCT02449551)

The VIKTORY study is a biomarker-based, Phase II umbrella trial in gastric cancer conducted by the Samsung Medical Center in South Korea. Patients were allocated to one of 12 biomarker-driven arms, based on a master screening protocol with tissue-based molecular analyses. Patients that tested positive for MET amplification or overexpression were treated with either savolitinib monotherapy or a combination of savolitinib and Taxotere.

A total of 715 gastric cancer patients were successfully sequenced and MET amplification was observed in 3.5% of these patients (25/715). Of the 10 associated clinical trials under the VIKTORY umbrella, the highest ORR was observed in the MET amplification arm in patients treated with savolitinib monotherapy, which reported an ORR of 50% (10/20, 95% confidence interval: 28.0-71.9) and met pre-specified 6-week PFS rates. While the savolitinib and Taxotere combination was well

tolerated, the VIKTORY study investigators decided to stop enrollment in the two combination cohorts in order to direct patients to the savolitinib monotherapy arm of the VIKTORY study as discussed above.

The VIKTORY study investigators have concluded that encouraging clinical efficacy of savolitinib in MET-amplified gastric cancer warrants further study.

In-Planning – China Phase II study with potential for registration intent in 2L+ gastric cancer with MET amplification

In the third quarter of 2021, we intend to initiate a Phase II registration-intent study in MET-amplified gastric cancer in China. This is a two-stage, single-arm study which targets advanced gastric cancer patients who have failed at least one line of treatment. The primary endpoint is ORR. Subject to the results of the first-stage of this study we will discuss with the CDE of NMPA the appropriate approach and necessary criteria for registration.

Savolitinib Exploratory Development

The table below shows a summary of the clinical study that is underway for savolitinib in other solid tumors.

Clinical Trial of Savolitinib in CRC

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[1]	Phase	Status/Plan	NCT #
Savolitinib monotherapy	National Cancer Institute	MET-driven mCRC	U.S. (33)	II	Enrolling. Started in July 2018.	NCT03592641

Note:

(1) Expected maximum number of sites.

Phase II study of savolitinib monotherapy in mCRC (Status: enrolling; NCT03592641)

This study is sponsored by the National Cancer Institute and targets to screen up to 150 patients in order to enroll approximately 15 patients with MET amplified mCRC. The primary objective of the study is ORR. Secondary objectives include additional measures of clinical efficacy, safety and tolerability.

Partnership with AstraZeneca

In December 2011, we entered into a global licensing, co-development and commercialization agreement for savolitinib with AstraZeneca. As noted above, given the complexity of many of the signal transduction pathways and resistance mechanisms in oncology, the industry is increasingly studying combinations of targeted therapies (tyrosine kinase inhibitors, monoclonal antibodies and immunotherapies) and chemotherapy as potentially the best approach to treating this complex and constantly mutating disease. Based on savolitinib showing early clinical benefit as a highly selective MET inhibitor in a number of cancers, in August 2016 and December 2020 we and AstraZeneca amended our global licensing, co-development and commercialization agreement for savolitinib. We believe that AstraZeneca's portfolio of proprietary targeted therapies is well suited to be used in combinations with savolitinib, and we are studying combinations with Tagrisso (EGFRm+, T790M+) and Imfinzi (PD-L1). These combinations of multiple global first-in-class compounds are difficult to replicate, and we believe represent a significant opportunity for us and AstraZeneca.

For more information regarding our partnership with AstraZeneca, see "*– Overview of Our Collaborations – AstraZeneca.*"

2. Surufatinib VEGFR 1, 2 and 3, FGFR1 and CSF-1R Inhibitor

Surufatinib is an oral small molecule angio-immuno kinase inhibitor targeting VEGFR and FGFR, which both inhibit angiogenesis, and CSF-1R, which regulates tumor-associated macrophages, promoting the body's immune response against tumor cells. Its unique angio-immuno kinase profile could help improve the anti-tumor activity of PD-1 antibodies.

Surufatinib is the first oncology medicine that we have taken through proof-of-concept in China and expanded globally ourselves. Surufatinib is in proof-of-concept clinical trials in the United States, successfully completed two late-stage clinical trials, is in further late-stage clinical trials in China and is expected to start late-stage trials in the United States and Europe as a monotherapy. Furthermore, it is being investigated in combination with PD-1 inhibitors.

Surufatinib was approved by the NMPA in December 2020 for the treatment of non-pancreatic NETs and is now being marketed in China under the brand name Sulanda.

Mechanism of Action

Both VEGFR and FGFR signaling pathways can mediate tumor angiogenesis. CSF-1R plays an important role in the functions of macrophages. Recently, the roles in increasing tumor immune evasion of VEGFR, FGFR in regulation of T cells, tumor-associated macrophages and myeloid-derived suppressor cells have been demonstrated. Therefore, blockade of tumor angiogenesis and tumor immune evasion by simultaneously targeting VEGFR 1, 2 and 3, FGFR1 and CSF-1R kinases may represent a promising approach for oncology therapy. See "*Business – Our Clinical Pipeline – 3. Fruquintinib VEGFR 1, 2 and 3 Inhibitor – Mechanism of Action*", "*Industry Overview – Overview of Molecular Targets and Market Landscape – VEGFR Pathway – Overview of VEGFR inhibitors", "– FGFR Pathway – Overview of FGFR inhibitors" and "– CSF-1R Pathway – Overview of CSF-1R inhibitors*" for more information.

Surufatinib Pre-clinical Evidence

Surufatinib inhibited VEGFR 1, 2, and 3, FGFR1 and CSF-1R kinases with IC_{50} in a range of 1 nM to 24 nM. It also strongly blocked VEGF-induced VEGFR2 phosphorylation in HEK293 cells and CSF-1R phosphorylation in RAW264.7 cells with an IC_{50} of 2 nM and 79 nM, respectively. Surufatinib also reduced VEGF- or FGF-stimulated human umbilical vein endothelial cell proliferation with an $IC_{50} < 50$ nM. In animal studies, a single oral dose of surufatinib inhibited VEGF-stimulated VEGFR2 phosphorylation in lung tissues of nude mice in an exposure-dependent manner. Furthermore, elevation of FGF23 levels in plasma 24 hours post dosing suggested suppression of FGFR signaling.

Surufatinib demonstrated potent tumor growth inhibition in multiple human xenograft models and decreased cluster of differentiation 31 expression remarkably, suggesting strong inhibition on angiogenesis through VEGFR and FGFR signaling. In a syngeneic murine colon cancer model, surufatinib demonstrated moderate tumor growth inhibition after single-agent treatment. Flow cytometry and immunohistochemistry analysis revealed an increase of certain T cells and a significant reduction in certain tumor-associated macrophages, including CSF-1R mutation positive tumor-associated macrophages in tumor tissue, indicating surufatinib has a strong effect on CSF-1R. Interestingly, a combination of surufatinib with a PD-L1 antibody resulted in enhanced anti-tumor effect. These results suggested that surufatinib has a strong effect in modulating angiogenesis and cancer immunity.

Surufatinib Clinical Trials

We currently have various clinical trials of surufatinib ongoing or expected to begin in the near term in patients with NETs and BTC, and in combination with checkpoint inhibitors.

Neuroendocrine Tumors

NETs begin in the specialized cells of the body's neuroendocrine system. Cells have traits of both hormone-producing endocrine cells and nerve cells. NETs are found throughout the body's organ system and have complex and fragmented epidemiology with about 65-75% of NETs originating in the gastrointestinal tract and pancreas, 25-35% in the lung or bronchus, and a further 20%-30% in other organs or unknown origins.

In China, there were about 71,300 newly diagnosed NET patients in 2020. While no China prevalence data exists, according to Frost & Sullivan, there could be over 300,000 patients living with the disease.

NETs can be functional, releasing hormones and peptides that cause symptoms like diarrhea and flushing, or non-functional with no symptoms. Early-stage NETs, which are often functional, can be treated with somatostatin analogue subcutaneous injections, which are approved and reimbursed in China and alleviate symptoms and slow NET growth, but have limited tumor reduction efficacy.

Advanced NETs grow more quickly. In China, Sutent is approved in pancreatic NET while Afinitor, an m-TOR inhibitor, is approved in non-functional neuroendocrine tumors in the pancreas, lung and gastrointestinal tract. These approvals, however, cover only about half of advanced NET patients.

The table below shows a summary of the clinical trials that we have completed or are in planning for surufatinib in neuroendocrine cancer patients. Our Phase Ib study in planning for the United States and Europe will also include expansion cohorts to explore surufatinib in patients with BTC and sarcoma.

Clinical Trials of Surufatinib in NETs

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
Surufatinib monotherapy	HUTCHMED	SANET-ep: Non-pancreatic NET	China (24)	III	Approved; launched in 2021	NCT02588170
Surufatinib monotherapy	HUTCHMED	SANET-p: Pancreatic NET	China (21)	III	Met primary endpoint; NDA accepted (Sept 2020)	NCT02589821
Surufatinib monotherapy[(2)]	HUTCHMED	NETs	U.S. (16)	Ib	NDA rolling submission completed in April 2021	NCT02549937
Surufatinib monotherapy	HUTCHMED	NETs	Europe (N/A)	Ib	Expect to file MAA in mid-2021	N/A

Notes:

(1) Expected maximum number of sites.

(2) FDA granted surufatinib orphan drug designation for the treatment of pancreatic NETs in November 2019 and Fast Track Designation for our pancreatic and non-pancreatic NET development programs in April 2020.

NET = neuroendocrine tumor; BTC = biliary tract cancer; and MAA = marketing authorization application.

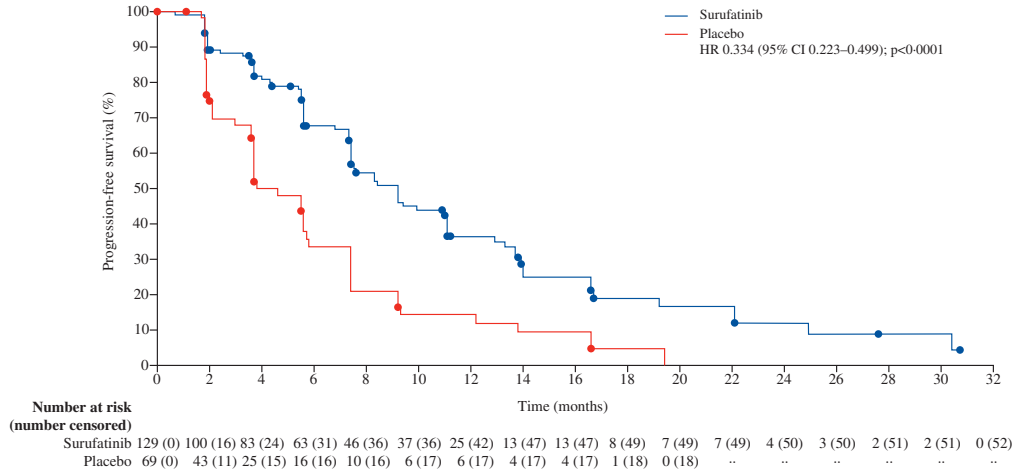
SANET-ep study: Phase III study of surufatinib monotherapy in non-pancreatic NETs (Status: completed and product launched in China in January 2021; NCT02588170)

In 2015, we initiated the SANET-ep study, which is a Phase III study in China in patients with grade 1 and 2 advanced non-pancreatic NETs. In this study, patients were randomized at a 2:1 ratio to receive either an oral dose of 300 mg of surufatinib or a placebo once daily on a 28-day treatment cycle. The primary endpoint was PFS, with secondary endpoints including ORR, disease control rate, time to response, duration of response, OS, safety and tolerability.

A 198-patient interim analysis was conducted on SANET-ep in mid-2019, leading the IDMC, to determine that it had met the pre-defined primary endpoint of PFS and should be stopped early. The

positive results of this trial were highlighted in an oral presentation at the 2019 European Society for Medical Oncology Congress, and subsequently published in The Lancet Oncology in September 2020. Median PFS per investigator assessment was 9.2 months for patients treated with surufatinib, as compared to 3.8 months for patients in the placebo group (HR 0.334; 95% CI: 0.223, 0.499; p<0.0001). Efficacy was also supported by a blinded independent image review committee assessment. Surufatinib was well-tolerated in this study and the safety profile was consistent with observations in prior clinical studies. CTC grade 3 or above TEAEs in this study with greater than 5% incidence were hypertension (36%), proteinuria (19%) and anemia (7%).

SANET-ep Clearly Succeeded in Meeting Primary Endpoint of PFS



Notes: P-value is obtained from the stratified one-sided log-rank test; Hazard ratio is obtained from stratified Cox model; CI = confidence interval; and HR = hazard ratio.

Source: Xu J, Shen L, Zhou Z, et al. Surufatinib in advanced extrapancreatic neuroendocrine tumours (SANET-ep): a randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncol. 2020;21(11):1500-1512. doi:10.1016/S1470-2045(20)30496-4.

In late 2020, surufatinib was granted approval for drug registration by the NMPA for the treatment of non-pancreatic NET, followed by launch in mid-January 2021 within three weeks of approval. We believe the benefit of surufatinib as a monotherapy to patients with non-pancreatic NETs in China could be significant as compared to the minimal treatment alternatives currently available to them.

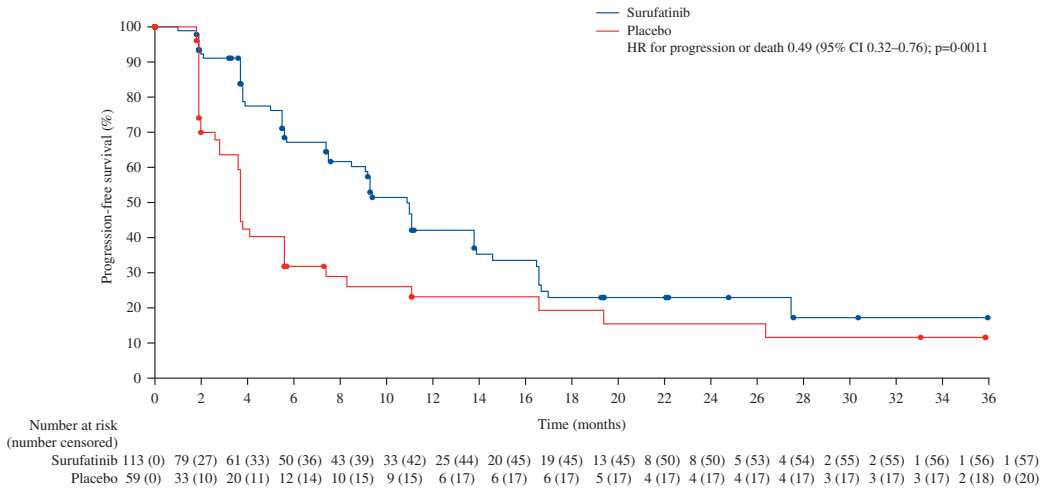
SANET-p study: Phase III study of surufatinib monotherapy in pancreatic NETs (Status: met primary endpoint early; NDA accepted in September 2020; NCT02589821)

In 2016, we initiated the SANET-p study, which is a Phase III study in China in patients with low- or intermediate-grade, advanced pancreatic NETs. In this study, patients are randomized at a 2:1 ratio to receive either an oral dose of 300 mg of surufatinib or a placebo once daily on a 28-day treatment cycle. The primary endpoint is PFS, with secondary endpoints including ORR, disease control rate, time to response, duration of response, OS, safety and tolerability.

In early 2020, an interim analysis was conducted on SANET-p, leading the IDMC to recommend that the study stop early as the pre-defined primary endpoint of PFS had already been met. Investigator-assessed median PFS was 10.9 months for patients treated with surufatinib, as compared to 3.7 months for patients in the placebo group (HR 0.491; 95% CI: 0.319-0.755; p=0.0011). ORRs were 19.2% for the efficacy evaluable patients in the surufatinib group versus 1.9% for the placebo group, with a DCR of 80.8% versus 66.0%, respectively. Most patients in the trial had Grade 2 disease with heavy tumor burden, including liver metastasis and multiple organ involvement. Efficacy was also supported by blinded independent image review committee assessment, with a median PFS of 13.9 months for surufatinib as compared to 4.6 months for placebo (HR 0.339; 95% CI 0.209-0.549; p<0.0001). The safety profile of surufatinib was manageable and consistent with observations in prior studies. Treatment was well

tolerated for most patients, with discontinuation rates as a result of TEAEs of 10.6% in the surufatinib group as compared to 6.8% in the placebo group. CTC grade 3 or above TEAEs in this study with greater than 5% incidence were hypertension (38%), proteinuria (10%) and hypertriglyceridemia (7%).

SANET-p Clearly Succeeded in Meeting Primary Endpoint of PFS



Notes: P-value is obtained from the stratified one-sided log-rank test; Hazard ratio is obtained from stratified Cox model; CI = confidence interval; and HR = hazard ratio.

Source: Xu J, Shen L, Bai C, et al. Surufatinib in advanced pancreatic neuroendocrine tumours (SANET-p): a randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncol. 2020;21(11):1489-1499. doi:10.1016/S1470-2045(20)30493-9.

Following the success of SANET-p, a second NDA was filed and accepted by the NMPA in September 2020. We believe the benefits of surufatinib as a monotherapy to the approximately 23,400 new patients with pancreatic NETs in China in 2018 could be significant as compared to the treatment alternatives currently available to them.

The positive SANET-ep and SANET-p Phase III studies now position surufatinib to potentially be approved in the full spectrum of advanced-NET disease in China. We believe that no other approved targeted therapy can address and treat all subtypes of NETs.

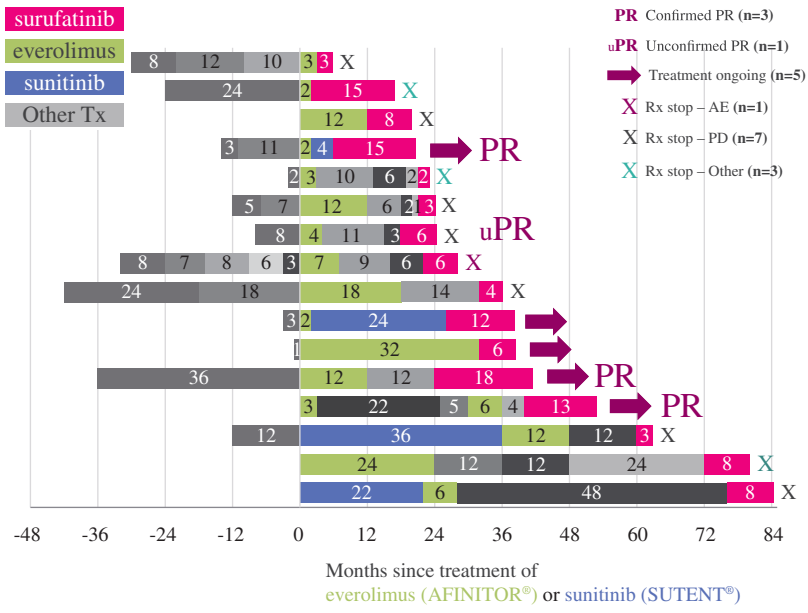
Phase Ib study of surufatinib monotherapy in heavily pretreated progressive NETs (Status: ongoing; NCT02549937)

We are conducting a multi-center, open-label, Phase Ib clinical study to evaluate the safety, tolerability and pharmacokinetics of surufatinib in U.S. patients, which has established the U.S. RP2D to be 300 mg, the same as that in China. At ASCO 2020, preliminary data presented from the two NET cohorts in the ongoing U.S. Phase Ib trial for surufatinib demonstrated efficacy comparable to China data in heavily pretreated patients, including Afinitor and Sutent, with pancreatic or non-pancreatic NETs. The safety profile was also consistent with the larger pool of surufatinib safety data. As of June 30, 2020, 16 patients with pancreatic NET were treated for a median of 8.5 months (range 2-23) and 16 patients with non-pancreatic NET were treated for a median of 8 months (range of 2-15). All 32 patients have pretreated progressive NETs (median prior lines of treatment: 3; range 1-8). Confirmed response was observed in 18.8% of pancreatic NET and disease control was observed in 87.5% of patients. In the non-pancreatic NET cohort confirmed response was observed in 6.3% of the patients and disease control was observed in 93.8% of patients. Median PFS was 11.5 months for patients in both cohorts (95% confidence interval: 6.5-17.5).

The FDA granted surufatinib orphan drug designation for the treatment of pancreatic NETs in November 2019 and Fast Track Designations for our pancreatic and non-pancreatic NET development programs in April 2020. In December 2020, we initiated the filing of an NDA to the U.S. FDA – the first

portion of a rolling submission for surufatinib for the treatment of pancreatic and non-pancreatic NET. We completed the NDA submission in April 2021, which is our first NDA in the U.S. Filing acceptance of the NDA is subject to FDA review of the complete application. We also plan to file a MAA to the EMA in mid-2021, based on scientific advice from the EMA's Committee for Medicinal Products for Human Use (CHMP).

US Phase Ib: Encouraging Preliminary Efficacy in Afinitor and Sutent Refractory/Intolerant NET Patients



Notes: Data cut-off as of April 21, 2020. PR = partial response; AE = adverse event; PD = progressive disease; Rx = treatment; Tx = treatment; and n = number of patients.

Source: Dasari, et al. Efficacy and safety of surufatinib in United States (US) patients (pts) with neuroendocrine tumors (NETs). Journal of Clinical Oncology 2020 38:15_suppl, 4610-4610.

Biliary Tract Cancer

BTC (also known as cholangiocarcinoma) is a heterogeneous group of rare malignancies arising from the biliary tract epithelia. Gemzar, a type of chemotherapy, is the currently approved first-line therapy for BTC patients, with median survival of less than 12 months for patients with unresectable or metastatic disease at diagnosis. As a result, this is an unmet medical need for patients who have progressed on chemotherapy. There is currently no standard of care for these patients. Surufatinib may offer a new targeted treatment option in this tumor type. The table below shows a summary of the clinical studies that we have underway for surufatinib in BTC patients.

Clinical Trials of Surufatinib in BTC

Treatment	Sponsors/ Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
Surufatinib monotherapy	HUTCHMED	Chemotherapy refractory BTC	China (5)	Ib/II	Enrollment complete. Supported progressing in Phase IIb/III	NCT02966821
Surufatinib monotherapy	HUTCHMED	Chemotherapy refractory BTC	China (26)	IIb/III	Ongoing Expect to conduct interim analysis in 2021	NCT03873532
Surufatinib monotherapy	HUTCHMED	BTC and soft tissue sarcoma	U.S. (16)	Ib	Ongoing. BTC cohort opened in April 2018. Sarcoma cohort opened in Oct 2019.	NCT02549937

Notes:

(1) Expected maximum number of sites.

Chemotherapy refractory = resistant to prior chemotherapy treatment; and BTC = biliary tract cancer.

Phase Ib/II surufatinib monotherapy in chemotherapy refractory BTC – China (Status: enrollment complete; NCT02966821)

In early 2017, we began a Phase Ib/II proof-of-concept study in patients with BTC. Preliminary efficacy led us to begin the Phase II/III study discussed below.

At ASCO 2021, results of this study were disclosed. Surufatinib demonstrated moderate efficacy and favorable tolerability profile.

After 16 weeks of treatment, 46% of the patients did not experience progression of their disease. Median PFS was 3.7 months and median OS was 6.9 months. The most common Grade 3 or higher TRAEs were blood bilirubin increase (21%), hypertension (18%), and proteinuria (13%).

Phase IIb/III study of surufatinib monotherapy in second line BTC – China (Status: ongoing; NCT03873532)

In March 2019, based on preliminary Phase Ib/IIa data, we initiated a registration-intent Phase IIb/III study comparing surufatinib with capecitabine in patients with unresectable or metastatic BTC whose disease progressed after first-line chemotherapy. The primary endpoint is OS. Enrollment for the BTC monotherapy Phase II portion (80 patients) was completed in 2020, and we expect to conduct an interim analysis for futility in 2021 when OS data are mature. The interim analysis will inform the Phase III study decision.

Surufatinib Combinations with Checkpoint Inhibitors

Surufatinib's ability to inhibit angiogenesis, block the accumulation of tumor associated macrophages and promote infiltration of effector T cells into tumors, could help improve the anti-tumor activity of PD-1 antibodies.

The table below shows a summary of the clinical trials that we have underway or in planning for surufatinib in combination with checkpoint inhibitors.

Clinical Trials of Surufatinib with Checkpoint Inhibitors

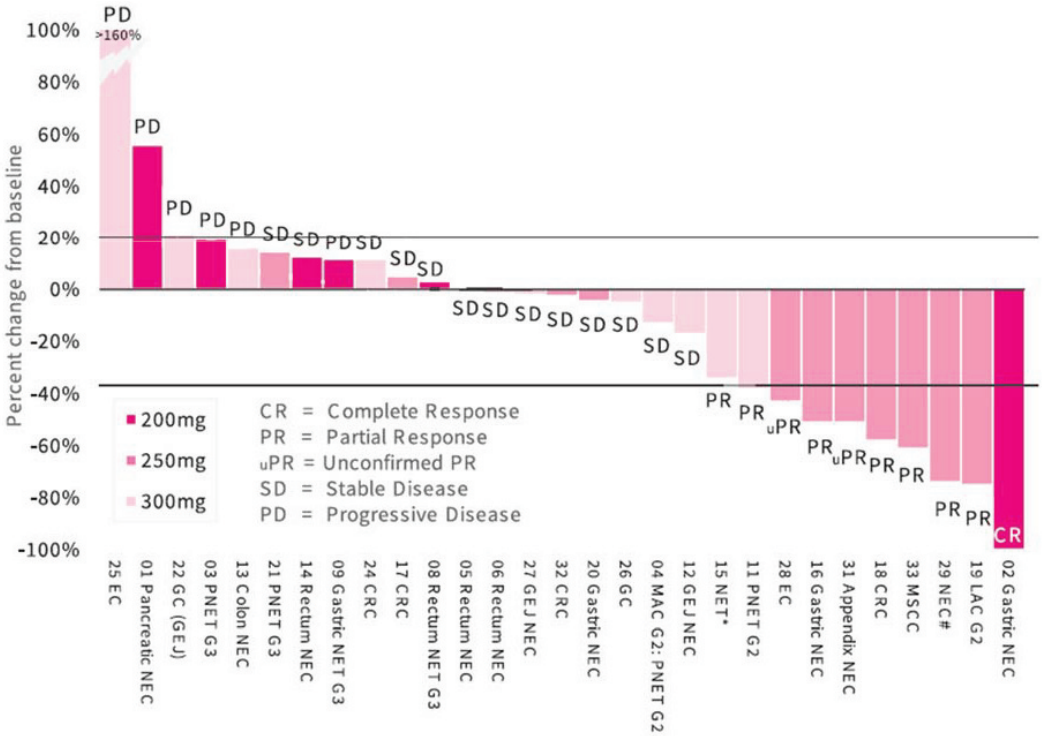
Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
Surufatinib and Tuoyi (PD-1)	HUTCHMED and Junshi	Neuroendocrine neoplasms	China (16)	II	Ongoing. Started in December 2019.	NCT04169672
Surufatinib and Tuoyi (PD-1)	HUTCHMED and Junshi	BTC	China (16)	II	Ongoing. Started in December 2019.	NCT04169672
Surufatinib and Tuoyi (PD-1)	HUTCHMED and Junshi	Gastric cancer	China (16)	II	Ongoing. Started in December 2019.	NCT04169672
Surufatinib and Tuoyi (PD-1)	HUTCHMED and Junshi	Thyroid cancer	China (16)	II	Ongoing. Started in December 2019.	NCT04169672
Surufatinib and Tuoyi (PD-1)	HUTCHMED and Junshi	Small cell lung cancer	China (16)	II	Ongoing. Started in December 2019.	NCT04169672
Surufatinib and Tuoyi (PD-1)	HUTCHMED and Junshi	Soft tissue sarcoma	China (16)	II	Ongoing. Started in December 2019.	NCT04169672
Surufatinib and Tuoyi (PD-1)	HUTCHMED and Junshi	Endometrial cancer	China (16)	II	Ongoing. Started in December 2019.	NCT04169672
Surufatinib and Tuoyi (PD-1)	HUTCHMED and Junshi	Esophageal cancer	China (16)	II	Ongoing. Started in December 2019.	NCT04169672
Surufatinib and Tuoyi (PD-1)	HUTCHMED and Junshi	NSCLC	China (16)	II	Ongoing. Started in December 2019.	NCT04169672
Surufatinib and Tyvyt (PD-1)	Innovent and HUTCHMED	Solid tumors	China (1)	I	Ongoing Started in July 2020	NCT04427774
Surufatinib and tislelizumab (PD-1)	HUTCHMED and BeiGene	Solid tumors	U.S./ Europe (24)	Ib/II	Ongoing First patient dosed in March 2021	NCT04579757

Note:

(1) Expected maximum number of sites.

In late 2018, we entered into a global collaboration with Junshi to evaluate the combination of surufatinib with Tuoyi. We completed a Phase I dose-finding study and presented the data at the AACR Conference in April 2020. The data showed that surufatinib plus Tuoyi were well tolerated with no unexpected safety signals observed. At the recommend Phase 2 dose, a DCR of 100% and ORR of 63.6% were reported for 11 efficacy evaluable patients, with 2 unconfirmed partial responses. Surufatinib plus Tuoyi showed encouraging antitumor activity in patients with advanced solid tumors. A Phase II China study is enrolling patients in nine solid tumor indications, including neuroendocrine neoplasms, BTC, gastric cancer, thyroid cancer, small cell lung cancer, soft tissue sarcoma, endometrial cancer, esophageal cancer and NSCLC.

Phase I Dose Finding Study: Encouraging Anti-Tumor Efficacy for Surufatinib Combined with the anti-PD-1 Antibody Tuoyi in G3 NET/NEC Patients



Notes: RP2D: Recommended Phase 2 Dose. NET/NEN: neuroendocrine tumor/neoplasm; NEC: neuroendocrine carcinoma; CRC: colorectal carcinoma; GC: gastric adenocarcinoma; EC: esophageal squamous cell carcinoma; GEJ: gastroesophageal junction; MAC G2: mediastinal atypical carcinoid; PNET G2: Pancreas NET G2; MSCC: metastatic squamous cell carcinoma with unknown primary; NSCLC: non-small cell lung cancer; LAC: Lung atypical carcinoid; *: Left supraclavicular lymph node neuroendocrine tumor; #: Merkel cell carcinoma.

Source: Cao Y, et al. "A phase I trial of surufatinib plus toripalimab in patients with advanced solid tumors." Presented at American Association for Cancer Research (AACR) Virtual Annual Meeting I on April 27, 2020.

At ASCO 2021, encouraging preliminary data were disclosed for the surufatinib and Tuoyi combination in the neuroendocrine carcinoma (NEC) and gastric cancer (GC) cohorts.

For the 20 patients in the NEC cohort who received an average of 5 cycles of treatments and are efficacy evaluable, ORR was 20% while DCR was 70%. Median PFS was 3.9 months (95% confidence interval: 1.3-NR). Grade 3 or higher TRAEs occurred in 33% of patients. We are preparing to initiate a Phase III study in 2L or above NEC.

Median duration of treatment for the GC cohort was 3 months, with 15 patients efficacy evaluable at the time of the analysis. For these 15 patients, confirmed ORR was 13% and an additional 20% of patients had unconfirmed OR. DCR was 73% and median PFS was 3.7 months (95% confidence interval: 1.4-NR). Grade 3 or higher TRAEs occurred in 14% of patients. Registration design for GC is under discussion.

In late 2019, we expanded our global collaboration agreement with Innovent to evaluate the safety and efficacy of Tyvyt in combination with surufatinib, and in July 2020, started a Phase I study in China to evaluate the safety and efficacy of the combination.

In addition, in May 2020, we entered into a global clinical collaboration agreement to evaluate the safety, tolerability and efficacy of combining surufatinib with BeiGene's anti-PD-1 antibody, tislelizumab, for the treatment of various solid tumor cancers in the United States, Europe, China and Australia. In March 2021, we dosed the first patient in an open-label, Phase Ib/II study of surufatinib in

combination with tislelizumab in the United States and Europe, evaluating the safety, tolerability, pharmacokinetics and efficacy in patients with advanced solid tumors, including CRC, NET, small cell lung cancer, gastric cancer and soft tissue sarcoma.

Surufatinib Exploratory Development

We are conducting multiple Phase Ib expansion cohorts in the United States to explore the use of surufatinib in BTC and soft tissue sarcoma. In China, we intend to initiate multiple exploratory studies, both as a single agent and in combinations, to evaluate the efficacy of surufatinib. We are also supporting dozens of investigator-initiated studies in various tumor settings.

3. Fruquintinib VEGFR 1, 2 and 3 Inhibitor

Fruquintinib (also known as HMPL-013) is a VEGFR inhibitor that we believe is highly differentiated due to its superior kinase selectivity compared to other small molecule VEGFR inhibitors, which can be prone to excessive off-target toxicities. Fruquintinib's selectivity on VEGFR 1, 2 and 3 results in fewer off-target toxicities, thereby allowing for better target coverage, as well as possible use in combination with other agents such as chemotherapies, targeted therapies and immunotherapies.

We believe these are meaningful points of differentiation compared to other approved small molecule VEGFR inhibitors such as Sutent, Nexavar and Stivarga, and can potentially significantly expand the use and market potential of fruquintinib. Consequently, we believe that fruquintinib has the potential to become a global small molecule VEGFR inhibitor with the best selectivity for many types of solid tumors.

We received full approval for launch of fruquintinib (under the brand name Elunate) in CRC in September 2018. In partnership with Eli Lilly, we launched fruquintinib in China in late November 2018. Elunate is indicated for the treatment of patients with mCRC that have been previously treated with fluoropyrimidine, oxaliplatin and irinotecan, including those who have previously received anti-VEGF therapy and/or anti-EGFR therapy (Ras wild type). We manufacture all commercial supplies of Elunate in our factory in Suzhou and have expanded our role in the commercialization of Elunate since October 1, 2020. For more information regarding the Elunate product launch, see "*– Overview of Elunate Commercial Launch*."

Mechanism of Action

During the development of cancer, tumors at an advanced stage can secrete large amounts of VEGF, a protein ligand, to stimulate formation of excessive vasculature (angiogenesis) around the tumor in order to provide greater blood flow, oxygen, and nutrients to fuel the rapid growth of the tumor. Since essentially all solid tumors require angiogenesis to progress beyond a few millimeters in diameter, VEGFR drugs have demonstrated benefits in a wide variety of tumor types. VEGF and other ligands can bind to three VEGF receptors, VEGFR 1, 2 and 3, each of which has been shown to play a role in angiogenesis. Therefore, inhibition of the VEGF/VEGFR signaling pathway can act to stop the growth of the vasculature around the tumor and thereby starve the tumor of the nutrients and oxygen it needs to grow rapidly.

This therapeutic strategy has been well validated with several first-generation VEGF inhibitors having been approved globally since 2005 and 2006. These include both small molecule multi-kinase inhibitor drugs such as Nexavar and Sutent as well as monoclonal antibodies such as Avastin. The success of these drugs validated VEGFR inhibition as a new class of therapy for the treatment of cancer.

See "*Industry Overview – Overview of Molecular Targets and Market Landscape – VEGFR Pathway – Overview of VEGFR inhibitors*" for more details.

Fruquintinib Pre-clinical Evidence

Pre-clinical trials have demonstrated that fruquintinib is a highly selective VEGFR 1, 2 and 3 inhibitor with high potency and low cell toxicity at the enzymatic and cellular levels. In a kinase selectivity

screening, fruquintinib was found to be approximately 250 times more selective to VEGFR 3 than to the next non-VEGFR kinase.

As a result of off-target side effects, existing VEGFR inhibitors are often unable to be dosed high enough to completely inhibit VEGFR, the intended target. In addition, the complex off-target toxicities resulting from inhibition of multiple signaling pathways are often difficult to manage in clinical practice. Combining such drugs with chemotherapy can lead to severe toxicities that can cause more harm than benefit to patients. To date, the first-generation VEGFR tyrosine kinase inhibitors have been rarely used in combination with other therapies, thereby limiting their potential. Because of the potency and selectivity of fruquintinib, we believe that it has the potential to be safely combined with other oncology drugs, which could significantly expand its clinical potential.

Fruquintinib Clinical Trials

Colorectal Cancer

The table below shows a summary of the clinical trials we have recently completed, are underway or are in planning for fruquintinib in CRC patients. We have two additional trials in progress for fruquintinib in CRC in combination with a checkpoint inhibitor as discussed in more detail below under "– *Fruquintinib Combinations with Checkpoint Inhibitors*."

Current Clinical Trials of Fruquintinib in CRC

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
Fruquintinib monotherapy	HUTCHMED and Eli Lilly	FRESCO:3L CRC; chemotherapy refractory	China (28)	III	Approved; launched in November 2018	NCT02314819
Fruquintinib monotherapy[(2)]	HUTCHMED	FRESCO-2: mCRC	U.S./ Europe/ Japan (expected to be 165 sites)	III	Ongoing Enrollment targeted to complete in late 2021	NCT04322539
Fruquintinib monotherapy	HUTCHMED	CRC, TN & HR+/HER2- breast cancer	U.S. (9)	Ib	Ongoing. CRC expansion cohort opened in March 2019. BC cohorts opened in Jan 2020.	NCT03251378

Notes:

(1) Expected maximum number of sites.

(2) The FDA granted Fast Track Designation for the development of fruquintinib for the treatment of patients with mCRC in June 2020.

CRC = colorectal cancer; >3L = third line or above; refractory = resistant to prior treatment; TN = triple-negative; HR+ = hormone receptor-positive; and HER2 = human epidermal growth factor receptor 2.

FRESCO study: Phase III study of fruquintinib monotherapy in third-line CRC (Status: completed and product launched in November 2018; NCT02314819)

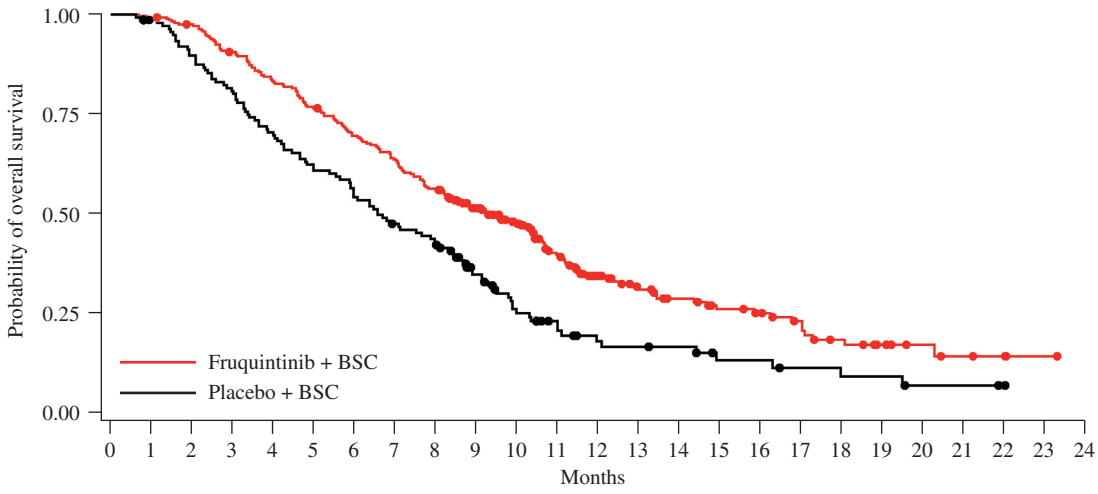
In 2014, we initiated the FRESCO study, which is a randomized, double-blind, placebo-controlled, multi-center, Phase III pivotal trial in China in patients with locally advanced or mCRC who had failed at least two prior systemic antineoplastic therapies, including fluoropyrimidine, Eloxatin and Camptosar. No drugs had been approved in third-line CRC in China with best supportive care being the general standard of care. This study followed a Phase II proof-of-concept trial in third-line CRC that met its primary endpoint of PFS in 2014.

Enrollment was completed in May 2016, and 519 patients were screened. The intent-to-treat population of 416 patients was randomized at a 2:1 ratio to receive either 5 mg of fruquintinib orally once daily, on a three-weeks-on/one-week-off cycle, plus best supportive care (278 patients) or placebo plus best supportive care (138 patients). Randomization was stratified for prior anti-VEGF therapy and K-RAS gene status. The trial concluded in January 2017.

In June 2017, we presented the results of the FRESCO study in an oral presentation during the ASCO Annual Meeting. Results showed that FRESCO met all primary and secondary endpoints including significant improvements in OS and PFS with a manageable safety profile and lower off-target toxicities compared to other targeted therapies.

The primary endpoint of median OS was 9.30 months (95% confidence interval: 8.18-10.45 months) in the fruquintinib group versus 6.57 months (95% confidence interval: 5.88-8.11 months) in the placebo group, with a hazard ratio of 0.65 (95% confidence interval: 0.51-0.83; two-sided p<0.001).

Phase III Study in China of Fruquintinib Monotherapy in Third-line CRC
FRESCO Clearly Succeeded in Meeting the Primary Efficacy Endpoint of Overall Survival

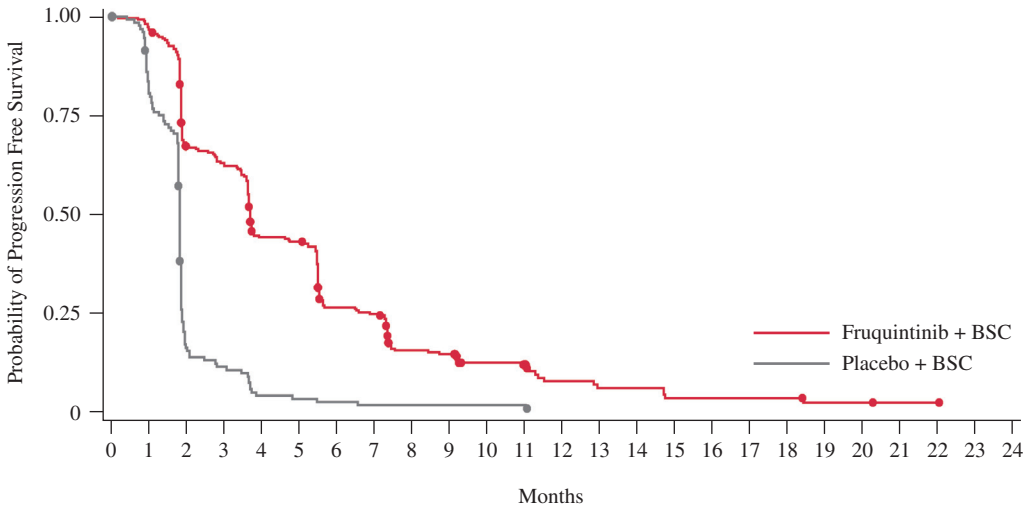


Notes: N = number of patients; BSC = best supportive care; 95% CI = 95% confidence interval; and HR = hazard ratio.

Source: Li J, Qin S, Xu RH, et al. Effect of Fruquintinib vs Placebo on Overall Survival in Patients With Previously Treated Metastatic Colorectal Cancer: The FRESCO Randomized Clinical Trial. JAMA. 2018;319(24):2486 2496. doi:10.1001/jama.2018.7855.

The secondary endpoint of median PFS was 3.71 months (95% confidence interval: 3.65-4.63 months) in the fruquintinib group versus 1.84 months (95% confidence interval: 1.81-1.84 months) in the placebo group, with a hazard ratio of 0.26 (95% confidence interval: 0.21-0.34; two-sided p<0.001). Significant benefits were also seen in other secondary endpoints. The disease control rate in the fruquintinib group was 62% versus 12% for placebo (p<0.001), while the ORR based on confirmed responses was 5% versus 0% for placebo (p=0.012).

FRESCO Clearly Succeeded in Meeting Endpoint of PFS



Note: BSC = best supportive care.

Source: Li J, Qin S, Xu RH, et al. Effect of Fruquintinib vs Placebo on Overall Survival in Patients With Previously Treated Metastatic Colorectal Cancer: The FRESCO Randomized Clinical Trial. JAMA. 2018;319(24):2486 -2496. doi:10.1001/jama.2018.7855.

We have not performed a head-to-head clinical trial of fruquintinib versus Stivarga. While it is difficult to directly evaluate and compare clinical results across separate trials, data from the FRESCO study compare favorably to the data from the CONCUR study, a Phase III study of Stivarga monotherapy in CRC conducted in Asia, and the CORRECT study, a global Phase III study of Stivarga in CRC. In particular, in the Chinese patient subgroup of the CONCUR study, Stivarga had a disease control rate of 46% versus 7% in the placebo group. Median PFS was 2.0 months in the Stivarga group versus 1.7 months in the placebo group, and median OS was 8.4 months in the Stivarga group versus 6.2 months in the placebo group. In the CORRECT study, Stivarga had a disease control rate of 41% versus 15% in the placebo group. Median PFS was 1.9 months in the Stivarga group versus 1.7 months for the placebo group, and median OS was 6.4 months in the Stivarga group versus 5.0 months in the placebo group.

In terms of safety, results showed that fruquintinib had a manageable safety profile with lower off-target toxicities compared to Stivarga, the other VEGFR tyrosine kinase inhibitor approved for third-line CRC. Of particular interest was that the CTC grade 3 or above hepatotoxicity was similar for the fruquintinib group as compared to the placebo group, which was in contrast to Stivarga which was markedly higher and often difficult to manage in the Chinese patient population in the CONCUR study. Adverse events led to dose interruptions in 69% of patients in the Chinese patient subgroup of the CONCUR study, compared to 35% in the FRESCO study. The most frequently reported fruquintinib-related CTC grade 3 or above TEAEs included hypertension (21%), hand-foot skin reaction (11%), proteinuria (3%) and diarrhea (3%), all possibly associated with VEGFR inhibition. No other CTC grade 3 or above TEAEs exceeded 2% in the fruquintinib population, including hepatic function adverse events such as elevations in bilirubin (1%), alanine aminotransferase (<1%) or aspartate aminotransferase (<1%).

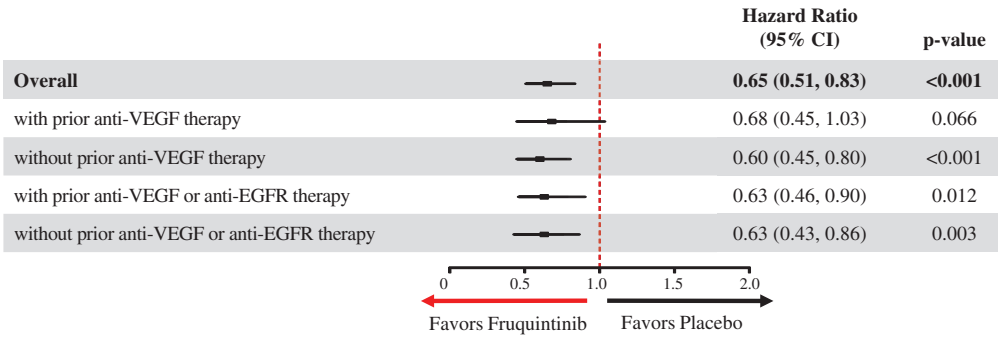
In terms of tolerability, dose interruptions or reductions occurred in only 35% and 24% of patients in the fruquintinib arm, respectively, and only 15% of patients discontinued treatment of fruquintinib due to adverse events versus 6% for placebo. The FRESCO study was published in the Journal of the American Medical Association in June 2018.

Subgroup analysis

In June 2018, a further subgroup analysis of data from the FRESCO Phase III study was presented during the ASCO Annual Meeting. This analysis explored possible effects of prior target therapy on the efficacy and safety of fruquintinib by analyzing the subgroups of patients with prior target therapy and those without prior target therapy.

Results showed that the benefits of fruquintinib were generally consistent across all subgroups. Among a total of 278 fruquintinib-treated patients, 111 had received prior target therapy while 55 of the 138 placebo-treated patients had received prior target therapy. In the prior target therapy subgroup, fruquintinib significantly prolonged OS and PFS. Median OS was 7.69 months for patients treated with fruquintinib versus 5.98 months for placebo (hazard ratio = 0.63; p = 0.012). Median PFS was 3.65 months for patients treated with fruquintinib versus 1.84 months for placebo (hazard ratio = 0.24; p < 0.001).

OS Subgroup Analysis by Prior Treatment.
Fruquintinib Demonstrated Consistent Results Across Sub-Groups



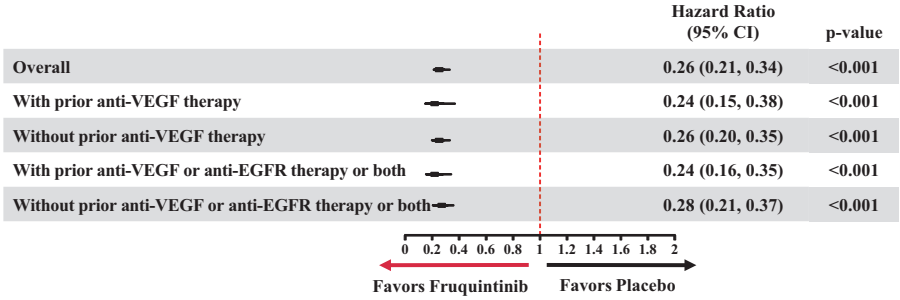
Notes: CI = confidence interval; and p-value = probability value.

Source: Xu RH, Li J, Bai YX, et al. Subgroup analysis by prior anti-VEGF or anti-EGFR target therapy in FRESCO, a randomized, double- blind, phase 3 trial comparing fruquintinib versus placebo plus best supportive care in Chinese patients with mCRC. Journal of Clinical Oncology. 2018;36:15_suppl, 3537-3537. doi:10.1200/JCO.2018.36.15_suppl.3537.

Among these 278 patients, the results showed that a subgroup of 84 patients who had received prior anti-VEGF treatment also benefited from fruquintinib. In this subgroup, the median OS was 7.20 months for fruquintinib versus 5.91 months for placebo (hazard ratio = 0.68; p=0.066) and the median PFS was 3.48 months for fruquintinib versus 1.84 months for placebo (hazard ratio = 0.24; p < 0.001).

In the subgroup of 250 patients without prior targeted therapies, the median OS was 10.35 months for 167 patients treated with fruquintinib versus 6.93 months for 83 patients treated with placebo (hazard ratio = 0.63; p = 0.003), and the median PFS for patients treated with fruquintinib was 3.81 months versus 1.84 months for placebo (hazard ratio = 0.28; p < 0.001).

PFS by Prior Therapy.
Fruquintinib Demonstrated Consistent Results Across Sub-Groups



Notes: CI = confidence interval; and p-value = probability value.

Source: Xu RH, Li J, Bai YX, et al. Subgroup analysis by prior anti-VEGF or anti-EGFR target therapy in FRESCO, a randomized, double- blind, phase 3 trial comparing fruquintinib versus placebo plus best supportive care in Chinese patients with mCRC. Journal of Clinical Oncology. 2018;36:15_suppl, 3537-3537. doi:10.1200/JCO.2018.36.15_suppl.3537.

Additional data showed that there were no observed cumulative CTC grade 3 or above TEAEs in the subgroup of patients with prior target therapy. The CTC grade 3 or above TEAEs rates of fruquintinib were similar in the subgroups with prior target therapy (61.3%) and without prior target therapy (61.1%). This subgroup analysis is consistent with the previously reported results from the FRESCO study's intent-to-treat population.

The results of this analysis showed that fruquintinib had clinically meaningful benefits in third-line mCRC patients regardless of prior target therapy without observed cumulative toxicity.

Quality-adjusted survival analysis

At the 2018 ASCO Annual Meeting, an analysis was presented that aimed to compare the quality-adjusted survival between the two arms of the FRESCO study using quality-adjusted time without symptoms or toxicity ("Q-TWiST") methodology and to investigate the Q-TWiST benefit of fruquintinib treatment among subgroups. Q-TWiST is a tool to evaluate relative clinical benefit-risk from a patient's perspective and has been widely used in oncology treatment assessment. The survival time for each patient was divided into three portions: time with CTC grade 3 or above toxicity before progression, time without symptoms or CTC grade 3 or above toxicity, and time from progression or relapse until death or end of follow-up.

Patients treated with fruquintinib had longer Q-TWiST periods compared to patients treated with placebo. Q-TWiST benefits were observed regardless of prior lines of chemotherapy and prior anti-VEGF or anti-EGFR targeted therapy. The relative improvement of Q-TWiST with fruquintinib represents a clinically important quality-of-life benefit for mCRC patients.

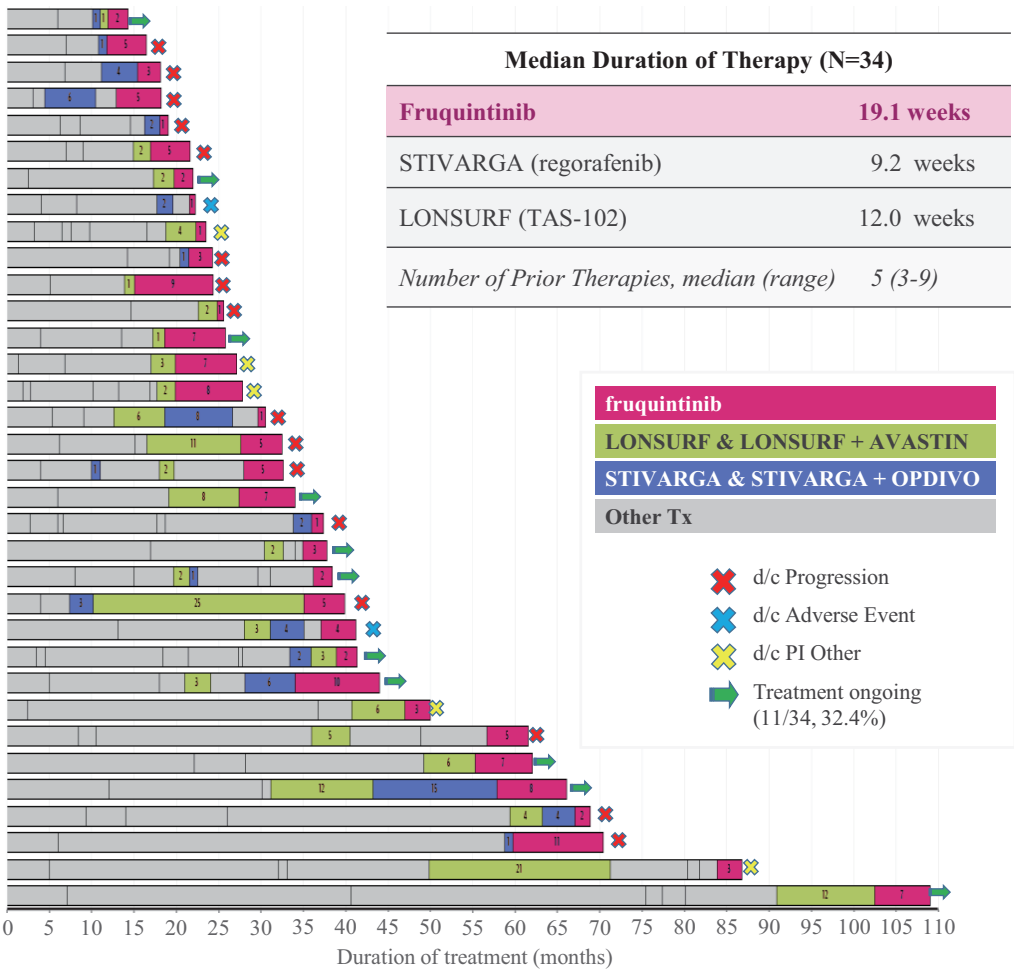
Supported by data from the successful FRESCO study, we submitted an NDA for fruquintinib in June 2017. Fruquintinib was subsequently awarded priority review status by the NMPA in view of its clinical value in September 2017, and in September 2018, the NMPA approved fruquintinib for the treatment of patients with advanced CRC and it was launched in November 2018. For more information regarding the Elunate product launch, see "*– Overview of Elunate Commercial Launch.*"

Phase Ib study of fruquintinib monotherapy in metastatic colorectal and breast cancers – U.S. (Status: enrolling; NCT03251378)

We are conducting a multi-center, open-label, Phase Ib clinical study to evaluate the safety, tolerability and pharmacokinetics of fruquintinib in U.S. patients, which has established the U.S. RP2D to be 5 mg, the same as that in China. This dose is being further evaluated in patients with mCRC and breast cancers.

Encouraging preliminary results of the U.S. Phase I/Ib study were presented at ESMO Congress 2020. As of the data cut-off in August 2020, fruquintinib was generally well-tolerated with preliminary evidence of anti-tumor activity in patients with heavily penetrated refractory mCRC. Among 34 total patients, 16 received prior Lonsurf treatment, 8 received Stivarga treatment and 10 received both Lonsurf and Stivarga treatments. The median duration of fruquintinib treatment was 19.1 weeks, higher than 12.0 weeks of Lonsurf and 9.2 weeks of Stivarga. DCR in 31 evaluable patients was 80.6%. The safety profile was consistent with that seen in the FRESCO study.

US Phase Ib: Encouraging Preliminary Efficacy in STIVARGA and LONSURF Refractory/Intolerant mCRC Patients



Notes: Data cut-off as of August 20, 2020. d/c = treatment discontinued; PI = primary inefficacy; N = number of patients; and Tx = treatment.

Source: Dasari, et al. Phase I/Ib Trial of Fruquintinib in Patients with Advanced Solid Tumors: Preliminary Results of the Dose Expansion Cohort in Refractory mCRC. ESMO 2020 Abstract #2217.

Phase III study of fruquintinib monotherapy in mCRC – Global (Status: enrolling; NCT04322539)

We initiated a global Phase III registration study, known as the FRESCO-2 study, in refractory mCRC which is expected to enroll over 680 patients from approximately 165 sites in 14 countries. The first patient was dosed in September 2020 in the United States and enrollment is targeted to complete in late 2021.

The U.S. FDA has acknowledged the totality of the fruquintinib clinical data, including the FRESCO-2 study (if positive), the prior positive Phase III FRESCO study demonstrating improvement

in OS that led to fruquintinib approval for mCRC in China in 2018, and additional completed and ongoing supporting studies in mCRC, could potentially support an NDA for the treatment of patients with mCRC in the third-line setting. The EMA and PMDA have reviewed and endorsed the FRESCO-2 study design.

Gastric Cancer

Advanced gastric cancer is a major medical need, particularly in Asian populations, with limited treatment options for patients who have failed first-line standard chemotherapy with 5-fluorouracil and platinum doublets. There were approximately 469,600 new cases of gastric cancer in China in 2020. The table below shows a summary of the clinical study we have underway for fruquintinib in gastric cancer patients.

Clinical Trials of Fruquintinib in Gastric Cancer

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
Fruquintinib and Taxol	HUTCHMED and Eli Lilly	FRUTIGA: 2L gastric cancer	China (36)	III	Ongoing; Completed second interim analysis	NCT03223376

Notes:

(1) Expected maximum number of sites.

2L = second line.

FRUTIGA study: Phase III study of fruquintinib in combination with Taxol in gastric cancer (second-line) (Status: first interim analysis reported; NCT03223376)

In October 2017, we initiated the FRUTIGA study, a pivotal Phase III clinical trial of fruquintinib in combination with Taxol for the treatment in advanced gastric or gastroesophageal junction adenocarcinoma patients in China. This randomized, double-blind, placebo-controlled, multi-center trial is being conducted in patients with advanced gastric cancer who have progressed after first-line standard chemotherapy. All subjects will receive fruquintinib or placebo combined with paclitaxel. Patients will be randomized at a 1:1 ratio and stratified according to factors such as stomach versus gastroesophageal junction tumors and ECOG performance status, a scale established by the Eastern Cooperative Oncology Group which determines ability of patient to tolerate therapies in serious illness, specifically for chemotherapy.

The primary efficacy endpoint is OS. Secondary efficacy endpoints include PFS, ORR, disease control rate, duration of response and quality-of-life score (EORTC QLQ-C30, version 3.0). Biomarkers related to the antitumor activity of fruquintinib will also be explored.

In June 2020, the IDMC of the FRUTIGA study completed a second planned interim data review and, based on the preset criteria, the IDMC and Joint Steering Committees recommended that the trial continue with a sample size increase to ~700 patients. We expect to complete enrollment of FRUTIGA around the end of 2021.

Fruquintinib Combinations with Checkpoint Inhibitors

The table below shows a summary of the clinical trials we have ongoing and in planning for fruquintinib in combination with checkpoint inhibitors.

Clinical Trials of Fruquintinib with Checkpoint Inhibitors

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
Fruquintinib and Tyvyt (PD-1)	Chinese PLA General Hospital and Innovent	CRC	China (6)	II	Ongoing. Started in Aug 2019.	NCT04179084
Fruquintinib and Tyvyt (PD-1)	HUTCHMED and Innovent	Hepatocellular carcinoma	China (9)	Ib/II	Ongoing. Expansion cohort started in mid-20.	NCT03903705
Fruquintinib and Tyvyt (PD-1)	HUTCHMED and Innovent	Endometrial cancer	China (10)	Ib/II	Ongoing. Expansion cohort started in mid-20.	NCT03903705
Fruquintinib and Tyvyt (PD-1)	HUTCHMED and Innovent	RCC	China (7)	Ib/II	Ongoing. Expansion cohort started in mid-20.	NCT03903705
Fruquintinib and Tyvyt (PD-1)	HUTCHMED and Innovent	Gastrointestinal tumor	China (6)	Ib/II	Ongoing. Expansion cohort started in mid-20.	NCT03903705
Fruquintinib and tislelizumab (PD-1)	HUTCHMED and BeiGene	Triple negative breast cancer	U.S. (13)	Ib/II	In planning Expected to initiate in 1H 2021	NCT04577963
Fruquintinib and tislelizumab (PD-1)	BeiGene and HUTCHMED	Solid tumors	Korea (4), China (5)	Ib/II	In planning	NCT04716634
Fruquintinib and geptanolimab (PD-1)	Genor and HUTCHMED	CRC	China (3)	Ib	Ongoing. Started in April 2019.	NCT03977090
Fruquintinib and geptanolimab (PD-1)	Genor and HUTCHMED	NSCLC	China (2)	Ib	Ongoing. Started in July 2019.	NCT03976856

Notes:

(1) Expected maximum number of sites.

CRC = colorectal cancer; and NSCLC = non-small cell lung cancer.

In November 2018, we entered into two collaboration agreements to evaluate the safety, tolerability and efficacy of fruquintinib in combination with checkpoint inhibitors. These include a global collaboration with Innovent to evaluate the combination of fruquintinib with Innovent's Tyvyt, a PD-1 monoclonal antibody approved in China, and a collaboration in China with Genor to evaluate the fruquintinib combination with geptanolimab, a PD-1 monoclonal antibody being developed by Genor. We are now approaching completion of the Phase I dose-finding study in China of fruquintinib in combination with Tyvyt, with the Phase I dose-expansion study already underway in five solid tumor indications. Phase Ib studies of fruquintinib in combination with geptanolimab in second-line CRC and NSCLC are ongoing.

At ASCO 2021, encouraging preliminary data were disclosed for fruquintinib in combination with two PD-1 inhibitors, Tyvyt and geptanolimab, in advanced CRC.

For the 15 patients in the CRC cohort of the fruquintinib and geptanolimab Phase Ib study, ORR was 26.7% (including 1 patient with unconfirmed PR) and 33% in the group that received the recommended Phase II dose (3mg/kg of geptanolimab every 2 weeks, 4mg of fruquintinib once daily for 3 weeks on, 1 week off). DCR for all evaluable patients were 80% and median PFS was 7.3 months (95% CI: 1.9-NR). Grade 3 TRAEs occurred in 47% of patients, and no incidences of grade 4 or 5 TRAEs were observed.

In the Tyvyt and fruquintinib combination study, 44 patients were enrolled into the CRC cohort, 22 of whom received the recommended Phase II dose of 200mg of Tyvyt every three weeks and 5mg of fruquintinib once daily for 2 weeks on, 1 week off. ORR was 23% for all patients and 27% for those who received the recommended Phase II dose. DCR was 86% for all patients and 96% for those who received the recommended Phase II dose. Median PFS was 5.6 months for all patients, and 6.9 months for those who received the recommended Phase II dose. Median OS was 11.8 months for all patients. We are formulating the registration study for mCRC. Outside of CRC, registration strategy for additional indications are in various stage of being formulated, and 3 new cohorts are being added to the study.

In addition, in May 2020, we entered into a global clinical collaboration agreement to evaluate the safety, tolerability and efficacy of combining fruquintinib with BeiGene's anti-PD-1 antibody, tislelizumab, for the treatment of various solid tumor cancers in the United States, Europe, China and Australia. In the first half of 2021, we plan to initiate a Phase Ib/II study for fruquintinib in combination with tislelizumab in patients with advanced refractory triple negative breast cancer, to be followed by a further study in additional solid tumor types.

Fruquintinib Exploratory Development

We are conducting multiple Phase Ib expansion cohorts in the United States to explore fruquintinib in CRC and breast cancer. In China, we are currently supporting dozens of investigator-initiated studies in various solid tumor settings.

Overview of Elunate Commercial Launch

Fruquintinib capsules, sold under the brand name Elunate, were approved for marketing in China by the NMPA in September 2018 and commercially launched in late November 2018. Elunate is for the treatment of patients with mCRC that have been previously treated with fluoropyrimidine, oxaliplatin and irinotecan, including those who have previously received anti-VEGF therapy and/or anti-EGFR therapy (RAS wild type).

Starting on January 1, 2020, Elunate was included on China's NRDL at a 63% discount to its initial retail price, paving the way to significantly broaden access for advanced CRC patients and rapidly build penetration in China over the coming years.

The revenues we generate from Elunate are comprised of royalty revenue, revenue from the sales of Elunate to Eli Lilly which we manufacture and sell at cost and, starting in October 2020, revenue from promotion and marketing services. In 2019, we generated US$10.8 million in total revenue from Elunate, of which US$2.7 million was royalty revenue and US$8.1 million was revenue from sales to Eli Lilly. In 2020, we generated US$20.0 million in total revenue from Elunate, of which US$4.9 million was royalty revenue, US$11.3 million was revenue from sales of goods primarily to Eli Lilly and US$3.8 million was revenue from promotion and marketing services to Eli Lilly.

Partnership with Eli Lilly

In October 2013, we entered into a license and collaboration agreement with Eli Lilly in order to accelerate and broaden our fruquintinib development program in China. As a result, we were able to quickly expand the clinical development of fruquintinib into indications with unmet medical needs in China including CRC and gastric cancer, as discussed above. In December 2018, we amended our license and collaboration agreement with Eli Lilly. This amendment gives us, among other things, all planning, execution and decision making responsibilities for life cycle indication development of fruquintinib in China. Support from Eli Lilly has also helped us to establish our own manufacturing (formulation) facility in Suzhou, China, which now produces clinical and commercial supplies of fruquintinib. In July 2020, we reached an agreement with Eli Lilly to take over development and execution of all on-the-ground medical detailing, promotion and local and regional marketing activities for Elunate in China starting on October 1, 2020. Under the terms of the new agreement, we will share gross profits linked to

sales target performance. Subject to meeting pre-agreed sales targets, Eli Lilly will pay us an estimated total of 70% to 80% of Elunate sales in the form of royalties, manufacturing costs and service payments.

For more information regarding our partnership with Eli Lilly, see "– *Overview of Our Collaborations – Eli Lilly*."

4. HMPL-689 PI3Kδ Inhibitor

HMPL-689 is a novel, highly selective and potent small molecule inhibitor targeting the isoform PI3Kδ, a key component in the B-cell receptor signaling pathway. We have designed HMPL-689 with superior PI3Kδ isoform selectivity, in particular to not inhibit PI3Kγ and offering advantages over Zydelig to minimize the risk of serious infection caused by immune suppression. HMPL-689's strong potency, particularly at the whole blood level, also allows for reduced daily doses to minimize compound related toxicity, such as the high level of gastrointestinal and liver toxicity observed with several first-generation PI3Kδ inhibitors. HMPL-689's pharmacokinetic properties have been found to be favorable with good oral absorption, moderate tissue distribution and low clearance in pre-clinical pharmacokinetic studies. We also expect that HMPL-689 will have low risk of drug accumulation and drug-to-drug interaction.

Mechanism of Action

Targeting the B-cell signaling pathway is emerging as a potential means to treat both hematological cancer and immunological diseases. Inhibiting different kinases found along the B-cell signaling pathway has proven to have clinical efficacy in hematological cancers, with breakthrough therapies having been recently approved by the FDA.

The high efficacy and successful approvals of BTK inhibitors and PI3Kδ inhibitors are evidence that modulation of the B-cell signaling pathway is critical for the effective treatment of B-cell malignancies.

Class I PI3Ks are lipid kinases that, through a series of intermediate processes, control the activation of several important signaling proteins including the serine/threonine kinase AKT.

There are multiple sub-families of PI3K kinases, and PI3Kδ is a lipid kinase that, through a series of intermediate processes, controls the activation of several important signaling proteins, including the serine/threonine kinase AKT. In most cells, AKT is a key PI3Kδ affector that regulates cell proliferation, carbohydrate metabolism, cell motility and apoptosis and other cellular processes. Upon an antigen binding to B-cell receptors, PI3Kδ can be activated through the Lyn and Syk signaling cascade.

Aberrant B-cell function has been observed in multiple immunological diseases and B-cell mediated malignancies. Therefore, PI3Kδ is considered to be a promising target for drugs that aim to prevent or treat hematologic cancer, autoimmunity and transplant organ rejection and other related inflammation diseases.

See "*Industry Overview – Overview of Molecular Targets and Market Landscape – Syk and PI3Kδ/ B-cell signaling Pathways – Overview of PI3Kδ Inhibitors*" for more details.

HMPL-689 Pre-clinical Evidence

Compared to other PI3Kδ inhibitors, HMPL-689 shows higher potency and selectivity.

Enzyme Selectivity (IC_{50}, in nM) of HMPL-689 Versus Competing PI3Kδ Inhibitors; This Shows HMPL-689 is Approximately Five-fold More Potent than Zydelig on Whole Blood Level and, unlike Copiktra, does not Inhibit PI3Kγ.

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

Source: Company.

HMPL-689 Clinical Development

The table below shows a summary of the clinical studies for HMPL-689.

Clinical Trials of HMPL-689

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[1]	Phase	Status/Plan	NCT #
HMPL-689 monotherapy	HUTCHMED	Indolent non-Hodgkin's lymphoma	China (15)	Ib	Ongoing. Data supported progressing into Phase II registration-intent	NCT03128164
HMPL-689 monotherapy	HUTCHMED	r/r MZL and FL	China (36)	II registration-intent	Ongoing. First patient dosed in April 2021	NCT04849351
HMPL-689 monotherapy	HUTCHMED	Indolent non-Hodgkin's lymphoma	U.S./ Europe (18)	I/Ib	Ongoing. First patient dosed in Aug 2019. To support US regulatory interaction in 2H21.	NCT03786926
HMPL-689 monotherapy	HUTCHMED	Indolent non-Hodgkin's lymphoma	U.S./ Europe (N/A)	II registration-intent	In planning. Expect to complete US FDA regulatory interaction in 2H21	N/A

Note:

(1) Expected maximum number of sites.

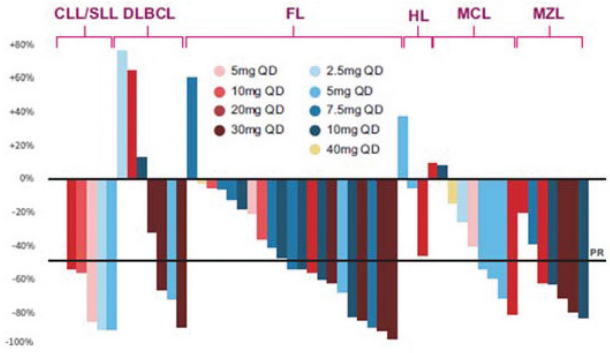
Phase Ib study of HMPL-689 in patients with Indolent non-Hodgkin's lymphoma (Status: enrolling; NCT03128164)

Our Phase I/Ib study of HMPL-689 in China has successfully established a Phase II dose and has now expanded into multiple sub-categories of indolent non-Hodgkin's lymphoma.

In December 2020, we presented preliminary results from a Phase I dose escalation study of HMPL-689 in Chinese patients with relapsed/refractory lymphoma at the American Society of Hematology (ASH) Annual Meeting. A total of 56 patients were enrolled resulting in an ORR of 51.9% (27/52) and complete response rate of 11.5% (6/52) in efficacy evaluable patients. The median time to response and duration of response were 1.8 months (1.8-1.9) and 9.2 months (3.9-NR), respectively. One patient with follicular lymphoma who achieved complete response (per post hoc independent radiologic

review) was on treatment for over 19 months. In the nine efficacy evaluable patients treated with the RP2D of 30mg QD orally, efficacy was encouraging with an ORR of 100% (4/4) in follicular lymphoma, 100% in marginal zone lymphoma (2/2) and 67% (2/3) in diffuse large B-cell lymphoma.

Phase 1 Dose Escalation Study: Promising HMPL-689 Single-agent Clinical Activity in Relapsed/refractory B-cell Symphoma Patients



Intent-to-treat population (n=56)	
Best Response	
Complete Response, %	11 (4-22)
Partial Response, %	37
Stable Disease, %	34
Progressive Disease, %	11
Overall Response Rate	48% (35-62)
Clinical Benefit Rate	82% (70-91)
Time on Treatment	5.6 months (0.7–23.2)
Time to Response	1.8 months (1.8–1.9)
Duration of Response	9.2 months (3.9–NR)
Progression Free Survival	10.1 months (5.5–15.7)
1-year PFS rate	40% (27–57)

Notes: CLL = chronic lymphocytic leukemia; SLL = small lymphocytic lymphoma; DLBCL = diffuse large B-cell lymphoma; FL = follicular lymphoma; HL = Hodgkin's lymphoma; MCL = mantle cell lymphoma; MZL = marginal zone lymphoma; BID = twice daily; QD = once daily; PR = partial response; n = number of patients; PFS = progression-free survival; and NA = not available.

Source: Cao JN, et al. "Results from a Phase 1 Dose Escalation Study of HMPL-689, a Selective Oral Phosphoinositide 3-Kinase-Delta Inhibitor, in Chinese Patients with relapsed/refractory (R/R) Lymphoma" Presented at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition on December 5, 2020. Abstract #1135.

HMPL-689 was well tolerated at the RP2D exhibiting dose-proportional pharmacokinetics and a manageable toxicity profile. Grade 3 or more non-hematologic TEAEs occurring in more than two patients were pneumonia, rash, hypertension, and increased lipase. Grade 3 or more hematologic TEAEs occurring in more than two patients were neutropenia, and no Grade 5 TEAEs were reported.

The Phase Ib dose expansion study in China is ongoing in multiple sub-categories of indolent non-Hodgkin's lymphoma.

Phase II registration-intent study of HMPL-689 in patients with relapsed/refractory follicular lymphoma and relapsed/refractory marginal zone lymphoma (Status: enrolling; NCT04849351)

In April 2021, we commenced a registration-intent Phase II trial of HMPL-689 in China in patients with relapsed or refractory follicular lymphoma and marginal zone lymphoma, two subtypes of non-Hodgkin's lymphoma. The clinical trial is a multi-center, single-arm, open-label clinical study to evaluate the efficacy and safety of HMPL-689 once a day oral monotherapy in approximately 100 patients with relapsed/refractory follicular lymphoma and approximately 80 patients with relapsed/refractory marginal zone lymphoma. Relapsed/refractory is defined when a patient has not achieved response (complete response or partial response) after the latest line of systemic treatment, or has progressive disease or relapse after achieving response. The primary endpoint is ORR, with secondary endpoints including CR rate, PFS, TTR and DoR. The trial is being conducted in over 35 sites in China. The initiation of the Phase II trial is based on the highly promising preliminary results from the Phase Ib expansion study ongoing in China, which has shown thus far that HMPL-689 was well tolerated, exhibiting dose-proportional pharmacokinetics, a manageable toxicity profile, and single-agent clinical activity in relapsed/refractory B-cell lymphoma patients.

Phase I/Ib study of HMPL-689 in patients with Indolent non-Hodgkin's lymphoma (Status: enrolling; NCT03786926)

In August 2019, we initiated an international Phase I/Ib study of HMPL-689 in patients with relapsed or refractory lymphoma. The international clinical study, with 17 sites in the United States and

Europe, is a multi-center, open-label, two-stage study, including dose escalation and expansion, investigating the effects of HMPL-689 administered orally to patients with relapsed or refractory lymphoma. The primary outcome measures are safety and tolerability. Secondary outcomes include pharmacokinetic measurements and preliminary efficacy such as ORR. Dose escalation is near complete and we expect to be able to engage with regulatory authorities in the second half of 2021 to discuss potential registration pathways.

5. HMPL-523 Syk Inhibitor

The result of our over six-year program of discovery and pre-clinical work against Syk is HMPL-523, a highly selective Syk inhibitor with a unique pharmacokinetic profile which provides for higher drug exposure in the tissue than on a whole blood level. We designed HMPL-523 intentionally to have high tissue distribution because it is in the tissue that the B-cell activation associated with rheumatoid arthritis and lupus occurs most often. Furthermore, and somewhat counter intuitively, in hematological cancer the vast majority of cancer cells nest in tissue, with a small proportion of cancer cells releasing and circulating in the blood where they cannot survive for long. We assessed that an effective small molecule Syk inhibitor would need to have superior tissue distribution.

However, many pharmaceutical and biotechnology companies had experienced difficulties in developing a safe and efficacious Syk-targeted drug. For example, the development of the Syk inhibitor Tavalisse for rheumatoid arthritis was one such failed program, although clear efficacy was observed in Phase II and Phase III trials. The main problem was off-target toxicities associated with poor kinase selectivity, such as hypertension and severe diarrhea. Therefore, we believe that kinase selectivity is critical to a successful Syk inhibitor. In addition, Tavalisse was designed as a prodrug in order to improve solubility and oral absorption. A prodrug is medication administered in a pharmacologically inactive form which is converted to an active form once absorbed into circulation. The rate of the metabolism required to release the active form can vary from patient to patient, resulting in large variation in active drug exposures that can impact efficacy. In addition to convenient oral dosing, we believe HMPL-523 offers important advantages over intravenous monoclonal antibody immune modulators in rheumatoid arthritis in that small molecule compounds generally clear the system faster, thereby reducing the risk of infections from sustained suppression of the immune system.

Mechanism of Action

Syk is a key kinase upstream to PI3Kδ and BTK within the B-cell signaling pathway and therefore thought to be an important target for modulating B-cell signaling.

Syk, a target for autoimmune diseases

The central role of Syk in signaling processes is not only in cells of immune responses but also in cell types known to be involved in the expression of tissue pathology in autoimmune, inflammatory and allergic diseases. Therefore, interfering with Syk could represent a possible therapeutic approach for treating these disorders. Indeed, several studies have highlighted Syk as a key player in the pathogenesis of a multitude of diseases, including rheumatoid arthritis, systemic lupus erythematosus and multiple sclerosis.

Syk, a target for oncology

In hematological cancer, we believe Syk is a high potential target. In hematopoietic cells, Syk is recruited to the intracellular membrane by activated membrane receptors like B-cell receptors or another receptor called Fc and then binds to the intracellular domain of the receptors. Syk is activated after being phosphorylated by certain kinases and then further induces downstream intracellular signals including B-cell linker, PI3Kδ, BTK and Phospholipase C-y2 to regulate B-cell proliferation, growth, differentiation, homing, survival, maturation, and immune responses. Syk not only involves the regulation of lymphatic cells but also signal transduction of non-lymphatic cells such as mast cells, macrophages, and basophils, resulting in different immunological functions such as degranulation to release immune

active substances, leading to immunological reaction and disease. Therefore, regulating B-cell signal pathways through Syk is expected to be effective for treating lymphoma.

Syk is upstream of both BTK and PI3Kδ, and we believe it could deliver the same outcome as inhibitors of BTK and PI3Kδ, assuming no unintentional toxicities are derived from Syk inhibition. Entospletinib, a Syk inhibitor developed by Gilead (now under the ownership of Kronos Bio), reported promising Phase II study results in late 2015 with a nodal response rate of 65% observed in chronic lymphocytic leukemia and small lymphocytic lymphoma. Nodal response is defined as a greater than 50% decrease from baseline in the sum of lymph node diameters. Gilead has also reported that entospletinib demonstrated a nodal response rate of 44% in an exploratory clinical study in chronic lymphocytic leukemia patients previously treated with Imbruvica and Zydelig, thereby indicating that Syk inhibition has the potential to overcome resistance to Imbruvica and Zydelig.

See "*Industry Overview – Overview of Molecular Targets and Market Landscape – Syk and PI3K*δ*/ B-cell signaling Pathways – Overview of Syk Inhibitors*" for more details.

HMPL-523 Research Background

The threshold of safety for a Syk inhibitor in chronic disease is extremely high, with no room for material toxicity. The failure of Tavalisse in a global Phase III registration study in rheumatoid arthritis provided important insights for us in the area of toxicity. While Tavalisse clearly showed patient benefit in rheumatoid arthritis, a critical proof-of-concept for Syk modulation, it also caused high levels of hypertension which is widely believed to be due to the high levels of off-target kinase insert domain receptor inhibition. In addition, Tavalisse has also been shown to strongly inhibit the Ret kinase, and in pre-clinical trials it was demonstrated that inhibition of the Ret kinase was associated with developmental and reproductive toxicities.

The requirement for Syk kinase activity in inflammatory responses was first evaluated with Tavalisse, which was co-developed by AstraZeneca/Rigel Pharmaceuticals, Inc. In 2013, AstraZeneca announced results from pivotal Phase III clinical trials that Tavalisse statistically significantly improved ACR20 (a 20% improvement from baseline based on the study criteria) response rates of patients inadequately responding to conventional disease-modifying anti-rheumatic drugs and a single anti-TNFα (a key pro-inflammatory cytokine involved in rheumatoid arthritis pathogenesis) antagonist at 24 weeks, but failed to demonstrate statistical significance in comparison to placebo at 24 weeks. As a result, AstraZeneca decided not to proceed. Rigel Pharmaceuticals subsequently chose to develop Tavalisse for immune thrombocytopenia instead, for which it was approved by the FDA in 2018 and the EMA in 2020.

Tavalisse was also in trials for B-cell lymphoma and T-cell lymphoma. It demonstrated some clinical efficacy in diffused large B-cell lymphoma patients with an ORR of 22%. Entospletinib has features of high potency and good selectivity toward kinases. However, while the Phase II study discussed above showed that it had significant efficacy in patients with chronic lymphocytic leukemia and small lymphocytic lymphoma, its poor solubility and permeability into intestinal epithelial cells resulted in unsatisfactory oral absorption and a great variation of individual drug exposure. In addition, entospletinib shows some inhibition of the CYP3A4, CYP2D6, and CYP1A2 enzymes involved in the metabolism of certain drugs, and therefore their inhibition could increase the risk of drug-to-drug interaction when used in combined therapy.

HMPL-523 Pre-clinical Evidence

The safety profile of HMPL-523 was evaluated in multiple in vitro and in vivo pre-clinical trials under good laboratory practice guidelines and found to be well tolerated following single dose oral administration. Toxic findings were seen in repeat dose animal safety evaluations in rats and dogs at higher doses and found to be reversible. These findings can be readily monitored in the clinical trials and fully recoverable upon drug withdrawal. The starting dose in humans was suggested to be 5 mg. This dose level is approximately 5% of the human equivalent dose extrapolated from the pre-clinical "no observed adverse event levels," which is below the 10% threshold recommended by FDA guidelines.

HMPL-523 Clinical Trials

As discussed below, we currently have various clinical trials of HMPL-523 ongoing in Australia, the United States, Europe and China as a monotherapy. The table below shows a summary of the clinical trials that we have underway for HMPL-523.

Current Clinical Trials of HMPL-523

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
HMPL-523 monotherapy	HUTCHMED	Immune thrombocytopenia purpura	China (10)	I/Ib	Ongoing. Supports initiation of Phase III in 2H21	NCT03951623
HMPL-523 monotherapy	HUTCHMED	Indolent non-Hodgkin's lymphoma	Australia (12)	Ib	Active, not recruiting.	NCT02503033
HMPL-523 monotherapy	HUTCHMED	Indolent non-Hodgkin's lymphoma	U.S./ Europe (22)	I/Ib	Ongoing. First patient dosed in Sept 2019.	NCT03779113
HMPL-523 monotherapy	HUTCHMED	Multiple sub-types of B-cell malignancies	China (18)	I/Ib	Enrollment completed	NCT02857998

Notes:

(1) Expected maximum number of sites.

Phase I/Ib study of HMPL-523 in patients with immune thrombocytopenia (Status: ongoing)

In mid-2019, we initiated a Phase I study of HMPL-523 in patients with immune thrombocytopenia purpura. Immune thrombocytopenia purpura is an autoimmune disorder characterized by low platelet count and an increased bleeding risk. Despite availability of several treatments with differing mechanisms of action, a significant proportion of patients develop resistance to treatment and are prone to relapse. In addition, there is a significant population of patients who have limited sensitivity to currently available agents and are in need of a new approach to treatment.

The study is a randomized, double-blinded, placebo-controlled Phase Ib clinical trial investigating the safety, tolerability, pharmacokinetics and preliminary efficacy of HMPL-523 in adult patients with immune thrombocytopenia purpura. The primary endpoint is the number of patients with any adverse event. The secondary endpoints are maximum plasma concentration, area under the concentration-time curve in a selected time interval, and rate of clinical remission at week eighty. The trial is comprised of a dose escalation stage and a dose expansion stage. Approximately 50 to 60 patients are expected to be enrolled. Dose escalation is near complete with planning and preparation for a Phase III trial in China now underway.

Phase Ib studies of HMPL-523 in indolent non-Hodgkin's lymphoma and multiple subtypes of B-cell malignancies (Status: enrolling; NCT02503033/NCT02857998)

In early 2016, we initiated a Phase I dose escalation study of HMPL-523 in Australia and have completed seven dose cohorts. A Phase I study in China began in early 2017 and has now completed five dose cohorts. In both Australia and China, we have established both efficacious once daily and twice daily dose regimens. Our Phase I/Ib dose escalation and expansion studies in Australia and China have now enrolled over 200 patients in a broad range of hematological cancers and have identified indications of interest for future development.

Phase I/Ib study of HMPL-523 in indolent non-Hodgkin's lymphoma (Status: enrolling; NCT03779113)

Based on extensive proof-of-concept clinical data in China and Australia, we have initiated a Phase I/Ib study in the United States and Europe. Patient enrollment is underway in 11 sites, multiple dose cohorts have been completed already and we are close to establishing our Phase II dose.

6. HMPL-453 FGFR Inhibitor

Mechanism of Action

FGFR belongs to a subfamily of receptor tyrosine kinases. Four different FGFRs (FGFR1-4) and at least 18 ligand FGFs constitute the FGF/FGFR signaling system. Activation of the FGFR pathway through the phosphorylation of various downstream molecules ultimately leads to increased cell proliferation, migration and survival. FGF/FGFR signaling regulates a wide range of basic biological processes, including tissue development, angiogenesis, and tissue regeneration. Given the inherent complexity and critical roles in physiological processes, dysfunction in the FGF/FGFR signaling leads to a number of developmental disorders and is consistently found to be a driving force in cancer. Deregulation of the FGFR can take many forms, including receptor amplification, activating mutations, gene fusions, and receptor isoform switching, and the molecular alterations are found at relatively low frequencies in most tumors. The incidence of FGFR aberrance in various cancer types is listed in the table below.

Common FGFR Alterations in Certain Tumor Types

	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 (5-10%)	Intra-hepatic biliary tract cancer (14%) Breast (n/a)	Endometrial (12-14%) Lung squamous (5%)
FGFR3	Bladder (3%) Salivary adenoid cystic (n/a) Breast (1%)	Bladder (3-6%) Lung squamous (3%) Glioblastoma (3-7%) Myeloma (15-20%)	Bladder (60-80% NMIBC; 15-20% MIBC) Cervical (5%)

Notes: H&N = head and neck; NMIBC = non-muscle invasive bladder cancer; MIBC = muscle invasive bladder cancer; and n/a = data not available.

Source: M. Touat et al., "Targeting FGFR Signaling in Cancer," Clinical Cancer Research (2015); 21(12); 2684-94.

See "Industry Overview – Overview of Molecular Targets and Market Landscape – FGFR Pathways – Overview of FGFR Inhibitors" for more details.

HMPL-453 Research Background

We noted a growing body of evidence has demonstrated the oncogenic potential of FGFR aberrations in driving tumor growth, promoting angiogenesis, and conferring resistance mechanisms to oncology therapies. Targeting the FGF/FGFR signaling pathway has therefore attracted attention from biopharmaceutical companies and has become an important exploratory target for new anti-tumor target therapies.

The main FGFR on-target toxicities observed to date in these compounds are all mild and manageable, including hyperphosphatemia, nail and mucosal disorder, and reversible retinal pigmented epithelial detachment. However, there are still many challenges in the development of FGFR-directed therapies. Uncertainties include the screening and stratifying of patients who are most likely to benefit from FGFR targeted therapy. Intra-tumor heterogeneity observed in FGFR amplified cancer may compromise the anti-tumor activity. In addition, the low frequency of specific FGFR molecular aberrance in each cancer type may hinder clinical trial enrollment.

HMPL-453 Pre-clinical Evidence

HMPL-453 is a highly selective and potent, small molecule that targets FGFR 1/2/3 with an IC_{50} in the low nanomolar range. Its good selectivity was revealed in the screening against 292 kinases. HMPL-453 exhibited strong anti-tumor activity that correlated with target inhibition in tumor models with abnormal FGFR activation.

HMPL-453 has good pharmacokinetic properties characterized by rapid absorption following oral dosing, good bioavailability, moderate tissue distribution and moderate clearance in all pre-clinical animal species. HMPL-453 was found to have little inhibitory effect on major cytochrome P450 enzymes, indicating low likelihood of drug-to-drug interaction issues.

HMPL-453 Clinical Development

The table below shows a summary of the clinical trials that we have recently completed and underway for HMPL-453.

Clinical Trials of HMPL-453

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
HMPL-453 monotherapy	HUTCHMED	Solid tumors	China (2)	I	Enrollment completed	NCT03160833
HMPL-453 monotherapy	HUTCHMED	Cholangiocarcinoma (IHCC)	China (15)	II	Ongoing. First patient dosed Sept 2020.	NCT04353375

Notes:

(1) Expected maximum number of sites.

Phase I HMPL-453 monotherapy in solid tumors – China (Status: enrollment completed; NCT03160833)

In June 2017, we initiated a Phase I clinical trial of HMPL-453 in China. This Phase I study is a multi-center, single-arm, open-label, two-stage study to evaluate safety, tolerability, pharmacokinetics and preliminary efficacy of HMPL-453 monotherapy in patients with solid tumors harboring FGFR genetic alterations. The dose-escalation stage is currently enrolling patients to further evaluate safety, tolerability and pharmacokinetics as well as preliminary anti-tumor efficacy at the RP2D. This stage will enroll primarily cancer patients harboring FGFR dysregulated tumors, including those with advanced bladder cancer, advanced cholangiocarcinoma and other solid tumors. For this second stage, the primary endpoint is ORR, with secondary endpoints including duration of response, disease control rate, PFS, OS and safety.

Phase II HMPL-453 monotherapy in advanced intrahepatic cholangiocarcinoma – China (Status: ongoing; NCT04353375)

In September 2020, we initiated a Phase II, single-arm, multi-center, open-label study, evaluating the efficacy, safety and pharmacokinetics of HMPL-453 in patients with advanced intrahepatic cholangiocarcinoma with FGFR2 fusion that had failed at least one line of systemic therapy. IHCC is a cancer that develops within the bile ducts, the second most common primary hepatic malignancy after hepatocellular carcinoma. Approximately 10-15% of IHCC patients have tumors that harbor FGFR2 fusion.

7. HMPL-306

HMPL-306 is a novel small molecule dual-inhibitor of IDH1 and 2 enzymes. IDH1 and IDH2 mutations have been implicated as drivers of certain hematological malignancies, gliomas and solid tumors, particularly among acute myeloid leukemia patients.

Mechanism of Action

IDHs are critical metabolic enzymes that help to break down nutrients and generate energy for cells. When mutated, IDH creates a molecule that alters the cell's genetic programming and prevents cells from maturing, 2-hydroxyglutarate ("2-HG"). Reduction in 2-HG levels can be used as a marker of target engagement by an IDH inhibitor. IDH1 or IDH2 mutations are common genetic alterations in various types of blood and solid tumors, including acute myeloid leukemia, with approximately 20% of patients having mutant IDH genes, myelodysplastic syndrome (MDS), myeloproliferative neoplasms (MPNs), low-grade glioma and intrahepatic cholangiocarcinoma. Mutant IDH isoform switching, either from cytoplasmic mutant IDH1 to mitochondrial mutant IDH2, or vice versa, is a mechanism of acquired resistance to IDH inhibition in acute myeloid leukemia and cholangiocarcinoma.

Cytoplasmic mutant IDH1 and mitochondrial mutant IDH2 have been known to switch to the other form when targeted by an inhibitor of IDH1 mutant alone or IDH2 mutant alone. By targeting both IDH1 and IDH2 mutations, HMPL-306 could potentially provide therapeutic benefits in cancer patients harboring either IDH mutation and may address acquired resistance to IDH inhibition through isoform switching.

Currently, the FDA has approved one drug for IDH1 mutation and one drug for IDH2 mutation, but no dual inhibitor targeting both IDH1 and IDH2 mutants has been approved.

See "*Industry Overview – Overview of Molecular Targets and Market Landscape – IDH – Overview of IDH1 and IDH2 Inhibition*" for more details.

HMPL-306 Clinical Trials

The table below shows a summary of the clinical trials that we have recently underway or in planning for HMPL-306.

Clinical Trials of HMPL-306

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
HMPL-306 monotherapy	HUTCHMED	Hematological malignancies	China (5)	I	Ongoing. First patient dosed in July 2020.	NCT04272957
HMPL-306 monotherapy	HUTCHMED	Solid tumors	U.S./ Europe (15)	I	Ongoing. First patient dosed in March 2021.	NCT04762602
HMPL-306 monotherapy	HUTCHMED	Hematological malignancies	U.S./ Europe (15)	I	Ongoing. First patient dosed in May 2021.	NCT04764474

Phase I HMPL-306 monotherapy – China (Status: ongoing; NCT04272957)

In July 2020, we initiated our Phase I development in China. This is a multi-center study to evaluate the safety, pharmacokinetics, pharmacodynamics and efficacy of HMPL-306 in patients of relapsed or refractory hematological malignancies with an IDH1 and/or IDH2 mutation. Multiple sites have been initiated and we anticipate to be able to establish the Phase II dose during 2021.

Phase I HMPL-306 monotherapy in solid tumors – U.S. and Europe (Status: ongoing; NCT04762602)

In March 2021, we initiated our Phase I development in the United States and Europe. This is a multi-center study to evaluate the safety, tolerability pharmacokinetics, pharmacodynamics and preliminary efficacy of HMPL-306 in solid tumors, including but not limited to gliomas, chondrosarcomas or cholangiocarcinomas.

Phase I HMPL-306 monotherapy in hematological malignancies – U.S. and Europe (Status: ongoing; NCT04764474)

In the United States, IND applications for solid tumors and hematologic malignancies were cleared in October 2020. In May 2021, we dosed the first patient with IDHm+ hematological malignancies.

8. HMPL-295

HMPL-295, a novel ERK inhibitor, is our tenth in-house discovered small molecule oncology drug candidate. ERK is a downstream component of the RAS-RAF-MEK-ERK signaling cascade (MAPK pathway). This is our first of multiple candidates in discovery addressing the MAPK pathway.

Mechanism of Action

RAS-MAPK pathway is dysregulated in human diseases, particularly cancer, in which mutations or nongenetic events hyperactivate the pathway in more than 50% of cancers. Activating mutations in RAS genes occur in more than 30% of cancers. RAS and RAF predict worse clinical prognosis in a wide variety of tumor types, mediate resistance to targeted therapies, and decrease the response to the approved standards of care, namely, targeted therapy and immunotherapy. On the MAPK pathway, KRAS inhibitors are under clinical evaluation, and acquired resistance develops for RAF/MEK targeted therapies. ERK inhibition has the potential to overcome or avoid the intrinsic or acquired resistance from upstream mechanisms such as these.

See "*Industry Overview – Overview of Molecular Targets and Market Landscape – ERK – Overview of ERK Inhibitions*" for more details.

HMPL-295 Clinical Trials

The table below shows a summary of the clinical trials that we have recently underway or in planning for HMPL-295.

Clinical Trial of HMPL-295

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
HMPL-295 monotherapy	HUTCHMED	Solid tumors	China (5)	Ib/II	In planning. Intend to initiate in mid-2021	N/A

Note:

(1) Expected maximum number of sites.

We currently retain all rights to HMPL-295 worldwide. The IND was cleared in China in late 2020. Planning for the Phase I study in China is now underway and set to start in mid-2021.

9. Epitinib EGFR Inhibitor

Mechanism of Action

Epitinib (also known as HMPL-813) is a potent and highly selective oral EGFR inhibitor designed to optimize brain penetration. A significant portion of patients with EGFR activating mutations go on to develop brain metastasis. Patients with brain metastasis suffer from poor prognosis and low quality of life with limited treatment options. EGFR inhibitors have revolutionized the treatment of NSCLC with EGFR activating mutations. However, many approved EGFR inhibitors such as Iressa and Tarceva cannot penetrate the blood-brain barrier effectively, leaving the majority of patients with primary brain tumors or brain metastasis without an effective targeted therapy.

Our strategy has been to create targeted therapies in the EGFR area that would go beyond the already approved EGFRm+ patient population to address certain areas of unmet medical needs that represent market opportunities, including: (i) brain metastasis and/or primary brain tumors with EGFRm+, which we seek to address with epitinib; and (ii) tumors with EGFR gene amplification or EGFR overexpressed.

See "*Industry Overview – Overview of Molecular Targets and Market Landscape – EGFR Pathway – Overview of EGFR Inhibitors*" for more details.

Epitinib Pre-clinical Evidence

Pre-clinical trials and orthotopic brain tumor models have shown that epitinib demonstrated brain penetration and efficacy superior to that of certain globally marketed EGFRm+ inhibitors such as Iressa and Tarceva. In orthotopic brain tumor models, epitinib demonstrated good brain penetration, efficacy and pharmacokinetic properties as well as a favorable safety profile.

Epitinib Clinical Development

The table below shows a summary of the clinical trial that is underway for epitinib.

Clinical Trial of Epitinib

Treatment	Sponsors/Partners	Name, Line, Patient Focus	Sites[(1)]	Phase	Status/Plan	NCT #
Epitinib monotherapy	HUTCHMED	Glioblastoma	China (2)	Ib/II	Enrolling. First patient dosed in March 2018	NCT03231501

Note:

(1) Expected maximum number of sites.

Phase Ib/II epitinib monotherapy in glioblastoma (Status: enrolling; NCT03231501)

Glioblastoma is the most aggressive of the gliomas, which are tumors that arise from glial cells or their precursors within the central nervous system. Glioblastoma is classified as grade IV under the World Health Organization grading of central nervous system tumors, and is the most common brain and central nervous system malignancy, accounting for about half of such tumors according to the Cancer Genome Atlas Research Network. The standard of care for treatment is surgery, followed by radiotherapy and chemotherapy. Median survival is approximately 15 months, and the five-year OS rate is 6%. There are currently no target therapies approved for glioblastoma.

Epitinib is a highly differentiated EGFR inhibitor designed for optimal blood-brain barrier penetration. EGFR gene amplification has been identified in about half of glioblastoma patients, according to The Cancer Genome Atlas Research Network, and hence is a potential therapeutic target in glioblastoma.

In March 2018, we initiated a Phase Ib/II proof-of-concept study of epitinib in glioblastoma patients with EGFR gene amplification in China. This Phase Ib/II study is a multi-center, single-arm, open-label study to evaluate the efficacy and safety of epitinib as a monotherapy in patients with EGFR gene amplified, histologically confirmed glioblastoma.

10. Theliatinib EGFR Inhibitor

Like epitinib, theliatinib (also known as HMPL-309) is a novel small molecule EGFR inhibitor. Tumors with wild-type EGFR activation, for instance, through gene amplification or protein over-expression, are less sensitive to current EGFR tyrosine kinase inhibitors such as Iressa and Tarceva due to sub-optimal binding affinity. Theliatinib has been designed with strong affinity to the wild-type EGFR kinase and has demonstrated five to ten times the potency than Tarceva in pre-clinical trials. This holds importance because tumors with wild-type EGFR activation have been found to be less sensitive to current EGFR inhibitors and is notable in certain cancer types such as esophageal cancer, where 15-28% have EGFR gene amplification and 50-70% have EGFR overexpressed. As a result, we believe that theliatinib could potentially be more effective than existing EGFR tyrosine kinase inhibitor products and benefit patients with tumor types with a high incidence of wild-type EGFR activation. We currently retain all rights to theliatinib worldwide. Phase I/Ib studies of theliatinib have been completed, and we are evaluating further development strategies.

Theliatinib Pre-clinical Evidence

EGFR is overexpressed in a significant proportion of epithelium-derived carcinomas, which are cancers that begin in a tissue that lines the inner or outer surfaces of the body. Theliatinib inhibits the epidermal growth factor-dependent proliferation of cells at nanomolar concentrations. Of most interest is the strong binding affinity to wild-type EGFR enzyme demonstrated by theliatinib. The data indicated that upon withdrawal of the drug, the EGFR phosphorylation rapidly returned to higher levels for Iressa and Tarceva, while EGFR phosphorylation remained low for theliatinib after drug withdrawal, suggesting theliatinib may demonstrate a sustained target occupancy or "slow-off" characteristic due to strong binding.

Theliatinib Clinical Development

Results showed that doses up to 500 mg once daily were determined to be safe and well-tolerated, with no dose-limiting toxicities and no clear maximum tolerated dose. Pharmacokinetic exposure increased with dose, with a 300 mg once daily or more considered to be sufficient to inhibit EGFR phosphorylation. Among the 21 patients that received 120 mg to 500 mg once daily, there were only four treatment-emergent adverse events of grade >3: gastrointestinal bleeding, decreased white blood cell count, anemia or decreased platelet count (1/21 = 5% each). There were no incidences of grade >3 rash or diarrhea. Among seven esophageal cancer patients, five had measurable lesions and could be evaluated for response. All five had stable disease. Of the efficacy evaluable patients in the 120 mg to 500 mg cohorts, 44% (8/18) had stable disease after 12 weeks.

Although we observed efficacy, primarily in the form of stable disease or short duration response, we have decided that it does not warrant continued development of theliatinib monotherapy in esophageal cancer at this time.

OUR RESEARCH AND DEVELOPMENT APPROACH

Our core research and development philosophy is to take a holistic approach to the treatment of cancer and immunological diseases, through multiple modalities and mechanisms, including targeted therapies, immunotherapies and other pathways. A primary objective of our research efforts has been to develop next generation drug candidates with:

- unique selectivity to limit target-based toxicity;
- high potency to optimize the dose selection with the objective to lower the required dose and thereby limit compound-based toxicity;
- chemical structures deliberately engineered to improve drug exposure in the targeted tissue; and
- ability to be combined with other therapeutic agents, including targeted therapies, immunotherapies and chemotherapies.

We have built a drug discovery engine, with which we strive to create differentiated novel oncology and immunology treatments with global potential. These include furthering both small molecule and biologic therapies which address aberrant genetic drivers and cancer cell metabolism; modulate tumor immune microenvironment; and target immune cell checkpoints. We design drug candidates with profiles that enable them to be used in innovative combinations with other therapies, such as chemotherapy, immunotherapy and other targeted therapy in order to attack disease simultaneously through multiple modalities and pathways. We believe that this approach can significantly improve treatment outcomes for patients.

We believe our ability to successfully develop innovative drug candidates through our Oncology/Immunology operations will be the primary factor affecting our long-term competitiveness, as well as our future growth and development. Creating high quality global first-in-class or best-in-class drug candidates requires a significant investment of resources over a prolonged period of time, and a core part

of our strategy is to continue making sustained investments in this area. As a result of this commitment, our pipeline of drug candidates has been steadily advancing and expanding, with ten clinical-stage drug candidates, seven of which are either in or about to start clinical development. See "– *Our Clinical Pipeline*" for more details.

In addition, we have three more novel oncology drug candidates in preclinical stage. We retain all global rights to these three drug candidates and are targeting dual U.S. and China IND submissions for some of them during 2021. We have also partnered with Inmagene to further develop four novel immunological disease drug candidates that we discovered and are in preclinical stage.

Beyond these clinical and preclinical stage candidates, we continue to conduct research into discovering new types of drug candidates, including among others, small molecules addressing cancer-related apoptosis, cell signaling, epigenetics and protein translation; biologic drug candidates including bispecific antibodies; and novel technologies including antibody-drug conjugates and heterobifunctional small molecules.

We have incurred and will continue to incur significant research and development costs for pre-clinical studies and clinical trials as all of the drug candidates of our Oncology/Immunology operations, other than fruquintinib and surufatinib, are still in development. We expect that our research and development expenses will significantly increase in future periods in line with the advance and expansion of the development of our drug candidates, including fruquintinib and surufatinib.

We and our collaboration partners have invested over US$970 million in our Oncology/Immunology operations as of December 31, 2020, with almost all of these funds used for research and development expenses for the development of our drug candidates. Oncology/Immunology expenses include:

- employee compensation related expenses, including salaries, benefits and equity compensation expense;
- expenses incurred for payments to CROs, investigators and clinical trial sites that conduct our clinical trials;
- the cost of acquiring, developing, and manufacturing clinical study materials;
- facilities, depreciation and other expenses, which include office leases and other overhead expenses; and
- costs associated with pre-clinical activities and regulatory operations.

As of the Latest Practicable Date, our Oncology/Immunology operations had approximately 680 scientists and staff, including 32 M.D.s and 82 doctorate degrees. We staff our research and development teams for each project based on employees' experience, education, and availability. Our research and development team operates primarily in two major facilities in Shanghai, totaling approximately 11,000 square meters, a formulation facility in Suzhou as well as our office in New Jersey.

OVERVIEW OF OUR COLLABORATIONS

Collaborations and joint ventures with corporate partners have provided us with significant funding and access to our partners' scientific, development, regulatory and commercial capabilities. Our current oncology collaborations focus on savolitinib (collaboration with AstraZeneca) and fruquintinib (collaboration with Eli Lilly). When we entered into these collaborations, we had already conducted the discovery research and early clinical development of each drug candidate and, following our agreements, continued to conduct the clinical development and manage the engagement with regulatory authorities in China up to and including filing the NDAs with the NMPA. Our collaboration partners fund a significant portion of our research and development costs for drug candidates developed in collaboration with them. In addition, we receive upfront payments upon our entry into these collaboration arrangements and upon the achievement of certain development milestones for the relevant drug candidate. We have received upfront payments, equity contributions and milestone payments totaling

approximately US$158.5 million mainly from our collaborations with AstraZeneca and Eli Lilly as of December 31, 2020. In return, our collaboration partners are entitled to a significant proportion of any future revenue from our drug candidates developed in collaboration with them, as well as a degree of influence over the clinical development process for such drug candidates. In addition, we have entered into other clinical collaborations for combination studies of fruquintinib and surufatinib with drug candidates belonging to BeiGene, Innovent and Junshi. We also have an immunology collaboration with Inmagene.

AstraZeneca

In 2008, our in-house teams started research on MET inhibitors, subsequently discovering our drug candidate, savolitinib, and conducting its pre-clinical development in-house. In 2011, we submitted applications for clinical development and initiated Phase I clinical trials. In December 2011, we entered into an agreement with AstraZeneca under which we granted to AstraZeneca co-exclusive, worldwide rights to develop, and exclusive worldwide rights to manufacture and commercialize savolitinib for all diagnostic, prophylactic and therapeutic uses. In August 2016 and December 2020, we and AstraZeneca amended the terms of the agreement. We refer to this agreement, including the amendments thereto, as the AstraZeneca Agreement.

AstraZeneca paid US$20.0 million upon execution of the AstraZeneca Agreement and agreed to pay royalties and additional amounts upon the achievement of development and sales milestones. Under the original terms of the AstraZeneca Agreement, we and AstraZeneca agreed to share the development costs for savolitinib in China, with AstraZeneca being responsible for the development costs for savolitinib in the rest of the world. With respect to global pivotal Phase III development in patients with MET-driven PRCC, we subsequently agreed to contribute up to US$50 million and to share any additional costs equally with AstraZeneca. As of December 31, 2020, we had received US$24.9 million in milestone payments in addition to approximately US$44.4 million in reimbursements for certain development costs. We may potentially receive future clinical development and first sales milestones payments for clinical development and initial sales of savolitinib, plus significant further milestone payments based on sales. AstraZeneca also reimburses us for certain development costs. Subject to approval of savolitinib in PRCC, under the AstraZeneca Agreement, AstraZeneca is obligated to pay us increased tiered royalties from 14% to 18% annually on all sales made of any product outside of China, which represents a five percentage point increase over the original terms, subject to a potential downward adjustment on such point increase based on the amount of any contribution by AstraZeneca to the Phase III development in patients with such indication. After total aggregate additional royalties have reached five times our contribution to the Phase III development in patients with such indication, this royalty will step down over a two-year period, to an ongoing royalty rate of 10.5% to 14.5%. AstraZeneca is also obligated to pay us a fixed royalty of 30% on all sales made of any product in China.

Development and collaboration under this agreement are overseen by a joint steering committee that is comprised of three of our senior representatives as well as three senior representatives from AstraZeneca. AstraZeneca is responsible for the development of savolitinib and all regulatory matters related to this agreement in all countries and territories other than China, and we are responsible for the development of savolitinib and all regulatory matters related to this agreement in China. Since entering this Agreement, we have continued to lead the development of savolitinib in China.

Subject to earlier termination, the AstraZeneca Agreement will continue in full force and effect on a country-by-country basis as long as any collaboration product is being developed or commercialized. The AstraZeneca Agreement is terminable by either party upon a breach that is uncured, upon the occurrence of bankruptcy or insolvency of either party, or by mutual agreement of the parties. The AstraZeneca Agreement may also be terminated by AstraZeneca for convenience with 180 days' prior written notice. Termination for cause by us or AstraZeneca or for convenience by AstraZeneca will have the effect of, among other things, terminating the applicable licenses granted by us. Termination for convenience by AstraZeneca will have the effect of obligating AstraZeneca to grant to us all of its rights

to regulatory approvals and other rights necessary to commercialize savolitinib. Termination by AstraZeneca for convenience will not have the effect of terminating any license granted by AstraZeneca to us.

Eli Lilly

In 2007, our in-house research into VEGFR inhibitors led to the discovery of our drug candidate, fruquintinib. We conducted pre-clinical development in-house and initiated a Phase I clinical trial in 2010. In October 2013, we entered into an agreement with Eli Lilly whereby we granted Eli Lilly an exclusive license to develop, manufacture and commercialize fruquintinib for all uses in China and Hong Kong. In December 2018, following the commercial launch of fruquintinib in China, we and Eli Lilly amended the terms of the agreement and further amended the terms of the agreement in July 2020. We refer to this agreement, including the amendments thereto, as the Eli Lilly Agreement.

Subsequent to the entering of the Eli Lilly Agreement, the Company continued to lead the development of fruquintinib, including all clinical trial development. Eli Lilly reimbursed the Company for a majority of the development costs and provided input over the course of the development of fruquintinib. Development, collaboration and manufacture of the products under this agreement are overseen by a joint steering committee comprised of equal numbers of representatives from each party.

Eli Lilly paid a US$6.5 million upfront fee following the execution of the Eli Lilly Agreement in 2013 and agreed to pay royalties and additional amounts upon the achievement of development and regulatory approval milestones. As of December 31, 2020, Eli Lilly had paid us US$37.2 million in milestone payments in addition to approximately US$53.2 million in reimbursements for certain development costs.

We could potentially receive future milestone payments for the achievement of development and regulatory approval milestones in China. Additionally, Eli Lilly is obligated to pay us tiered royalties from 15% to 20% annually on sales made of fruquintinib in China and Hong Kong, the rate to be determined based upon the dollar amount of sales made for all products in that year. Under the terms of our 2018 amendment, upon the first commercial launch of fruquintinib in China in a new life cycle indication, these tiered royalties increased to 15% to 29%. Under the terms of our 2020 amendment, we and Eli Lilly share gross profits linked to sales target performance. Subject to meeting pre-agreed sales targets, Eli Lilly will pay us an estimated total of 70% to 80% of Elunate sales in the form of royalties, manufacturing costs and service payments.

Under the terms of our 2018 amendment, we are entitled to determine and conduct future life cycle indication development of fruquintinib in China beyond the three initial indications specified in the original Eli Lilly Agreement. After the 2018 amendment, we assumed responsibility for all development activities and costs for fruquintinib in China in new life cycle indications, and we have the liberty to collaborate with third-parties to explore combination therapies of fruquintinib with various immunotherapy agents. Under the terms of our 2020 amendment, we took over development and execution of all on-the-ground medical detailing, promotion and local and regional marketing activities for Elunate in China.

We are responsible in consultation with Eli Lilly for the supply of, and have the right to supply, all clinical and commercial supplies for fruquintinib pursuant to an agreed strategy for manufacturing. For the term of the Eli Lilly Agreement, such supplies will be provided by us at a transfer price that accounts for our cost of goods sold.

The Eli Lilly Agreement is terminable by either party for breach that is uncured. The Eli Lilly Agreement is also terminable by Eli Lilly for convenience with 120 days' prior written notice or if there is a major unexpected safety issue with respect to a product. Termination by either us or Eli Lilly for any reason will have the effect of, among other things, terminating the applicable licenses granted by us, and will obligate Eli Lilly to transfer to us all regulatory materials necessary for us to continue development efforts for fruquintinib.

BeiGene

In May 2020, we entered into a clinical collaboration agreement with BeiGene to evaluate the safety, tolerability and efficacy of combining surufatinib and fruquintinib with BeiGene's anti-PD-1 antibody tislelizumab, for the treatment of various solid tumor cancers, in the United States, Europe, China and Australia. Under the terms of the agreement, we and BeiGene each plan to explore development of the combination of surufatinib with tislelizumab or fruquintinib with tislelizumab in different indications and regions. We have agreed to provide mutual drug supply and other support.

Inmagene

In January 2021, we and Inmagene entered into a strategic partnership to further develop four novel preclinical drug candidates (HMPL-A28, HMPL-727, HMPL-662 and HMPL-958) discovered by us for the potential treatment of multiple immunological diseases. We will work together to move the drug candidates towards IND submission. If successful, Inmagene will then move the drug candidates through global clinical development.

Under the terms of the agreement, we have granted Inmagene exclusive options to four drug candidates solely for the treatment of immunological diseases. If Inmagene exercises an option, it will have the right to further develop, manufacture and commercialize that specific drug candidate worldwide, while we retain first right to co-commercialization in China. For each of the drug candidates, we will be entitled to development milestones of up to US$95 million and up to US$135 million in commercial milestones, as well as up to double-digit royalties upon commercialization.

Other Collaborations

In October and November 2018, we entered into multiple collaborations to evaluate combinations of fruquintinib and surufatinib. These include a global collaboration with Innovent to evaluate the combination of fruquintinib with Tyvyt and a global collaboration with Junshi to evaluate the combination of surufatinib with Tuoyi. In September 2019, we expanded our global collaboration agreement with Innovent to evaluate the safety and efficacy of Tyvyt in combination with surufatinib.

OTHER VENTURES

Other Ventures is our large-scale, high-performance drug marketing and distribution platform covering about 320 cities and towns in China with approximately 4,800 manufacturing and commercial personnel as of December 31, 2020. Built over the past 20 years, it has been focused on the sale of prescription drug products and consumer health products conducted through the following entities:

Shanghai Hutchison Pharmaceuticals

Shanghai Hutchison Pharmaceuticals, our non-consolidated joint venture, primarily engages in the manufacture and sale of prescription drug products originally contributed by our joint venture partner, as well as third-party prescription drugs with a focus on cardiovascular medicine. Shanghai Hutchison Pharmaceuticals' proprietary products are sold under the "Shang Yao" brand, literally meaning "Shanghai pharmaceuticals," a trademark that has been used for over 37 years in the pharmaceutical retail market, primarily in Eastern China. In early 2019, Shanghai Hutchison Pharmaceuticals was awarded the 2018 State Scientific and Technological Progress Award – Second Prize, which was presented by President Xi Jinping, Premier Li Keqiang and other state leaders of the PRC at the National Science and Technology Awards Ceremony. This award was one of only two such awards given that year to studies in the botanical drug industry.

Its key product is She Xiang Bao Xin pills, a vasodilator for the long-term treatment of coronary artery and heart disease and for rapid control and prevention of acute angina pectoris, a form of chest pain. There are over one million deaths due to coronary artery disease per year in China. She Xiang Bao Xin pill is the third largest botanical prescription drug in this indication in China, with market share in

2020 of 18.2% (2019: 17.9%) nationally and 46.8% (2019: 50.0%) in Shanghai. She Xiang Bao Xin pills' sales represented 90.5% of all Shanghai Hutchison Pharmaceuticals sales in 2020.

She Xiang Bao Xin pills were first approved in 1983 and subsequently enjoyed 22 proprietary commercial protections under the prevailing regulatory system in China. In 2005, Shanghai Hutchison Pharmaceuticals was able to attain "Confidential State Secret Technology" status protection, as certified by China's Ministry of Science and Technology and State Secrecy Bureau, which extended proprietary protection in China until late 2016. The Science and Technology Commission of Shanghai Municipality has subsequently extended such protection. Shanghai Hutchison Pharmaceuticals holds an invention patent in China covering its formulation, which extends proprietary protection through 2029. She Xiang Bao Xin pill is one of less than two dozen proprietary prescription drugs represented on China's National Essential Medicines List, which means that all Chinese state-owned health care institutions are required to carry it. She Xiang Bao Xin pill is fully reimbursed in all of China.

Shanghai Hutchison Pharmaceuticals manufactures its products at its 78,000 square meter production facility located in Feng Pu district outside the center of Shanghai. Shanghai Hutchison Pharmaceuticals holds 74 drug product manufacturing licenses, of which 17 are included in National Essential Medicines List, and three are in active production. The factory is operated by over 530 manufacturing staff.

As of December 31, 2020, Shanghai Hutchison Pharmaceuticals had a commercial team of about 2,200 medical sales representatives allowing for the promotion and scientific detailing of our products not just in hospitals in provincial capitals and medium-sized cities, but also in the majority of county-level hospitals in China. Shanghai Hutchison Pharmaceuticals, through its GSP-certified subsidiary, sells its products and its third-party licensed prescription drugs directly to distributors who on-sell such products to hospitals and clinics, pharmacies and other retail outlets in their respective areas, as well as to other local distributors. As of December 31, 2020, Shanghai Hutchison Pharmaceuticals engaged a group of approximately 650 primary distributors to cover China. These primary distributors in turn used over 2,600 secondary distributors to work directly with hospitals, on a local level, to manage logistics. Shanghai Hutchison Pharmaceuticals' own prescription drugs sales representatives promote its products to doctors and purchasing managers in hospitals, clinics and pharmacies as part of its marketing efforts. See "– *Sales and Marketing*" for further information relating to sales through our distributors.

Hutchison Sinopharm

Hutchison Sinopharm is our consolidated joint venture with Sinopharm. Based in Shanghai, Hutchison Sinopharm focuses on providing logistics services to, and distributing and marketing prescription drugs in China. As of December 31, 2020, Hutchison Sinopharm had a dedicated team of over 120 commercial staff focused on two key areas of operation – a commercial team that markets approximately 1,000 third-party prescription drug and other products directly to over 500 public and private hospitals in the Shanghai region and through a network of approximately 40 distributors to cover all other provinces in China, and a second commercial team that markets our Zhi Ling Tong infant nutrition brand through a network of over 29,000 promoters in over 7,500 outlets in China.

Since early 2015, Hutchison Sinopharm has been the exclusive marketing agent for Seroquel tablets in China. In June 2018, AstraZeneca sold and licensed its rights to Seroquel to Luye Pharma Group, Ltd., including its rights in China. The terms of our agreement with AstraZeneca were assigned to Luye Pharma Hong Kong Ltd., or Luye HK. In May 2019, we received a notice from Luye HK purporting to terminate our agreement. We believe that Luye HK has no basis for termination and have commenced confidential legal proceedings to seek damages which are ongoing as of the Latest Practicable Date and there will be no negative material impact to the Group. During the three financial years ended December 31, 2020 ("Track Record Period"), revenues from the distribution of Seroquel were US$29.2 million, US$7.3 million and nil for the years ended December 31, 2018, 2019 and 2020, respectively.

In 2019, we began building an in-house oncology commercial sales and marketing team at Hutchison Sinopharm to support the launch of certain of our innovative oncology drugs. By December 31, 2020, this team had grown to over 360 commercial sales and marketing staff.

During the Track Record Period, a substantial portion of Hutchison Sinopharm's sales were made directly to hospitals and clinics, with the remaining sales being made through distributors. As of December 31, 2020, Hutchison Sinopharm had approximately 590 customers of which approximately 6% were distributors, and the revenue generated from these distributors accounted for approximately 26% of the revenue of Hutchison Sinopharm for the financial year ended December 31, 2020. See "– *Sales and Marketing*" for further information relating to sales through our distributors.

Hutchison Baiyunshan

Hutchison Baiyunshan, our non-consolidated joint venture, focuses primarily on the manufacture, marketing and distribution of over-the-counter pharmaceutical products. Hutchison Baiyunshan's "Bai Yun Shan" brand is a market-leading household-name, established over 40 years ago and is known by the majority of Chinese consumers. As of December 31, 2020, Hutchison Baiyunshan held 185 registered drug licenses in China. In addition, 30 of Hutchison Baiyunshan's products, of which six are in active production, are represented on China's National Essential Medicines List. In addition to about 1,000 manufacturing staff in Guangdong and Anhui provinces, Hutchison Baiyunshan has a commercial team of about 900 sales staff that covers the national retail pharmacy channel in China.

Hutchison Baiyunshan's key products are two generic over-the-counter therapies:

- **Banlangen granules –** for the treatment of viral flu, fever, and respiratory tract infections which represented approximately 35.9% of the sales of Hutchison Baiyunshan in 2020; and
- **Fu Fang Dan Shen tablets –** generic over-the-counter drugs for the treatment of chest congestion and angina pectoris to promote blood circulation and relieve pain, which represented approximately 16.5% of the sales of Hutchison Baiyunshan in 2020.

Hutchison Baiyunshan's products are mainly manufactured in-house at facilities in Guangzhou, Guangdong province and Bozhou, Anhui province. Third-party contract manufacturers are also used. Hutchison Baiyunshan also operates cultivation sites through its subsidiaries for growing and sourcing the herbs used in its over-the-counter products in Guangdong, Yunnan and Heilongjiang provinces in China. In addition, Hutchison Baiyunshan generates revenue by supplying raw materials produced by its cultivation operations to its collaboration partner, Guangzhou Pharmaceuticals.

Hutchison Baiyunshan sells its products directly to regional distributors across China who on-sell to local distributors, hospitals and clinics, pharmacies and other retailers, and employs its own sales representatives at a local level to market its products and promote over-the-counter sales to retailers.

In June 2020, Hutchison Baiyunshan entered into a land compensation agreement with the Guangzhou government for the return of its land use rights for an approximately 30,000 square meter unused plot of land in Guangzhou for cash compensation of up to approximately US$100 million. As of December 31, 2020, Hutchison Baiyunshan had surrendered the land use rights certificate for deregistration, had satisfied all major obligations under the land compensation agreement and received approximately US$40 million in compensation. Hutchison Baiyunshan is expected to receive approximately US$60 million in 2021. The land return had no impact on manufacturing operations, which continue to be conducted at larger sites in Guangzhou and Bozhou.

On March 24, 2021, we entered into a sale and purchase agreement with GL Mountrose Investment Two Limited, a company controlled and managed by GL Capital Group, to sell our entire investment in Hutchison Baiyunshan. The disposal is subject to regulatory approval in China and is expected to be completed in the second half of 2021.

Hutchison Hain Organic

Hutchison Hain Organic is a consolidated joint venture with Hain Celestial, a Nasdaq-listed, natural and organic food and personal care products company. Hutchison Hain Organic distributes a broad range of over 500 imported organic and natural products. Pursuant to its joint venture agreement, Hutchison Hain Organic has rights to manufacture, market and distribute Hain Celestial's products within nine Asian territories. We believe the key strategic product for Hutchison Hain Organic is Earth's Best organic baby products, a leading brand in the United States. Hutchison Hain Organic's other products are distributed to hypermarkets, specialty stores and other retail outlets in Hong Kong, China and across seven other territories in Asia mainly through third-party local distributors, including retail chains owned by affiliates of CK Hutchison.

Hutchison Healthcare

Hutchison Healthcare is our wholly-owned subsidiary and is primarily engaged in the manufacture and sale of health supplements. Hutchison Healthcare's major product is Zhi Ling Tong DHA capsules, a health supplement made from algae DHA oil for the promotion of brain and retinal development in babies and young children, which is distributed by Hutchison Sinopharm.

The majority of Hutchison Healthcare's products are contract manufactured at a dedicated and certified manufacturing facility operated by a third-party.

Hutchison Consumer Products

Hutchison Consumer Products is our wholly-owned subsidiary that is primarily engaged in the distribution of third-party consumer products in Asia.

PATENTS AND OTHER INTELLECTUAL PROPERTY

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our Oncology/Immunology drugs and drug candidates, our Other Ventures' products and other know-how. Our policy is to seek to protect our proprietary and intellectual property position by, among other methods, filing patent applications in various jurisdictions related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

Patents

We and our joint ventures file patent applications directed to our Oncology/Immunology drugs and drug candidates and our Other Ventures' products in an effort to establish intellectual property positions with regard to new small molecule compounds and/or extracts of natural herbs, their compositions as well as their medical uses in the treatment of diseases. In relation to our Oncology/Immunology operations, we also file patent applications directed to crystalline forms, formulations, processes, key intermediates, and secondary uses as clinical trials for our drug candidates evolve. We file such patent applications in major market jurisdictions, including the United States, Europe, Japan and China as well as Argentina, Australia, Brazil, Canada, Chile, India, Indonesia, Israel, Mexico, Malaysia, New Zealand, Peru, the Philippines, Singapore, South Korea, Ukraine and South Africa.

Our Onocology/Immunology Patents

As of December 31, 2020, we had 235 issued patents, including 19 Chinese patents, 22 U.S. patents and 13 European patents, 155 patent applications pending in the above major market jurisdictions, and six pending PCT patent applications relating to the drugs and drug candidates of our Oncology/Immunology operations. The intellectual property portfolios for our most advanced drug candidates are summarized below. With respect to most of the pending patent applications covering our drug candidates,

prosecution has yet to commence. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the relevant patent office is often significantly narrowed by the time when they issue, if they issue at all. We expect this to be the case for our pending patent applications referred to below.

Savolitinib – The intellectual property portfolio for savolitinib contains two patent families.

The first patent family for savolitinib is directed to novel small molecule compounds as well as methods of treating cancers with such compounds. As of December 31, 2020, we owned 48 patents in this family, including patents in China, the United States, Europe and Japan, and we had 15 patent applications pending in various other jurisdictions. Our European patent is also registered in Hong Kong. Our issued patents will expire in 2030.

The second patent family is directed to the method for the preparation of savolitinib. With respect to this family, we have PCT, Argentina and Taiwan applications pending, each of which, if issued, would have an expiration date in 2039. This patent family is co-owned by us and AstraZeneca.

Our collaboration partner AstraZeneca is responsible for maintaining and enforcing the intellectual property portfolio for savolitinib.

Surufatinib – The intellectual property portfolio for surufatinib contains five patent families.

The first patent family for surufatinib is directed to novel small molecule compounds as well as methods of treating tumor angiogenesis-related disorders with such compounds. As of December 31, 2020, in this patent family we owned one Chinese patent expiring in 2027 and 12 patents in various other jurisdictions, including the United States expiring in 2031, and Europe and Japan, each expiring in 2028. As of December 31, 2020, we also had one patent application pending in Brazil.

The second patent family is directed to the crystalline forms of surufatinib as well as methods of treating tumor angiogenesis-related disorders with such forms. As of December 31, 2020, in this patent family we owned two patents in China expiring in 2029 and 2030, respectively, and we owned 15 patents in other countries, including the United States which will expire in 2031 and Europe which will expire in 2030. As of December 31, 2020, we also had one patent application pending in Brazil.

The third patent family is directed to the formulation of a micronized active pharmaceutical ingredient used in surufatinib as well as methods of treating tumor angiogenesis-related disorders with such formulation. As of December 31, 2020, in this patent family, we owned three patents in Europe, Russia and Indonesia expiring in 2036. We also had 15 patent applications pending in various jurisdictions, including China, the United States and Japan, each of which, if issued, would have an expiration date in 2036.

The fourth patent family is directed to clinical indications of surufatinib. With respect to this patent family, we have four patent applications pending in China, the United States, Hong Kong and Japan, which, if issued, will each have expiration dates in 2036.

The fifth patent family is subject to confidential review by the patent authorities. With respect to this family, we had one patent application pending in China, which, if issued, would have an expiration date in 2040.

Fruquintinib – The intellectual property portfolio for fruquintinib contains five patent families.

The first patent family for fruquintinib is directed to novel small molecule compounds as well as methods of treating tumor angiogenesis-related disorders with such compounds. As of December 31, 2020, we owned three United States patents, one Chinese patent and one Taiwanese patent in this family, each of which will expire in 2028. We also owned patents in Europe and 14 other jurisdictions expiring in 2029 and had one patent application pending in Brazil.

The second patent family is directed to crystalline forms of fruquintinib as well as methods of treating tumor angiogenesis-related disorders with such forms. As of December 31, 2020, we owned 13

patents in this family in various jurisdictions, including the United States, China, Europe and Japan, each of which will expire in 2035, and we had 13 patent applications pending in various jurisdictions, including Brazil, Peru and Chile.

The third patent family is directed to the method of preparing one of the critical intermediates used in the manufacturing process of fruquintinib. With respect to this patent family, we have one patent in China, which has an expiration date in 2034.

The fourth patent family is directed to the pharmaceutical composition of fruquintinib. With respect to this family, we have one patent application pending in China, which, if issued, would have an expiration date in 2038. We also have PCT, Argentina and Taiwan applications pending for this family, which, if issued, would have an expiration date in 2039.

The fifth patent family is subject to confidential review by the patent authorities. With respect to this family, we had one patent application pending in China, which, if issued, would have an expiration date in 2040. This patent family is co-owned by us and Genor.

HMPL-523 Syk Inhibitor – The intellectual property portfolio for HMPL-523 contains two patent families.

The first patent family is directed to novel small molecule compounds as well as methods of treating cancers, inflammatory diseases, allergic diseases, cell-proliferative diseases, and immunological diseases with such compounds. As of December 31, 2020, we owned 22 patents in this family in various jurisdictions, including the United States, China and South Korea, each of which will expire in 2032. As of December 31, 2020, we also had three patent applications in this family pending in other jurisdictions.

The second patent family is directed to the salts of HMPL-523. As of December 31, 2020, in this patent family we had 22 patent applications pending in various jurisdications, including China, the United States, Europe and Taiwan, each of which, if issued, would have an expiration date in 2038.

HMPL-689 – The intellectual property portfolio for HMPL-689 contains two patent families.

The first patent family is directed to novel small molecule compounds as well as uses of such compounds. As of December 31, 2020, we owned 21 patents in this family in various jurisdictions, including China, the United States, Europe, Australia and Japan, each of which will expire in 2035. As of December 31, 2020, we also had six patent applications pending in this family in other various jurisdictions.

The second patent family is directed to crystalline forms of HMPL-689. With respect to this family, we had one patent application pending in China as of December 31, 2020, which, if issued, would have an expiration date in 2038. We also had 22 patent applications in this family pending in various jurisdictions, including China, the United States, Europe and Taiwan, each of which, if issued, would have an expiration date in 2039.

HMPL-453 – The intellectual property portfolio for HMPL-453 contains two patent families.

The first patent family is directed to novel small molecule compounds as well as methods of treating cancers with the compounds. As of December 31, 2020, we owned 21 patents in this family in various jurisdictions, including China, Europe, Japan and the United States, each of which will expire in 2034. As of December 31, 2020, we had four patent applications pending in other various jurisdictions.

The second patent family is subject to confidential review by the patent authorities. With respect to this family, we have PCT, Argentina and Taiwan applications pending, each of which, if issued, would have an expiration date in 2040.

HMPL-306 – The intellectual property portfolio for HMPL-306 contains one patent family.

The patent family is directed to novel small molecule compounds as well as methods of treating cancers with the compounds. As of December 31, 2020, in this patent family we had 24 patent

applications pending in various jurisdictions, including China, the United States, Europe and Taiwan, each of which, if issued, would have an expiration date in 2038.

Epitinib – The intellectual property portfolio for epitinib contains two patent families.

The first patent family is directed to novel small molecule compounds as well as methods of treating cancers with such compounds. As of December 31, 2020, we owned two patents in China and Taiwan expiring in 2028, one patent in the United States expiring in 2031 and 14 patents in other jurisdictions, including Europe, each expiring in 2029.

The second patent family is directed to the salts and solvates of epitinib and crystalline forms thereof, as well as methods of treating cancers with such forms. As of December 31, 2020, we had one patent application pending in China in this family, which, if issued, would have an expiration date in 2038.

Theliatinib – The intellectual property portfolio for theliatinib contains three patent families.

The first patent family is directed to novel small molecule compounds as well as methods of treating cancers with such compounds. As of December 31, 2020, we owned 18 patents in this family in various jurisdictions, including China and Japan, each of which will expire in 2031. As of December 31, 2020, we also had one patent application in this family pending in Brazil. Our Chinese patent was also registered in Hong Kong and Macau.

The second patent family is directed to the crystalline forms of theliatinib as well as methods of treating cancers with such forms. As of December 31, 2020, we had one patent application pending in China in this family, which, if issued, will have an expiration date in 2037.

The third patent family is directed to the salts and solvates of theliatinib and crystalline forms thereof. With respect to this family, we have one Chinese application pending, which, if issued, would have an expiration date in 2038.

Other Ventures Patents

As of December 31, 2020, our joint venture Shanghai Hutchison Pharmaceuticals had 58 issued patents and 22 pending patent applications in China, including patents for its key prescription products described below.

She Xiang Bao Xin Pills. As of December 31, 2020, Shanghai Hutchison Pharmaceuticals held an invention patent in China directed to the formulation of the She Xiang Bao Xin pill. Under PRC law, invention patents are granted for new technical innovations with respect to products or processes. Invention patents in China have a maximum term of 20 years. This patent will expire in 2029. The "Confidential State Secret Technology" status protection on the She Xiang Bao Xin pill technology held by Shanghai Hutchison Pharmaceuticals, as certified by China's Ministry of Science and Technology and State Secrecy Bureau, is currently active.

Danning Tablets. As of December 31, 2020, Shanghai Hutchison Pharmaceuticals also held an invention patent in China directed to the formulation of the Danning tablet. This patent will expire in 2027.

Many of the products sold by our joint venture Hutchison Baiyunshan, including its Banlangen granules and Fu Fang Dan Shen tablets, are generic, over-the-counter products for which Hutchison Baiyunshan does not hold patents. As of December 31, 2020, Hutchison Baiyunshan had 80 issued patents and 26 pending patents in China, two PCT patents and one in Australia.

Patent Term

The term of a patent depends upon the laws of the country in which it is issued. In most jurisdictions, a patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a

patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. In the future, if and when our drug candidates receive approval by the FDA or other regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, depending upon the length of the clinical trials for each drug and other factors. There can be no assurance that any of our pending patent applications will be issued or that we will benefit from any patent term extension.

As with other pharmaceutical companies, our or our joint ventures' ability to maintain and solidify our proprietary and intellectual property position for our drugs and drug candidates or our or their products and technologies will depend on our or our joint ventures' success in obtaining effective patent claims and enforcing those claims if granted. However, our or our joint ventures' pending patent applications and any patent applications that we or they may in the future file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our or our joint ventures' patents. Any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority of filing covered by pending third-party patent applications. If third parties prepare and file patent applications in the United States, China or other markets that also claim technology or therapeutics to which we or our joint ventures have rights, we or our joint ventures may have to participate in interference proceedings, which could result in substantial costs to us, even if the eventual outcome is favorable to us, which is highly unpredictable. In addition, because of the extensive time required for clinical development and regulatory review of a drug candidate we may develop, it is possible that, before any of our drug candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting protection such patent would afford the respective product and any competitive advantage such patent may provide.

Trade Secrets

In addition to patents, we and our joint ventures rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our or their competitive position. We and our joint ventures seek to protect our proprietary information, in part, by executing confidentiality agreements with our collaborators and scientific advisors, and non-competition, non-solicitation, confidentiality, and invention assignment agreements with our employees and consultants. We and our joint ventures have also executed agreements requiring assignment of inventions with selected scientific advisors and collaborators. The confidentiality agreements we and our joint ventures enter into are designed to protect our or our joint ventures' proprietary information and the agreements or clauses requiring assignment of inventions to us or our joint ventures, as applicable, are designed to grant us or our joint ventures, as applicable, ownership of technologies that are developed through our or their relationship with the respective counterpart. We cannot guarantee, however, that these agreements will afford us or our joint ventures adequate protection of our or their intellectual property and proprietary information rights.

Trademarks and Domain Names

We conduct our business using trademarks with various forms of the "Hutchison", "Chi-Med", "Hutchison China MediTech", "Hutchmed", "Elunate" and "Sulanda" brands, the logo used by Hutchison MediPharma, as well as domain names incorporating some or all of these trademarks. In April 2006, we entered into a brand license agreement (as amended and restated on June 15, 2021) with Hutchison Whampoa Enterprises Limited, an indirect wholly-owned subsidiary of CK Hutchison, pursuant to which we have been granted a non-exclusive, non-transferrable, royalty-free right to use the "Hutchison", "Hutchison China MediTech", "Chi-Med", "Hutchmed" trademarks, domain names and other intellectual property rights owned by the CK Hutchison group in connection with the operation of our business worldwide. The Elunate trademark is licensed to us in China by our collaboration partner Eli Lilly. The trademarks for the Hutchison MediPharma logo and "Sulanda" are owned by us.

In addition, our joint ventures seek trademark protection in China for their products. As of December 31, 2020, our joint ventures Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan owned a total of 316 trademarks in the aggregate related to products sold by them. For example, the name "Shang Yao" is a registered trademark of Shanghai Hutchison Pharmaceuticals in China for certain uses including pharmaceutical preparations. In addition, our joint venture Hutchison Baiyunshan has been granted a royalty-free license to use the registered trademark "Bai Yun Shan" for a term equal to its operational period of the joint venture by Guangzhou Baiyunshan.

RAW MATERIALS AND SUPPLIES

Raw materials and supplies are ordered based on our or our joint ventures' respective sales plans and reasonable order forecasts and are generally available from our or our joint ventures' own cultivation operations and various third-party suppliers in quantities adequate to meet our needs. We typically order raw materials on short-term contract or purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements.

For our Oncology/Immunology operations, the active pharmaceutical ingredient used in our drug candidates are supplied to us from third-party vendors. Our ability to successfully develop our drug candidates, and to ultimately supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the active pharmaceutical ingredients for these drugs in accordance with regulatory requirements and in sufficient quantities for commercialization and clinical testing.

We generally aim to identify and qualify one or more manufacturers to provide such active pharmaceutical ingredients prior to submission of an NDA to the FDA and/or NMPA. We contract with a single supplier to manufacture and supply us with the active pharmaceutical ingredient for fruquintinib for commercial purposes and are in the process of engaging a second supplier. We have already validated the second supplier's cGMP production processes and submitted an application for its approval to the NMPA. We also contract with a single supplier to manufacture and supply us with the active pharmaceutical ingredient for surufatinib for commercial purposes. We manage the risk of price fluctuations and supply disruptions of active pharmaceutical ingredients by purchasing them in bulk quantities as these ingredients have a relatively long shelf life. Other than the foregoing, we do not currently have arrangements in place for a contingent or second-source supply of the active pharmaceutical ingredients for fruquintinib or surufatinib in the event any of our current suppliers of such active pharmaceutical ingredients cease their operations for any reason, which may lead to an interruption in our production. However, to date, while we have experienced price fluctuations associated with our raw materials, we have not experienced any material disruptions in the supply of the active pharmaceutical ingredients or the other raw materials we and our joint venture partners use. See "*Risk Factors – Risks Relating to Sales of our Internally Developed Drugs and other Drugs – Certain of our joint ventures' principal products involve the cultivation or sourcing of key raw materials including botanical products, and any quality control or supply failure or price fluctuations could adversely affect our ability to manufacture our products and/or could materially and adversely affect our operating results.*" and *"Risk Factors – Risks Relating to Our Dependence on Third Parties – The third-party vendors upon whom we rely for the supply of the active pharmaceutical ingredients used in some of our drug candidates and drug products are our sole source of supply, and the loss of any of these suppliers could significantly harm our business.*" in Item 3D. of our 2020 Annual Report.

CROs

Although we or our collaboration partners design the clinical trials for our drug candidates, CROs conduct most of the clinical trials. Our agreements with CROs are usually structured as master service agreements which set out the services to be performed, payment schedule, term and confirmation that all intellectual rights arising out of or made in performance of the services are owned by us. We and our collaboration partners work with major global and Chinese CROs.

PRODUCTION

Our and our joint ventures' manufacturing operations consist of bulk manufacturing and formulation, fill, and finishing activities that produce products and drug candidates for both clinical and commercial purposes. Our and our joint ventures' manufacturing capabilities have a large operation scale for our own-brand products. We and our joint ventures manufacture and sell about 4.9 billion doses of medicines a year, in the aggregate, through our well-established GMP manufacturing base.

The principal products sold by our Other Ventures are mainly produced at our joint ventures' manufacturing facilities in Shanghai, Guangzhou and Bozhou, China. Our commercial supplies of fruquintinib and surufatinib are manufactured at our GMP-certified production facility in Suzhou, China, which has a maximum production capacity of 50 million tablets and capsules per year. During the Track Record Period, we produced 26.2 million tablets and capsules. We have commenced construction of a large-scale manufacturing plant for innovative drugs in Shanghai. The Shanghai factory is expected to be completed in 2025 and will be our largest manufacturing facility, with production capacity estimated to be five times that of our facility in Suzhou. The first phase will be primarily for small molecule production, with production capacity expected to be able to produce 250 million tablets and capsules per year.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements governing recordkeeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our manufacturing facilities and the contract manufacturing organizations we use to manufacture our drugs and drug candidates operate under cGMP conditions. cGMP are regulatory requirements for the production of pharmaceuticals that will be used in humans.

CUSTOMERS AND SUPPLIERS

In the financial years ended December 31, 2018, 2019 and 2020, we generated revenue of US$75.8 million, US$75.7 million and US$102.3 million from our five largest customers, respectively. For the financial years ended December 31, 2018, 2019 and 2020, revenue from our five largest customers represented approximately 35%, 37% and 45% of our total revenue, respectively, and revenue from our largest customer in those periods represented approximately 11%, 13% and 16% of our revenue in the same periods, respectively. Save for Sinopharm, our five largest customers were independent third parties and none of our Directors or their close associates or, to the knowledge of our Directors, any Shareholder who owned more than 5% of our issued Shares had any interest in any of our five largest customers as of the Latest Practicable Date.

During the Track Record Period, Sinopharm, which will be a connected person of the Company from the Listing, was one of our five largest customers. Sales to Sinopharm and/or its associates contributed 12%, 14% and 16% of the Group's revenue in 2018, 2019 and 2020, respectively. Purchases from Sinopharm and/or its associates contributed less than 1% of the Group's total purchases in 2018, 2019 and 2020, respectively.

In the financial years ended December 31, 2018, 2019 and 2020, the total purchases from our five largest suppliers were US$57.2 million, US$46.8 million and US$58.0 million, respectively. For the financial years ended December 31, 2018, 2019 and 2020, our purchases from our five largest suppliers represented less than 20% of our total purchases. Save for Shanghai Hutchison Pharmaceuticals and Hain Celestial, all of our five largest suppliers were independent third parties and none of our Directors or their close associates or, to the knowledge of our Directors, any Shareholder who owned more than 5% of our issued Shares had any interest in any of our five largest suppliers as of the Latest Practicable Date.

QUALITY CONTROL AND ASSURANCE

We have our own independent quality control system and devote significant attention to quality control for the designing, manufacturing and testing of our products. We have established a strict quality

control system in accordance with the NMPA regulations. Our laboratories fully comply with the Chinese manufacturing guidelines and are staffed with highly educated and skilled technicians to ensure quality of all batches of product release. We monitor in real time our operations throughout the entire production process, from inspection of raw and auxiliary materials, manufacture, delivery of finished products, clinical testing at hospitals, to ethical sales tactics. Our quality assurance team is also responsible for ensuring that we are in compliance with all applicable regulations, standards and internal policies. Our senior management team is actively involved in setting quality policies and managing internal and external quality performance of our Company and our non-consolidated joint ventures, Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan.

CERTIFICATES AND PERMITS

We are required to obtain and renew certain certificates and permits for our business operations.

Hutchison MediPharma (Suzhou) Limited holds a pharmaceutical manufacturing permit issued by its local regulatory authority expiring on September 13, 2025. It also holds a GMP certificate issued by its local regulatory authority expiring on September 16, 2023.

Hutchison Sinopharm holds a pharmaceutical trading license issued by its local regulatory authority expiring on July 30, 2024. Hutchison Sinopharm also holds a GSP certificate issued by its local regulatory authority which expires on July 30, 2024.

Shanghai Hutchison Pharmaceuticals holds a pharmaceutical manufacturing permit from its local regulatory authorities expiring on December 31, 2025. Shanghai Hutchison Pharmaceuticals also holds three GMP certificates issued by its local regulatory authority. The three GMP certificates will expire on August 14, 2021, November 16, 2021 and December 3, 2022, respectively.

Shanghai Shangyao Hutchison Whampoa GSP Company Limited, a subsidiary of Shanghai Hutchison Pharmaceuticals, holds a pharmaceutical trading license from its local regulatory authority expiring on November 17, 2024. It also holds a GSP certificate issued by its local regulatory authority expiring on November 17, 2024.

Hutchison Baiyunshan holds a pharmaceutical manufacturing permit issued by its local regulatory authority expiring on November 26, 2025. Hutchison Baiyunshan also holds a GMP certificate issued by its local regulatory authority expiring on December 11, 2023.

Hutchison Whampoa Guangzhou Baiyunshan Pharmaceuticals Limited, a subsidiary of Hutchison Baiyunshan, holds a GSP certificate issued by its local regulatory authority expiring on October 14, 2024. It also holds a pharmaceutical trading license issued by its local regulatory authority expiring on November 5, 2024.

Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine (Bozhou) Company Limited, a subsidiary of Hutchison Baiyunshan, holds a GMP certificate issued by its local regulatory authority expiring on January 18, 2022. It also holds a pharmaceutical manufacturing license issued by its local regulatory authority expiring on December 31, 2025.

Hutchison Whampoa Baiyunshan Lai Da Pharmaceutical (Shan Tou) Company Limited, a subsidiary of Hutchison Baiyunshan, holds a pharmaceutical manufacturing license issued by its local regulatory authority expiring on October 25, 2025.

During the Track Record Period and up to the Latest Practicable Date, we had obtained all requisite certificates, permits and approvals that are material for our operations, and all of such certificates, permits and approvals were within their respective effective periods. We did not experience any material difficulty in renewing such certificates, permits and licenses during the Track Record Period and up to the Latest Practicable Date, and we currently do not expect to have any material difficulty in renewing them when they expire, if applicable. During the Track Record Period and up to the Latest Practicable Date, we had

not been penalized by any government authorities for any non-compliance relating to maintenance and renewal of our material licenses, permits and approvals.

EMPLOYEES

As of December 31, 2018, 2019 and 2020, we had 714, 853 and 1,280 full-time employees, respectively. None of our employees are represented by labor unions or covered by collective bargaining agreements. As of the Latest Practicable Date, we have not experienced any strikes or labor disputes which had a material effect on our business and consider our relations with our employees to be good. The number of employees by function as of December 31, 2018, 2019 and 2020 was as follows:

	2018	2019	2020
By Function:			
Oncology/Immunology	418	500	643
Other Ventures[(1)]	267	315	594
Corporate Head Office	29	38	43
Total	714	853	1,280

Note:

(1) Hutchison Sinopharm employees are categorized under the Other Ventures function.

Additionally, under our Other Ventures operations, our joint venture Shanghai Hutchison Pharmaceuticals employed a total of 2,898 full time employees, and Hutchison Baiyunshan employed a total of 1,700 full time employees and 1,864 outsourced contract staff, who are mostly sales representatives and manufacturing employees, as of December 31, 2020. Their employees are represented by labor unions and covered by collective bargaining agreements.

As of the Latest Practicable Date, neither Shanghai Hutchison Pharmaceuticals nor Hutchison Baiyunshan has experienced any strikes, labor disputes or industrial actions which had a material effect on their business, and consider their relations with the union and their employees to be good.

PROPERTY, PLANT AND EQUIPMENT

We are headquartered in Hong Kong where we have our main administrative offices.

We rent and operate a 2,107 square meter GMP-certified manufacturing facility for fruquintinib and surufatinib in Suzhou, Jiangsu Province in Eastern China, and own a 5,024 square meter facility in Shanghai which houses research and development operations. We lease 7,036 square meters of office space in Shanghai which houses Hutchison MediPharma's management and staff. In 2020, we entered into a 50-year land use rights agreement for a 28,771 square meter site in Shanghai. We have commenced construction of a new almost 55,000 square meter large-scale manufacturing facility for innovative drugs on the site.

We also lease a 26,989 square foot facility in Florham Park, New Jersey where we house our U.S.-based clinical, regulatory and commercial management and staff.

Our non-consolidated joint ventures, Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan, operate two large-scale research and development and manufacturing facilities for which they have obtained land use rights and property ownership certificates.

Shanghai Hutchison Pharmaceuticals relocated to its current facility outside of Shanghai in September 2016, and it has an aggregate site area of approximately 78,000 square meters (compared to approximately 58,000 square meters for its old facility located in Shanghai). Shanghai Hutchison Pharmaceuticals agreed to surrender its land use rights for the property where its old production facility was located to the Shanghai government for cash consideration. The total cash and subsidies paid by the Shanghai government to Shanghai Hutchison Pharmaceuticals was approximately US$113 million,

including approximately US$101 million for land compensation and US$12 million in government subsidies related to research and development projects.

Hutchison Baiyunshan's facilities are in Guangzhou on a 59,000 square meter site and Bozhou on a 230,000 square meter site. In 2020, Hutchison Baiyunshan surrendered for deregistration its land use rights for an unused portion of its Guangzhou property to the local government for cash consideration. Hutchison Baiyunshan also operates cultivation sites through its subsidiary in Heilongjiang province in China.

See "– *Other Ventures – Shanghai Hutchison Pharmaceuticals*" and "– *Other Ventures – Hutchison Baiyunshan*" for more details on the new facilities of Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan mentioned above.

SALES AND MARKETING

For our Oncology/Immunology operations, our oncology drug sales team in China comprised about 390 staff as of December 31, 2020 (which has expanded to about 520 as of the Latest Practicable Date) to support the commercialization of Elunate, Sulanda and our other innovative drugs, if approved, throughout China. Our oncology drug sales team has the capability to cover over 2,500 oncology hospitals and over 20,000 oncology physicians in China, a network that we estimate represents over 90% of oncology drug sales in China.

For our Other Ventures operations, our in-house sales and marketing team as well as sales representatives of our joint ventures' prescription drugs business directly market and promote prescription drugs and other products to hospitals, clinics, pharmacies and other customers. As of December 31, 2020, Shanghai Hutchison Pharmaceuticals and Hutchison Sinopharm operated a network of approximately 2,300 medical sales representatives covering over 25,300 hospitals in about 320 cities and towns in China.

As is common in the PRC pharmaceutical industry, sales of oncology drugs, other prescription drugs and other products are carried out through third-party distributors. Shanghai Hutchison Pharmaceutical and Hutchison Baiyunshan, both of which are non-consolidated joint ventures of our Company, primarily conduct sales of their products through third-party distributors, while Hutchison Sinopharm, a consolidated joint venture of our Company, relies primarily on direct sales to hospitals and clinics and to a lesser extent on third-party distributors.

We select our distributors based on their business qualifications and marketing capabilities, such as distribution network, customer portfolio, number of sales personnel, credit record, financial strength, market position, logistics, compliance standard and past performance. We also check the qualification of our distributors to ensure that they have obtained the necessary permits, licenses and certifications for the distribution of relevant products, including drug operation permits and GSP certifications.

Our relationship with our distributors is that of seller and buyer and not principal and agent. Legal title to the products as well as all significant risks and rewards associated with the products are transferred to the distributors upon sale. We have no ownership or management control over our distributors.

We enter into distribution agreements with our distributors. While specific terms vary from distributor to distributor, in summary, the key terms of our typical distribution agreements are as follows:

Duration:	Typical term of 12 months, subject to termination by us in certain circumstances, such as breach of applicable law by the distributor.
Rights and obligations of parties involved and geographic or other exclusivity:	The distributor is generally authorized to sell the specified products only within the designated geographical area set out in the distribution agreement and is prohibited from selling the products outside the designated geographical area without our prior consent.

Sales and pricing policies:	The distributor is typically required to sell the products at a price which is not less than the price set out in the price list. Consistent with pharmaceutical industry practice, we offer a discount or rebate if certain sales targets are achieved.
Obsolete stock and products return arrangements:	The distributor is generally not permitted to return products to us unless the products are defective.
Minimum purchase amounts/sales targets:	The distributor is generally not required to purchase a minimum amount of the products but the distribution agreement will generally set out sales targets to be achieved by the distributor.
Sales and inventory reports and estimates:	The distributor is generally required to provide us with monthly reports on sales volumes and inventory levels of the products.
Payment and credit terms:	The distributor is typically required to pay for the products at the time the order is made. We may extend a credit period of up to 90 days for some distributors.

To the best of our knowledge, during the Track Record Period, we did not experience any material non-compliance by our distributors with respect to the terms and conditions of our distribution agreements.

We actively monitor the performance of our distributors, and our distributors are generally required to provide us with periodic market information related to our products that they distribute. Sales returns are only accepted with the requisite approvals from relevant departmental managers. We regularly monitor the inventory level of our distributors in order to identify any unusual inventory levels and the volume of relevant products the distributor resells to hospitals and other medical institutions, which allows us to manage the risk of channel stuffing. Our sales representatives regularly communicate with target hospitals and retail pharmacies as part of our efforts to assess the performance of our distributors. Our distributors generally may not return any unsold products (except for defective products). We regularly monitor the level of sales returns in order to identify and investigate any unusual or material issues. During the Track Record Period, sales returns in our Other Ventures operations were immaterial and accounted for less than 0.5% of the revenue generated by our Other Ventures operations, and there were no sales returns in our Oncology/Immunology operations. We consider that these internal control measures are sufficient to mitigate the risk of channel stuffing for our distributors.

See "*Risk Factors – Risks Relating to Our Dependence on Third Parties – We and our joint ventures rely on our distributors for logistics and distribution services.*" in Item 3D. of our 2020 Annual Report.

In China, prices of pharmaceutical products are regulated by the government to ensure that drugs are offered at affordable prices. In June 2015, the Chinese government abolished the 15-year-old government-led pricing system for drugs, and lifted the maximum retail price requirement for most drugs, including drugs reimbursed by government medical insurance funds, patented drugs, and some other drugs. The government regulates prices mainly by establishing a consolidated procurement mechanism, restructuring medical insurance reimbursement standards and strengthening regulation of medical and pricing practices.

In China, generic prescription drugs must go through a centralized procurement process in the form of government-administered public tenders organized on a provincial or municipal basis in order to be commercially available at public medical institutions owned by the government or owned by state-owned or controlled enterprises. Assessment of the bids takes a number of factors into consideration, including but not limited to bid price, product quality, clinical effectiveness, product safety, level of technology, qualifications and reputation of the manufacturer, after-sale services and innovation. As a result, the prices of our generic prescription drugs under our Other Ventures segment are affected by the bidding process. In addition, in order for our generic prescription drugs to be included in the NRDL and critical illness insurance reimbursement listings, we are subject to price negotiation with the Ministry of Human Resources and Social Security and the relevant authorities at provincial level.

INSURANCE

We maintain insurance policies based on the assessment of our operational needs and industry practice and believe the coverage of the insurance obtained by us is adequate and consistent with the industry norm for our business and operations. Our principal insurance policies cover product liability for fruquintinib, surufatinib, certain prescription drugs and health supplements, property loss due to accidents or natural disasters and adverse events in clinical trials. We do not maintain "key person" insurance. See "*Risk Factors – Other Risks and Risks Relating to Doing Business in China – Product liability claims or lawsuits could cause us, our collaborators or our joint ventures to incur substantial liabilities.*" and "*Risk Factors – Risks Relating to Our Oncology/Immunology Operations and Development of Our Drug Candidates – Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.*" in Item 3D. of our 2020 Annual Report.

INTERNAL CONTROL AND RISK MANAGEMENT

We have established and maintained risk management and internal control policies and procedures that we consider to be appropriate for our business operations, and we are dedicated to continuously improving these policies and procedures. We have adopted and implemented comprehensive risk management policies in various aspects.

Financial Reporting Risk Management

As a public company in the United States, we are subject to the Sarbanes-Oxley Act, together with rules implemented by the SEC, and applicable market regulators. The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal control for financial reporting and disclosure controls and procedures. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements in accordance with U.S. GAAP. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness of our internal control over financial reporting to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, assesses the effectiveness of our internal control over financial reporting based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (2013 Framework) in order to report on the effectiveness of our internal control over financial reporting and describe any material weakness in internal control over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. The effectiveness of our internal control over financial reporting is also tested by our independent registered public accounting firm on an annual basis.

Audit Committee Oversight

Our Audit Committee reviews the effectiveness of our internal control and financial reporting risk management and reviews the policies and procedures for the identification, assessment and reporting of financial and non-financial risks and our management of those risks in accordance with the requirements of the Sarbanes-Oxley Act and other applicable laws, rules and regulations and the applicable requirements of any stock exchange.

Information Security Policy

Our Board has adopted an information security policy to define and help communicate the common policies for information confidentiality, integrity and availability to be applied to the Group and our joint ventures. The purpose of the information security policy is to ensure business continuity by preventing and minimizing the impact of security risks within our company and our joint ventures. Our information security policy applies to all of our and our joint ventures' business entities across all countries. It applies to the creation, communication, storage, transmission and destruction of all different

types of information. It applies to all forms of information, including but not limited to electronic copies, hardcopy, and verbal disclosures whether in person, over the telephone, or by other means.

During the Track Record Period and up to the Latest Practicable Date, we do not believe that we have experienced any material information leakage or loss of sensitive data.

Human Resources Risk Management

We provide regular and specialized training tailored to the needs of our employees in different departments. We regularly organize internal training sessions conducted by senior employees or outside consultants on topics of interest. Our long term goal is to further increase the number of trainings available to all employees as well as measure the success of the trainings.

Our Board has adopted a Code of Ethics to set standards for our directors, officers and employees as are reasonably necessary to promote (i) honest and ethical conduct, including the ethical handling of actual or apparent conflicts of interest between personal and professional relationships; (ii) full, fair, accurate, timely and understandable disclosure in the reports and documents that we file or submit to the applicable stock exchanges, and in any other public communications; (iii) compliance with applicable governmental and regulatory laws, rules, codes and regulations; (iv) prompt internal reporting of any violations of the code of ethics; and (v) accountability for adherence to the code of ethics.

To safeguard against any corruption with the Group, we also have in place an Anti-Bribery and Anti-Corruption Policy, which explains potential corrupt conduct and our anti-corruption measures. The policy imposes restrictions on, among other things, giving or receiving business gifts and hospitality to or from business partners, and each company within our Group has procedures in place for documenting and recording any such business courtesies outside the normal course of business and for employees to report any business courtesies they are offered or receive to a supervisor who then reports it to our management. In addition, it prohibits any employee from using any funds or assets of our Group for political or charitable contributions.

Each of our business units, including our joint ventures, is required to comply with our Anti-Bribery and Anti-Corruption Policy, and they have certain policies, procedures and controls at an entity-level to ensure compliance. Our Anti-Bribery and Anti-Corruption Policy also includes guidelines on the procurement of goods and services by our Group and other business partners which require, among other things, that appropriate levels of diligence are conducted by our personnel in the selection and renewal of new and existing contractors and suppliers and other business partners (such as a joint venture partner) commensurate with the bribery risk associated with a particular relationship. The policy further requires that our business partners and any third parties engaged by our Group be made aware of this policy, all fees and expenses paid to such third parties represent appropriate and justifiable remuneration, which is commercially reasonable under the circumstances, for legitimate services rendered, and we maintain accurate financial records of all payments made and received by us. Moreover, with respect to our sales, each of our distributors is required to enter into a sales or distribution agreement which contains anti-bribery and anti-corruption provisions applicable to the distributor as well as their acknowledgement of our Anti-Bribery and Anti-Corruption Policy.

Compliance with our Anti-Bribery and Anti-Corruption Policy is subject to ongoing review and checking by our internal compliance team which also conducts regular training for our personnel regarding such policy. Our training programs aim to enhance regulation compliance awareness among our employees and summarize the risk points where corruption is likely to occur in the pharmaceutical industry.

Our Board has also adopted a Complaints Procedures, which are anonymous whistle-blowing systems, such as complaint hotlines and e-mail boxes, for the confidential receipt, retention, and treatment of complaints from, or concerns raised by, employees regarding accounting, internal accounting controls and auditing matters as well as illegal or unethical matters. The Complaint Procedures are reviewed by the Audit Committee from time to time as warranted to ensure their

continuing compliance with applicable laws and listing standards as well as their effectiveness. Any complaints received are reviewed and investigated and, if warranted, reported to the chairman of our Audit Committee.

In addition to the foregoing, on a semi-annual basis an internal controls assessment is completed by our Group, as well as our joint ventures, which assesses the effectiveness of internal controls with respect to anti-bribery and anti-corruption measures. Fraud risk assessments are included as part of the foregoing, including assessing various process level controls of each department such as finance, purchase, production, marketing and sales, warehouse, human resources, information technology and research and development. Upon completion of the assessment, our management consolidates the results and investigates any irregularities or exceptions.

Ongoing Measures to Monitor the Implementation of Risk Management Policies

Our Board and management together monitor the implementation of our risk management policies on an ongoing basis to ensure our policies and implementation are effective and sufficient.

ENVIRONMENTAL, WORKPLACE, HEALTH AND SAFETY MATTERS

We and our joint ventures are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We and our joint ventures are therefore subject to PRC laws and regulations concerning the discharge of waste water, gaseous waste and solid waste during our manufacturing processes. We and our joint ventures are required to establish and maintain facilities to dispose of waste and report the volume of waste to the relevant government authorities, which conduct scheduled or unscheduled inspections of our facilities and treatment of such discharge. We and our joint ventures generally contract with third parties for the disposal of these materials and wastes. In addition, we have adopted policies and procedures to instill a culture of environmental management, and our joint venture Shanghai Hutchison Pharmaceuticals has earned ISO 14001 certification (environmental management) and ISO 50001 certification (energy management). Moreover, to help ensure our preparedness and resilience in the event of an environmental incident or emergency, such as fire or leakage of hazardous waste, we have developed an Emergency Plan for Environmental Incidents which is designed to cover risks analysis, internal warning mechanisms, and emergency plans and responses for our Company and our subsidiaries. Our goal is for such plan to enable relief work and contingency arrangements to be made efficiently and effectively. See "*Risk Factors – Other Risks and Risks Relating to Doing Business in China – If we or our joint ventures fail to comply with environmental, health and safety laws and regulations, we or they could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business*." in Item 3D. of our 2020 Annual Report.

We also consider the potential impact of our operations on climate change. To mitigate such impact, we actively explore options for greener manufacturing and operations. For example, our manufacturing facility in Suzhou features equipment and technology that provides purified air conditioning, purified water production, compressed air and an environmental monitoring system. In addition, a new management strategy, named "the three parallels", has been adopted by us. This means that when facilities or installations are planned, measures to prevent pollution and emissions must be included in the (i) design, (ii) construction, and (iii) operation phases in tandem with the principal project.

We focus on protecting the occupational health and safety (OHS) of our employees at work, especially in laboratories and facilities. Our internal Environment, Health and Safety unit offers regular OHS training, ensures that we communicate and engage with employees on related issues, and reviews and improves our safety measures, facilities, equipment and overall infrastructure. We carry out daily, monthly and unscheduled inspections of our laboratories and their safety measures. To continually improve awareness of OHS, safety training and education are tailored and provided for all personnel. Before beginning their roles, new hires are required to attend workshop-level and on-the-job safety

training. In particular, personnel handling hazardous chemicals must receive appropriate training and pass assessments specific to those tasks. Every year, they are trained again to update their OHS qualifications. Furthermore, our laboratories internally disseminate information on safety, environmental protection, regulations and policies from time to time to maintain a high level of awareness among frontline personnel.

We also endorse and support the proposition that "enterprises should give back to society and bear social responsibility". As part of this endeavor, among other activities, we and Shanghai Hutchison Pharmaceuticals have jointly made donations to the Shanghai Charity Foundation to support frontline work towards COVID-19 prevention and control in Hubei Province. In addition, Shanghai Hutchison Pharmaceuticals have donated thermometers to Fengxian District, Shanghai, to support local COVID-19 prevention work. Separately, we have paid visits to various schools under the Shanghai Hutchison Pharmaceuticals School Bookroom project – a national public welfare project launched in 2010 with a theme of "passing knowledge and lighting hope," by which we aim to support the learning and development of primary and secondary school children living in remote areas, ethnic minority areas and rural areas. We have also built a number of book rooms in various provinces or cities, encouraging children's comprehension of books and exploration of knowledge.

In addition to the foregoing, we have adopted a Code of Ethics and Anti-Bribery and Anti-Corruption Policy which are described above under the heading "– Human Resources Risk Management".

During the Track Record Period and up to the Latest Practicable Date, the Group has not had any material non-compliance and has not been subject to any fines or other penalties due to material noncompliance with health, safety or environmental regulations.

We plan to adopt and implement additional policies on environment, social and governance consistent with industry standards and in compliance with the requirements of the Listing Rules within a period of 12 months from the Listing. For example, we plan to establish a sustainability committee to oversee management and advise the Board on the development and implementation of the corporate social responsibility and sustainability initiatives of the Group, which committee will operate pursuant to a written charter. Moreover, we plan to establish additional internal training programs on environment, social and governance compliance requirements, regulatory updates and practicable points to our employees within a period of 12 months from the Listing.

LEGAL AND REGULATORY MATTERS AND COMPLIANCE

Legal Proceedings

From time to time, we may become subject to legal proceedings and claims in the ordinary course of our business, including claims of alleged infringement of patents and other intellectual property rights. As of the Latest Practicable Date, there were no legal or arbitration proceedings pending or, to our knowledge, threatened against us that could have a material adverse effect on our financial condition or results of operations.

Compliance with Laws and Regulations

During the Track Record Period and up to the Latest Practicable Date, we did not have any non-compliance incidents which our Directors believe would, individually or in the aggregate, have a material adverse effect on our financial condition or results of operations.

The following section sets forth supplemental financial information as at and for the years ended December 31, 2018, 2019 and 2020, including certain new disclosures made in connection with the Listing.

The following consolidated financial data for the periods and as of the dates indicated are qualified by reference to and should be read in conjunction with our consolidated financial statements and related notes and Item 5. "Operating and Financial Review and Prospects" in our 2020 Annual Report as well as our unaudited consolidated financial statements as of March 31, 2021 and for the three months ended March 31, 2020 and 2021, which are available on our company website, and the related disclosures contained herein and therein.

CRITICAL ACCOUNTING POLICIES AND SIGNIFICANT JUDGMENTS AND ESTIMATES

Impairment of Goodwill

Goodwill is recorded when the purchase price of an acquisition exceeds the fair value of the net tangible and identified intangible assets acquired. Goodwill is allocated to our reporting units based on the relative expected fair value provided by the acquisition. Reporting units may be operating segments as a whole or an operation one level below an operating segment, referred to as a component. Goodwill is attributable to our Other Ventures' operations.

We perform an annual impairment assessment in the fourth quarter of each year, or more frequently if indicators of potential impairment exist, to determine whether it is more likely than not that the fair value of a reporting unit in which goodwill resides is less than its carrying value. For reporting units in which this assessment concludes that it is more likely than not that the fair value is more than its carrying value, goodwill is not considered impaired and we are not required to perform the goodwill impairment test. Qualitative factors considered in this assessment include industry and market considerations, overall financial performance, and other relevant events and factors affecting the reporting unit. Additionally, as part of this assessment, we may perform a quantitative analysis to support the qualitative factors above by applying sensitivities to assumptions and inputs used in measuring a reporting unit's fair value. For reporting units in which the impairment assessment concludes that it is more likely than not that the fair value is less than its carrying value, we perform the goodwill impairment test, which compares the fair value of the reporting unit to its carrying value. If the fair value of the reporting unit exceeds the carrying value of the net assets assigned to that reporting unit, goodwill is not considered impaired. If the carrying value of the net assets assigned to the reporting unit exceeds the fair value of the reporting unit, an impairment loss shall be recognized in an amount equal to that excess, limited to the total amount of goodwill allocated to that reporting unit.

Our goodwill impairment test uses the income method to estimate a reporting unit's fair value. The income method is based on a discounted future cash flow approach that uses the following assumptions and inputs: revenue, based on assumed market segment growth rates; and appropriate discount rates based on a reporting unit's weighted average cost of capital as determined by considering the observable weighted average cost of capital of comparable companies. Our estimate of market segment growth is based on historical data, various internal estimates, and a variety of external sources. This estimate is developed as part of our routine long-range planning process. We test the reasonableness of the inputs and outcomes of our discounted cash flow analysis against available comparable market data. A reporting unit's carrying value represents the assignment of various assets and liabilities, excluding certain corporate assets and liabilities, such as cash, investments, and debt. We performed the goodwill impairment test and determined that the fair values of the reporting units exceeded their carrying values and considered that impairment was not necessary for any reporting unit.

Our goodwill during the Track Record Period consisted of two components: (i) goodwill attributable to Hutchison Sinopharm of US$2.8 million, US$2.7 million and US$2.9 million as of December 31, 2018, 2019 and 2020, respectively, and (ii) goodwill attributable to Hutchison Healthcare

of US$0.4 million as of December 31, 2018, 2019 and 2020. We completed the annual impairment evaluation of each component and concluded that no impairment of goodwill was necessary during the Track Record Period.

Hutchison Sinopharm – We performed a quantitative analysis of Hutchison Sinopharm's fair value using five-year cash flow projections based on estimated average annual revenue growth rates not exceeding 11.9%, 6.2% and 18.8% for the years ended December 31, 2018, 2019 and 2020, respectively, and estimated post-tax discount rates of 15.7%, 14.0% and 13.0% for the years ended December 31, 2018, 2019 and 2020, respectively. Based on this analysis, the headroom between the fair value and carrying value of Hutchison Sinopharm was approximately US$5.0 million, US$7.1 million and US$51.1 million as of December 31, 2018, 2019 and 2020, respectively. Neither decreasing the estimated average annual revenue growth rate by 1% nor increasing the estimated post-tax discount rate by 1% would have resulted in impairment of goodwill. The headroom would decrease to US$47.3 million (2018: US$2.3 million, 2019: US$5.3 million) with a 1% decrease in the estimated average annual revenue growth rate or to US$43.9 million (2018: US$3.0 million, 2019: US$4.1 million) with a 1% increase in the estimated post-tax discount rate. A 15.9% decrease (2018: 1.9%, 2019: 4.0%) in the estimated average annual revenue growth rate and a 18.3% increase (2018: 2.9%, 2019: 2.7%) in the estimated post-tax discount rate, each taken in isolation, would remove the remaining headroom.

Hutchison Healthcare – We performed a quantitative analysis of Hutchison Healthcare's fair value using five-year cash flow projections based on estimated average annual revenue growth rates not exceeding 14.0%, 10.0% and 10.0% for the years ended December 31, 2018, 2019 and 2020, respectively, and estimated post-tax discount rates of 15.7%, 14.0% and 13.0% for the years ended December 31, 2018, 2019 and 2020, respectively. Based on this analysis, the headroom between fair value and carrying value of Hutchison Healthcare was US$5.4 million, US$11.9 million and US$3.5 million as of December 31, 2018, 2019 and 2020, respectively. Neither decreasing the estimated average annual revenue growth rate by 1% nor increasing the estimated post-tax discount rate by 1% would have resulted in impairment of goodwill. The headroom would decrease to US$2.6 million (2018: US$4.6 million, 2019: US$10.3 million) with a 1% decrease in the estimated average annual revenue growth rate or to US$2.9 million (2018: US$4.8 million, 2019: US$10.4 million) with a 1% increase in the estimated post-tax discount rate. A 4.0% decrease (2018: 7.0%, 2019: 8.5%) in the estimated average annual revenue growth rate and a 10.8% increase (2018: 29.5%, 2019: 25.4%) in the estimated post-tax discount rate, each taken in isolation, would remove the remaining headroom.

In respect of the goodwill recorded in the financial statements of the Company's non-consolidated joint venture Hutchison Baiyunshan prepared under IFRS, an impairment assessment was performed by comparing its carrying value to its recoverable value. The recoverable value was determined based on value-in-use calculations using cash flow projections covering a five-year period with average annual revenue growth rates not exceeding 5.0%, 3.0% and 3.0% for the years ended December 31, 2018, 2019 and 2020, respectively and estimated pre-tax discount rates of 18.1%, 15.9% and 14.9% for the years ended December 31, 2018, 2019 and 2020, respectively. Based on this analysis, the headroom between recoverable value and carrying value of Hutchison Baiyunshan was approximately US$75.3 million, US$230.3 million and US$48.4 million as of December 31, 2018, 2019 and 2020, respectively. A sensitivity analysis was performed, and it was determined that no reasonable change to any key assumptions would cause the carrying value to exceed its recoverable value. No impairment indicator was noted as of December 31, 2020.

KEY COMPONENTS OF RESULTS OF OPERATIONS

Revenues

The following table sets forth the components of revenues of our Other Ventures by product type for the years indicated.

	Year Ended December 31,					
	2018		2019		2020	
	US$'000	%	US$'000	%	US$'000	%
Revenues – Other Ventures						
Prescription drug products	121,169	70.1	141,124	79.2	165,072	83.5
Consumer health products	40,047	23.2	34,390	19.3	32,689	16.5
Services	11,660	6.7	2,584	1.5	—	—
	172,876	100.0	178,098	100.0	197,761	100.0

Operating Expenses

Cost of Revenues

The following table sets forth the components of costs of revenues of our Other Ventures by product type for the years indicated.

	Year Ended December 31,					
	2018		2019		2020	
	US$'000	%	US$'000	%	US$'000	%
Cost of Revenues – Other Ventures						
Prescription drug products	110,168	77.4	133,896	86.2	158,910	90.1
Consumer health products	23,579	16.6	19,447	12.5	17,500	9.9
Services	8,620	6.0	1,929	1.3	—	—
	142,367	100.0	155,272	100.0	176,410	100.0

Equity in Earnings of Equity Investees

Investments in equity investees mainly consisted of our investments in Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan. The fluctuations in the investments in equity investees was primarily due to recording our equity in earnings of equity investees, net of tax, offset by dividends declared by the equity investees.

The following table shows our investments in our equity investee non-consolidated joint ventures as of the dates indicated.

	As of December 31,		
	2018	2019	2020
		US$'000	
Shanghai Hutchison Pharmaceuticals	68,812	76,226	79,408
Hutchison Baiyunshan	60,992	22,271	59,712
Nutrition Science Partners and Others	8,514	447	385
Total	138,318	98,944	139,505

The following table shows the financial position of Shanghai Hutchison Pharmaceuticals, Hutchison Baiyunshan and Nutrition Science Partners as of the dates indicated.

	Shanghai Hutchison Pharmaceuticals			Hutchison Baiyunshan			Nutrition Science Partners		
	As of December 31,								
	2018	2019	2020	2018	2019	2020	2018	2019	2020
	US$'000								
Current assets[1]	124,512	141,268	175,965	116,020	124,704	177,888	17,320	—	—
Non-current assets	98,532	91,098	93,361	100,353	95,096	95,731	—	—	—
Current liabilities	(84,357)	(79,533)	(109,873)	(73,974)	(124,051)	(137,179)	(1,117)	—	—
Non-current liabilities	(6,909)	(6,074)	(6,739)	(17,302)	(48,690)	(16,034)	—	—	—
Net assets[2]	131,778	146,759	152,714	125,097	47,059	120,406	16,203	—	—
Non-controlling interests	—	—	—	(3,113)	(2,518)	(982)	—	—	—
	131,778	146,759	152,714	121,984	44,541	119,424	16,203	—	—

(1) The expected credit loss rates on trade and bills receivables for Shanghai Hutchison Pharmaceuticals and Hutchison Baiyunshan was insignificant and close to zero for the years indicated.

(2) Shanghai Hutchison Pharmaceuticals' balance with related parties are all related to trade except for lease balances and other payables to our Group. Hutchison Baiyunshan's balance with related parties are all related to trade except for dividend balances and other payables to our Group. Nutrition Science Partners' amounts due to related parties are all not related to trade.

PERIOD-TO-PERIOD COMPARISON OF RESULTS OF OPERATIONS

Year Ended December 31, 2019 Compared to Year Ended December 31, 2020

Revenues

Our revenue increased by 11.3% from US$204.9 million for the year ended December 31, 2019 to US$228.0 million for the year ended December 31, 2020, which was caused by increased revenue from both Oncology/Immunology and Other Ventures operations.

Revenue from Oncology/Immunology increased by 12.8% from US$26.8 million for the year ended December 31, 2019 to US$30.2 million for the year ended December 31, 2020, primarily due to an increase in revenue related to the sale of Elunate from US$10.8 million for the year ended December 31, 2019 (of which US$2.7 million was royalty revenue and US$8.1 million was revenue from sales to Eli Lilly) to US$20.0 million for the year ended December 31, 2020 (of which US$4.9 million was royalty revenue, US$11.3 million was revenue from sales of goods primarily to Eli Lilly and US$3.8 million was revenue from promotion and marketing services to Eli Lilly which commenced in October 2020) as a result of the inclusion of Elunate in the 2020 China NRDL. Elunate was included on China's NRDL at an approximately 60% discount to its initial retail price. The inclusion of Elunate resulted in a substantial improvement in sales volume due to the availability of third-party reimbursements. This increase was offset in part by a decrease in revenue related to collaboration research and development services from US$15.5 million for the year ended December 31, 2019 to US$9.8 million for the year ended December 31, 2020 as there was less clinical activity subject to reimbursement from our collaboration partners.

Revenue from our Other Ventures increased by 11.0% from US$178.1 million for the year ended December 31, 2019 to US$197.8 million for the year ended December 31, 2020, primarily due to an increase in sales of prescription drug products. Revenue from sales of prescription drugs increased by 17.0% from US$141.1 million for the year ended December 31, 2019 to US$165.1 million for the year ended December 31, 2020 primarily due to increased sales by our consolidated joint venture Hutchison Sinopharm. The increase was offset in part by lower provision of services which decreased from

US$2.6 million for the year ended December 31, 2019 to nil for the year ended December 31, 2020 after the discontinuation of our distribution of Seroquel in May 2019. This increase was also offset in part by a decrease in sales of consumer health products which decreased by 4.9% from US$34.4 million for the year ended December 31, 2019 to US$32.7 million for the year ended December 31, 2020. This decrease was primarily attributable to decreased sales of infant nutrition products.

Our Other Ventures' results of operations are affected by seasonality.

Equity in Earnings of Equity Investees

Shanghai Hutchison Pharmaceuticals

The following table shows a summary of the results of operations of Shanghai Hutchison Pharmaceuticals for the years indicated:

	Year Ended December 31,			
	2019		2020	
	US$'000	%	US$'000	%
Revenue	272,082	100.0	276,354	100.0
Cost of sales	(77,313)	(28.4)	(72,163)	(26.1)
Selling expenses	(110,591)	(40.6)	(111,892)	(40.5)
Administrative expenses	(14,761)	(5.4)	(17,907)	(6.5)
Other net operating income	2,941	1.1	3,473	1.3
Taxation charge	(11,015)	(4.0)	(10,833)	(3.9)
Profit for the year	61,301	22.5	67,020	24.3
Equity in earnings of equity investee attributable to our Company	30,654	11.3	33,502	12.1

Other net operating income is primarily comprised of government grants and interest income. Other net operating income increased by 18.1% from US$2.9 million for the year ended December 31, 2019 to US$3.5 million for the year ended December 31, 2020, primarily due to higher interest income of US$0.4 million.

Hutchison Baiyunshan

The following table shows a summary of the results of operations of Hutchison Baiyunshan for the years indicated:

	Year Ended December 31,			
	2019		2020	
	US$'000	%	US$'000	%
Revenue	215,403	100.0	232,368	100.0
Cost of sales	(100,279)	(46.6)	(115,564)	(49.7)
Selling expenses	(74,013)	(34.4)	(74,066)	(31.9)
Administrative expenses	(23,817)	(11.1)	(25,664)	(11.0)
Other net operating income	5,626	2.6	6,071	2.6
Gain on return of land	—	—	84,667	36.4
Taxation charge	(3,634)	(1.7)	(16,494)	(7.1)
Profit attributable to equity holders of Hutchison Baiyunshan	19,792	9.2	91,276	39.3
Equity in earnings of equity investee attributable to our Company	9,899	4.6	45,641	19.6

Other net operating income is primarily comprised of government grants, interest income, brand-licensing income and rental income. Other net operating income increased by 7.9% from US$5.6 million for the year ended December 31, 2019 to US$6.1 million for the year ended December 31, 2020, primarily due to higher government grants of $0.3 million and higher brand-licensing income of $0.2 million.

Year Ended December 31, 2018 Compared to Year Ended December 31, 2019

Revenues

Our revenue decreased by 4.3% from US$214.1 million for the year ended December 31, 2018 to US$204.9 million for the year ended December 31, 2019, resulting from decreased revenue from our Oncology/Immunology operations.

Revenue from our Oncology/Immunology operations decreased by 35.0% from US$41.2 million for the year ended December 31, 2018 to US$26.8 million for the year ended December 31, 2019. The decrease was primarily due to the fact that the prior period included the milestone payment of US$13.5 million that we received from Eli Lilly following the approval in September 2018 of Elunate in China for the treatment of mCRC. The decrease was also due to a US$7.0 million reduction in service fees from Nutrition Science Partners. These decreases were partially offset by an increase in revenue related to the sale of Elunate from US$3.6 million for the year ended December 31, 2018 to US$10.8 million for the year ended December 31, 2019.

Revenue from our Other Ventures increased by 3.0% from US$172.9 million for the year ended December 31, 2018 to US$178.1 million for the year ended December 31, 2019. The increase was primarily due to an increase in revenue from our prescription drug products. Revenue from prescription drugs increased by 16.5% from US$121.2 million for the year ended December 31, 2018 to US$141.1 million for year ended December 31, 2019 primarily due to increased sales by our consolidated joint venture Hutchison Sinopharm, despite the depreciation of the renminbi against the U.S. dollar by approximately 5% between the periods (using the weighted average monthly exchange rate for the periods). The increase was offset in part by lower provision of services which decreased by 77.8% from US$11.7 million for the year ended December 31, 2018 to US$2.6 million for the year ended December 31, 2019 after the discontinuation of our distribution of Seroquel in May 2019. This increase was also partially offset by a decrease in sales of consumer health products which decreased by 14.1% from US$40.0 million for the year ended December 31, 2018 to US$34.4 million for the year ended December 31, 2019. This decrease was primarily attributable to decreased sales of products in Hong Kong.

Our Other Ventures' results of operations are affected by seasonality.

Equity in Earnings of Equity Investees

Shanghai Hutchison Pharmaceuticals

The following table shows a summary of the results of operations of Shanghai Hutchison Pharmaceuticals for the periods indicated.

	Year Ended December 31,			
	2018		2019	
	US$'000	%	US$'000	%
Revenue	275,649	100.0	272,082	100.0
Cost of sales	(82,710)	(30.0)	(77,313)	(28.4)
Selling expenses	(111,984)	(40.6)	(110,591)	(40.6)
Administrative expenses	(14,522)	(5.3)	(14,761)	(5.4)
Other net operating income	2,705	1.0	2,941	1.1
Taxation charge	(9,371)	(3.4)	(11,015)	(4.0)
Profit for the year	59,767	21.7	61,301	22.5
Equity in earnings of equity investee attributable to our Company	29,884	10.8	30,654	11.3

Other net operating income increased by 8.7% from US$2.7 million for the year ended December 31, 2018 to US$2.9 million for the year ended December 31, 2019, primarily due to higher government grants.

Hutchison Baiyunshan

The following table shows a summary of the results of operations of Hutchison Baiyunshan for the periods indicated.

	Year Ended December 31,			
	2018		2019	
	US$'000	%	US$'000	%
Revenue	215,838	100.0	215,403	100.0
Cost of sales	(102,701)	(47.6)	(100,279)	(46.6)
Selling expenses	(70,501)	(32.7)	(74,013)	(34.4)
Administrative expenses	(25,997)	(12.0)	(23,817)	(11.1)
Other net operating income	4,085	1.9	5,626	2.6
Taxation charge	(4,227)	(2.0)	(3,634)	(1.7)
Profit attributable to equity holders of Hutchison Baiyunshan	16,860	7.8	19,792	9.2
Equity in earnings of equity investee attributable to our Company	8,430	3.9	9,899	4.6

Other net operating income increased by 37.7% from US$4.1 million for the year ended December 31, 2018 to US$5.6 million for the year ended December 31, 2019, primarily due to higher brand-licensing income.

DISCUSSION OF CERTAIN KEY BALANCE SHEET ITEMS

The table below sets forth selected information from our consolidated balance sheets as of the dates indicated:

	As of December 31,		
	2018	2019	2020
		US$'000	
Total current assets	370,541	317,022	530,740
Total non-current assets	161,577	148,100	193,378
Total assets	532,118	465,122	724,118
Total current liabilities	85,479	113,101	158,397
Total non-current liabilities	34,384	39,118	46,772
Total liabilities	119,863	152,219	205,169
Ordinary shares	66,658	66,691	72,772
Additional paid-in capital	505,585	514,904	822,458
Accumulated losses	(183,004)	(289,734)	(415,591)
Accumulated other comprehensive (loss)/income	(243)	(3,849)	4,477
Total Company's shareholders' equity	388,996	288,012	484,116
Non-controlling interest	23,259	24,891	34,833
Total shareholders' equity	412,255	312,903	518,949

Net Current Assets

The following table sets forth our current assets and current liabilities as of the dates indicated:

	As of December 31,			As of April 30,
	2018	2019	2020	2021
	US$'000			
				(Unaudited)
Current assets:				
Cash and cash equivalents	86,036	121,157	235,630	295,617
Short-term investments	214,915	96,011	199,546	169,969
Accounts receivable – third parties	40,176	41,410	46,648	52,442
Accounts receivable – related parties	2,782	1,844	1,222	1,112
Other receivables, prepayments and deposits	13,434	15,769	26,786	27,694
Amounts due from related parties	889	24,623	1,142	1,142
Inventories	12,309	16,208	19,766	23,094
Total current assets	370,541	317,022	530,740	571,070
Current liabilities:				
Accounts payable	25,625	23,961	31,612	34,249
Other payables, accruals and advance receipts	56,327	81,624	120,882	153,596
Income tax payable	555	1,828	1,120	2,391
Deferred revenue	2,540	2,106	1,597	2,140
Amounts due to related parties	432	366	401	189
Lease liabilities	—	3,216	2,785	4,348
Total current liabilities	85,479	113,101	158,397	196,913
Net current assets	285,062	203,921	372,343	374,157

Our net current assets decreased from US$285.1 million as of December 31, 2018 to US$203.9 million as of December 31, 2019, primarily due to the continued investment in our research and development activities. Our net current assets increased from US$203.9 million as of December 31, 2019 to US$372.3 million as of December 31, 2020, primarily due to proceeds from our follow-on offering on the Nasdaq in January and February 2020 and private placements in July 2020 and November 2020, partially offset by the continued investment in our research and development activities.

As of April 30, 2021, the latest practicable date for the purpose of our net current asset position, our net current assets increased to US$374.2 million from US$372.3 million as of December 31, 2020, primarily due to proceeds from the private placement in April 2021, partially offset by the continued investment in our research and development activities.

Short-term investments

Short-term investments as of the dates indicated below consisted of the following bank deposits:

	As of December 31,		
	2018	2019	2020
		US$'000	
Bank deposits maturing over three months			
Denominated in:			
US$	214,538	73,986	187,961
RMB	—	—	612
HK$	377	22,025	10,973
Total	214,915	96,011	199,546

The weighted average effective interest rate on bank deposits for the years ended December 31, 2018, 2019, 2020 was 2.18% per annum, 2.65% per annum and 1.06% per annum respectively (with maturity ranging from 91 to 100 days, 91 to 129 days and 91 to 180 days, respectively).

Accounts receivable – third parties

Accounts receivable – third parties are recorded at their invoiced amounts, net of allowances for credit losses. An allowance for credit losses is recorded when the collection of the full amount is no longer probable. Management reviews accounts receivable regularly to determine if any receivable will potentially be uncollectible. Accounts receivable are written off after all collection efforts have been exhausted and ceased. The recorded allowance for credit losses was approximately less than US$0.1 million as of December 31, 2018 and 2019 and US$0.1 million as of December 31, 2020, respectively.

Our accounts receivable – third parties balance, net of allowance for credit losses, totaled US$40.2 million, US$41.4 million and US$46.6 million as of December 31, 2018, 2019 and 2020, respectively.

Substantially all accounts receivable are denominated in RMB, US$ and HK$ and are due within one year from the end of the reporting periods. The following table sets forth an aging analysis of our accounts receivable, gross, as of the dates indicated:

	As of December 31,		
	2018	2019	2020
		US$'000	
Not later than 3 months	37,326	37,899	42,434
Between 3 months to 6 months	2,704	2,414	3,118
Between 6 months to 1 year	61	24	23
Later than 1 year	126	1,089	1,168
Total	40,217	41,426	46,743

The movements on the allowance for credit losses are as follows:

	2018	2019	2020	2021
		US$'000		
As at January 1	258	41	16	95
Increase in allowance for credit losses	21	16	95	57
Decrease in allowance due to subsequent collection	(223)	(41)	(18)	(12)
Write-off	(1)	—	—	—
Exchange difference	(14)	—	2	1
As at December 31/April 30[(1)]	41	16	95	141

Note:

(1) As at December 31, 2018, 2019 and 2020 and as at April 30, 2021.

Our credit term for accounts receivable – third parties was generally 30-90 days during the Track Record Period. The average turnover days of such accounts receivable outstanding in 2018, 2019 and 2020 were 72 days, 76 days and 72 days, respectively. The average turnover days of accounts receivable – third parties is calculated by dividing the average balance of accounts receivable owed by third parties as of the beginning and end of the period by total third-party revenue for the relevant period, multiplied by the number of days for the period. As of April 30, 2021, US$41.4 million, or 89%, of the total accounts receivable – third parties outstanding as of December 31, 2020 had been settled. As of April 30, 2021, substantially all accounts receivable – third parties outstanding as of December 31, 2018 and 2019 had been settled (net of credit losses).

Accounts payable

The following table sets forth the total amounts of our accounts payable as of the dates indicated:

	As of December 31,		
	2018	2019	2020
		US$'000	
Accounts payable – third parties	14,158	19,598	26,756
Accounts payable – non-controlling shareholders of subsidiaries	4,960	4,363	4,856
Accounts payable – related party	6,507	—	—
Total	25,625	23,961	31,612

Substantially all accounts payable are denominated in RMB and US$ and are due within one year from the end of the reporting periods. The following table sets forth an aging analysis of our accounts payable as of the dates indicated:

	As of December 31,		
	2018	2019	2020
		US$'000	
Not later than 3 months	19,185	20,658	26,270
Between 3 months to 6 months	5,584	1,846	3,364
Between 6 months to 1 year	703	1,394	782
Later than 1 year	153	63	1,196
Total	25,625	23,961	31,612

Our credit term for accounts payable – third parties was generally 30-90 days during the Track Record Period. The average turnover days of such accounts payable outstanding in 2018, 2019 and 2020

were 49 days, 43 days and 51 days, respectively. The average turnover days of accounts payable – third parties is calculated by dividing the average balance of accounts payable owed to third-parties as of the beginning and end of the period by total cost of purchases from third party suppliers for the relevant period, multiplied by the number of days for the period. As of April 30, 2021, US$27.6 million, or 87% of the total accounts payable outstanding as of December 31, 2020 had been settled. As of April 30, 2021, substantially all accounts payable outstanding as of December 31, 2018 and 2019 had been settled.

Inventory

Our inventories are primarily comprised of prescription drugs and consumer health products sold by our Other Ventures operations and our self-discovered and developed drugs Elunate and Sulanda sold by our Oncology/Immunology operations since 2018 and 2021, respectively. Our average inventory turnover days were 32 days, 33 days and 36 days in 2018, 2019 and 2020, respectively. The average inventory turnover days is calculated by dividing the average balance of inventories as of the beginning and end of the period by total costs of goods for the relevant period, multiplied by the number of days for the period. As of April 30, 2021, we had utilized an aggregate of US$16.6 million, or 84%, of our total inventories as of December 31, 2020.

Other payables, accruals and advance receipts

Other payables, accruals and advance receipts consisted of the following:

	As of December 31,		
	2018	2019	2020
		US$'000	
Accrued salaries and benefits	8,962	13,258	21,982
Accrued research and development expenses[(1)]	28,883	48,531	72,697
Accrued selling and marketing expenses	4,675	3,337	5,747
Accrued administrative and other general expenses	5,934	8,411	10,319
Deferred government grants	1,817	445	374
Deposits	1,230	1,778	1,408
Dividend payable to non-controlling shareholder of a subsidiary	1,282	—	—
Others	3,544	5,864	8,355
Total	56,327	81,624	120,882

Note:

(1) The increase in accrued research and development expenses primarily resulted from a significant expansion of clinical activities.

Accumulated other comprehensive (loss)/income

As the U.S. dollar is the reporting currency used in our consolidated financial statements, the financial statements of our subsidiaries with a functional currency other than the U.S. dollar have been translated into U.S. dollars. All assets and liabilities of the subsidiaries are translated using year-end exchange rates and revenues and expenses are translated at average exchange rates for the year. Translation adjustments are reflected in accumulated other comprehensive (loss)/income in shareholders' equity. We recorded a foreign currency translation loss of US$6.6 million and US$4.3 million for the years ended December 31, 2018 and December 31, 2019, respectively, and a foreign currency translation gain of US$9.5 million for the year ended December 31, 2020 in our consolidated financial statements. These losses and gains primarily resulted from translating the financial statements of our subsidiaries which use the renminbi as their functional currency into U.S. dollars at exchange rates that fluctuated from year to year.

WORKING CAPITAL

Working Capital Sufficiency

Our liquidity and capital resource needs over the next 12 months primarily relate to progressing the development of our drug candidates towards receiving regulatory approval and commencing product commercialization, expanding our drug candidate portfolio, as well as operating expenses and working capital for our Oncology/Immunology marketed products and Other Ventures.

Working Capital Sufficiency Statement

After taking into consideration the financial resources available to us including our cash and cash equivalents on hand, short-term investments, available credit facilities, the expected proceeds from the disposal of Hutchison Baiyunshan, the expected proceeds from the Global Offering and expected dividends from our Other Ventures, in the absence of unforeseeable circumstances, the Directors confirm that we have sufficient working capital to satisfy our liquidity and capital resource needs over the next 12 months from the date of this document.

Our ability to obtain additional funding beyond our anticipated cash needs for the next 12 months following the date of this document, however, is subject to a variety of uncertainties, including our future results of operations, our future business plans, financial condition and cash flows and economic, political and other conditions in the markets where we and our customers and lenders operate.

After due consideration of the above and discussions with the Company, the Joint Sponsors concur with the view of the Directors regarding the working capital sufficiency statement above.

INDEBTEDNESS

During the Track Record Period, we had indebtedness primarily in the form of bank borrowings. The table below sets forth a breakdown of our overall indebtedness as reported in the consolidated balance sheets, as of the dates indicated. All amounts are unsecured and unguaranteed unless otherwise noted.

	As of December 31,			As of April 30,
	2018	2019	2020	2021
	US$'000			
				(Unaudited)
Non-current				
Bank borrowings	26,739	26,818	26,861	26,875
Loan from non-controlling shareholder of a subsidiary	579	579	579	579
Lease liabilities	—	3,049	6,064	6,094
Current				
Lease liabilities	—	3,216	2,785	4,348
Total indebtedness	**27,318**	**33,662**	**36,289**	**37,896**

Bank borrowings are presented net of unamortized debt issuance costs. Lease liabilities were recognized on January 1, 2019 after the adoption of ASC 842, Leases, and presented based on the present value of future lease payments under the Group's lease agreements.

The table below sets forth a maturity profile of our overall indebtedness as of the dates indicated:

	As of December 31,			As of April 30,
	2018	2019	2020	2021
	US$'000			
				(Unaudited)
Indebtedness repayable within:				
Less than one year	—	3,402	3,059	4,665
One to two years	26,923	1,302	29,352	30,031
Two to five years	—	28,865	3,484	2,852
Five years or more	579	579	1,063	989
	27,502	**34,148**	**36,958**	**38,537**
Less: unamortized debt issuance costs and interest	(184)	(486)	(669)	(641)
Total indebtedness	**27,318**	**33,662**	**36,289**	**37,896**

During the Track Record Period and up to the Latest Practicable Date, we had not been in violation of any of the covenants set out in our loan facilities. Our Directors confirm that we are not subject to other material covenants under any agreements with respect to any bank loans or other borrowings. Our Directors also confirm that there was no delay or default in the repayment of borrowings during the Track Record Period. Taking into consideration our financial position, our Directors are of the opinion that we are able to abide by the covenants in our loan facilities amid current market conditions and that our capital raising abilities were not materially affected as of December 31, 2020.

Except as discussed above and below, we did not have any material mortgages, charges, debentures, loan capital, debt securities, loans, bank overdrafts or other similar indebtedness, hire purchase commitments, liabilities under acceptances (other than normal trade bills), lease liabilities, acceptance credits, which are either guaranteed, unguaranteed, secured or unsecured, or guarantees or other contingent liabilities as at close of business on April 30, 2021.

Indebtedness Statement

As of April 30, 2021, being the latest practicable date for the purpose of the indebtedness statement:

- the total balance of our interest-bearing loans on demand or due within one year was nil;
- the total balance of our interest-bearing bank loans due after one year was US$26.9 million;
- the total balance of our loan from non-controlling shareholder of a subsidiary was US$0.6 million;
- lease liabilities were approximately US$10.4 million;
- we had unutilized loan and credit facilities of approximately US$69.4 million;
- other than as disclosed in "– *Indebtedness*" and "– *Contingent Liabilities*" and apart from intra-group liabilities, we had no other debt securities, borrowings, debts, mortgages, charges, acceptance credits, hire purchase commitments, liabilities under acceptances (other than normal trade bills), contingent liabilities or guarantees.

Since April 30, 2021, other than as disclosed above, there has been no material adverse change to our indebtedness. The US$0.6 million loan from non-controlling shareholder of a subsidiary was repaid in May 2021.

KEY FINANCIAL RATIOS

The table below sets forth, as at the dates indicated, certain of our key financial ratios:

	As at December 31,		
	2018	2019	2020
Current ratio[(1)]	433%	280%	335%
Quick ratio[(2)]	419%	266%	323%

Notes:

(1) Current ratio is calculated as current assets divided by current liabilities, multiplied by 100%.

(2) Quick ratio is calculated as current assets minus inventories then divided by current liabilities, multiplied by 100%.

Current Ratio

Our current ratio decreased from 433% as at December 31, 2018 to 280% as at December 31, 2019, primarily due to decrease in short-term investments and increased in other payables, accruals and advanced receipts. Our current ratio then increased to 335% as at December 31, 2020 primarily due to the increase in cash and cash equivalents and short-term investments after our follow-on offering on Nasdaq in January and February 2020 and two private placements completed in July 2020 and November 2020.

Quick Ratio

Our quick ratio decreased from 419% as at December 31, 2018 to 266% as at December 31, 2019, primarily due to decrease in short-term investments and increased in other payables, accruals and advanced receipts. Our quick ratio then increased to 323% as at December 31, 2020 primarily due to the increase in cash and cash equivalents and short-term investments after our follow-on offering on Nasdaq in January and February 2020 and two private placements completed in July 2020 and November 2020.

TREND INFORMATION

Other than as described elsewhere, we are not aware of any trends, uncertainties, demands, commitments or events that are reasonably likely to have a material adverse effect on our revenue, income, profitability, liquidity or capital resources, or that would cause our reported financial information to not be indicative of future operation results or financial condition.

OFF-BALANCE SHEET ARRANGEMENTS

We did not have during the periods presented, and we do not currently have, any material off-balance sheet arrangements.

CONTINGENT LIABILITIES

Other than as disclosed elsewhere, the Group does not have any other significant commitments or contingent liabilities.