亞 盛 醫 藥
Ascentage Pharma

Ascentage Pharma Group International

2023 Interim Results Presentation

August 22, 2023

Disclaimer

DISCLAIMER FOR INVESTOR MATERIALS

By attending the meeting where this presentation is made, or by reading the presentation materials, you agree to be bound by the following limitations:

The information in this presentation has been prepared by representatives of Ascentage Pharma Group International (the "**Company**", and together with its subsidiaries, the "**Group**") for use in presentations by the Group at investor meetings for information purposes. No part of this presentation should form the basis of, or be relied on in connection with, any contract or commitment or investment decision whatsoever.

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

This presentation is based on the economic, regulatory, market and other conditions as in effect on the date hereof. It should be understood that subsequent developments may affect the information contained in this presentation, which neither the Company nor any of its directors, supervisors, officers, partners, employees, affiliates, agents, advisors or representatives is under an obligation to update, revise or affirm.

The information communicated in this presentation contains certain statements that are or may be forward-looking. These statements typically contain words such as "will", "may", "expects", "forecasts", "plans" and "anticipates" and words of similar import. By their nature forward-looking statements involve risk and uncertainty because they relate to events and depend on circumstances that will occur in the future. There may be additional material risks that are currently not considered to be material or of which the Company and its advisors or representatives are unaware. Against the background of these uncertainties, readers should not rely on these forward-looking statements. The Company assumes no responsibility to update forward-looking statements or to adapt them to future events or developments.

This presentation and the information contained herein does not constitute or form part of any offer for sale or subscription of or solicitation or invitation of any offer to buy or subscribe for any securities of the Company or any of its subsidiaries or affiliates in any jurisdiction. This presentation and the information contained herein is highly confidential and being furnished to you solely for your information and may not be reproduced or redistributed in any manner to any other person, in whole or in part. In particular, neither the information contained in this presentation nor any copy hereof may be, directly or indirectly, taken or transmitted into or distributed in the United States, Canada, Australia, Japan, Hong Kong or any other jurisdiction which prohibits the same except in compliance with applicable securities laws. Any failure to comply with this restriction may constitute a violation of U.S. or other national securities laws. No money, securities or other consideration is being solicited, and, if sent in response to this presentation or the information contained herein, will be accepted.

By attending this presentation, you acknowledge that you will be solely responsible for your own assessment of the market and the market position of the Group and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of the business of the Group. Any decision to purchase securities in the context of a proposed offering of securities, if any, should be made solely on the basis of information contained in an offering circular or prospectus prepared in relation to such offering.

By reviewing this presentation, you are deemed to have represented and agreed that you and any customers you represent are either (i) a "qualified institutional buyer" (within the meaning of Rule 144A under the United States Securities Act of 1933, as amended), or (ii) outside the United States. You are also deemed to have represented and agreed that you and any customers you represent are professional investors as defined in the Securities and Futures Ordinance (Chapter 571 of the Laws of Hong Kong) and any rules made thereunder.

Ascentage Pharma

Patient-Centric Innovation | Global Breakthrough Therapies

MISSION To address China and global unmet medical needs

VISION To become a global leading integrated biopharmaceutical company

VALUE Patients first; Innovation-driven; Science-based

Patient-Centric Innovation | Global Breakthrough Therapies

Global leading proprietary innovative products

Olverembatinib is **global best-in-class[1] 3G BCR-ABL TKI** for CML, ALL and solid tumors

Lisaftoclax (APG-2575) is **potentially global best-in-class Bcl-2 inhibitor** and to be the 2nd approved Bcl-2 inhibitor globally

Multiple **first-in-class pipeline assets** in advanced clinical development stages, targeting unmet clinical needs

Rapidly expanding commercial footprint

NRDL covered, olverembatinib is the only marketed 3G BCR-ABL inhibitor in China

Due to olverembatinib's **efficacious, durable, safe and long DoT[2] properties**, number of patients on treatment growing steadily

Commercialization team equipped with **rich experience in hematology field**, laying solid foundation for future commercialization

World-class R&D and manufacturing capabilities

468 issued patents and 1,200+ applications globally

400+ R&D employees executing 40+ clinical trials globally

Comprehensive R&D capabilities, covering entire lifecycle from discovery to registration

cGMP manufacturing facilities qualified by international standards, passing EU QP audit with zero deficiency

Unique competitive advantages combining revolutionary hematology pipeline and powerful commercial model

Well-positioned to capture the US$10bn+ global blood cancer market opportunities

CML	ALL	CLL	AML	MM	MDS
$7.2bn	$2.3 bn	$13.2 bn	$3.1 bn	$25.7 bn	$3.3 bn

[1] Not head-to-head clinical results ; based on released data analysis ; [2] Duration of treatment
Source: Company data, published clinical data, GlobalData, Cerner, ResearchAndMarkets, Coherent Market Insights, company annual reports

Lisaftoclax (APG-2575) received clearance for global registrational Phase III trial for treatment of CLL/SLL

Lisaftoclax (APG-2575)

APPROVED

FDA

Global Phase III Registrational Trial for CLL/SLL

Potentially the 2nd approved Bcl-2 inhibitor globally

- Received clearance from U.S. FDA to initiate global registrational phase III clinical trial
- To treat previously treated CLL/SLL patients
- Lisaftoclax (APG-2575) in combination with BTK inhibitor
- ORR of 98% achieved in r/r CLL/SLL patients when given lisaftoclax (APG-2575) in combination with BTK inhibitor based on global Phase II clinical trial data

Olverembatinib

APPROVED

CDE

Global Phase III Registrational Trial for Ph+ ALL

To become the 1st 3rd generation TKI for first line treatment of Ph+ ALL in China

- Global registrational Phase III study approved by China CDE
- To treat newly diagnosed Ph+ ALL patients (i.e., 1st line treatment)
- Olverembatinib in combination with chemotherapy
- Abundant real-world patient and clinical data demonstrating efficacy and safety

Clinically validated products, well-designed clinical trials, maximizing probability of success

Source: Company data

Olverembatinib commercialization accelerated
Accumulated sales exceeded RMB300m since launch[1]

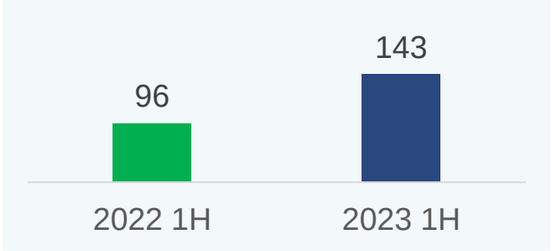
Continuously enhances commercialization capabilities to expand patient reach

Affordability significantly improved since NRDL effective in Mar 2023

Total Revenue
(RMB m)

2023 1H vs 2022 1H

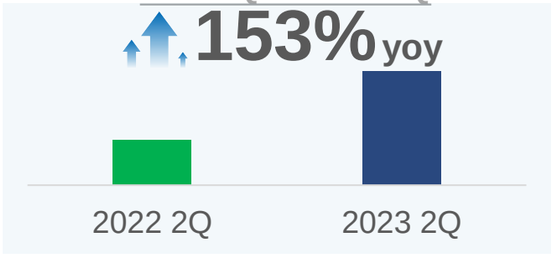
49% yoy



Olverembatinib revenue

2023 2Q vs 2022 2Q

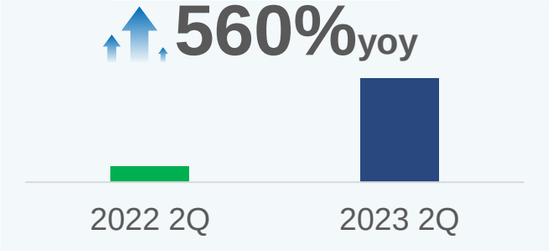
153% yoy



Olverembatinib sales volume

2023 2Q vs 2022 2Q

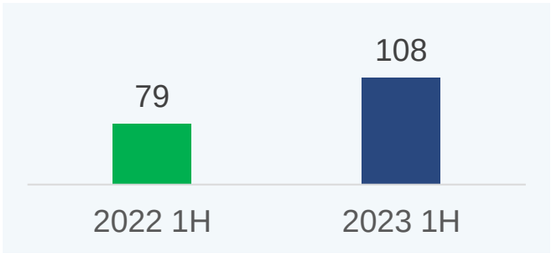
560% yoy



Olverembatinib revenue
(RMB m)

2023 1H vs 2022 1H

37% yoy



- Entered 110 hospitals and 260+ DTP pharmacies[2]
- Future growth drivers:
  - Longer DoT driving growth in number of patients on treatment
  - NDA for CML-CP resistant to 1G and 2G TKIs expected to be approved in China in near term, expanding number of on-label patients
  - Expand indications and potentially to be the 1st TKI for the first-line treatment of Ph+ ALL in China

First and only 3rd generation BCR-ABL TKI in China, establishing strong market position

[1] Since approved by NMPA to launch in Nov 2011, as of Jun 30, 2023; [2] As of Jun 30, 2023

Patient-centric innovation, global cutting-edge targeted therapies, hematology leader

耐立克®
奥雷巴替尼 olverembatinib

Commercialized

CML (Approved)

ALL (Ph 3 registrational trial for 1st line treatment approved)

GIST (Ph 1)

Lisaftoclax (APG-2575)

Registrational trial

CLL/SLL (China pivotal registrational ph 2 trial ongoing and global registrational ph 3 trial approved)

AML (Ph 2)

MDS (Ph 2)

MM (Ph 2)

...

Alrizomadlin (APG-115)

Pelcitoclax (APG-1252)

APG-2449

APG-1387

APG-5918

Other first-in-class

Hematological malignancies and solid tumors

Potential combination treatments

(e.g., alrizomadlin (APG-115) and lisaftoclax (APG-2575) combo to treat r/r pediatric neuroblastoma and other solid tumors)

Data Source: Company data

Pipeline covers all the hematological malignancies and targets US$10bn+ market opportunity

Market potential for indications:

- CML: US$7.2 bn
- ALL: US$2.3 bn

Olverembatinib

US$5.4bn+
market opportunity

Comparable product sales:[1]

- 2G TKI: US$4bn+
- Ponatinib: US$600m+
- Asciminib: US$800m+

+

Market potential for indications:

- CLL: US$13.2 bn
- AML: US$3.1 bn
- MM: US$25.7 bn
- MDS: US$3.3 bn

Lisaftoclax (APG-2575)

US$4bn+
market opportunity

Comparable product sales:[2]

- Venetoclax: US$4bn+

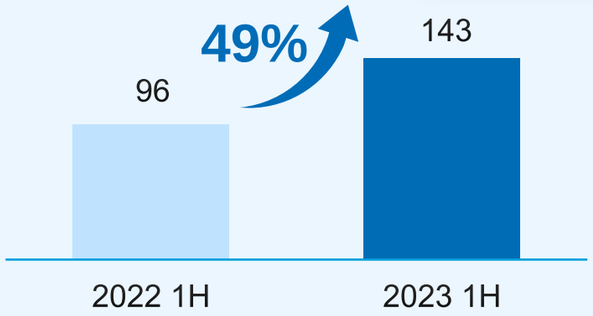
+

Global FIC Pipeline

[1] 2G TKI includes dasatinib and nilotinib, 2022 sales； Ponatinib 2025 forecast sales；Asciminib 2028 forecast sales. [2] Venetoclax 2029 forecast sales
Source: GlobalData, Cerner, Research And Markets, Coherent Market Insights, company annual reports

Financial overview for 1H 2023

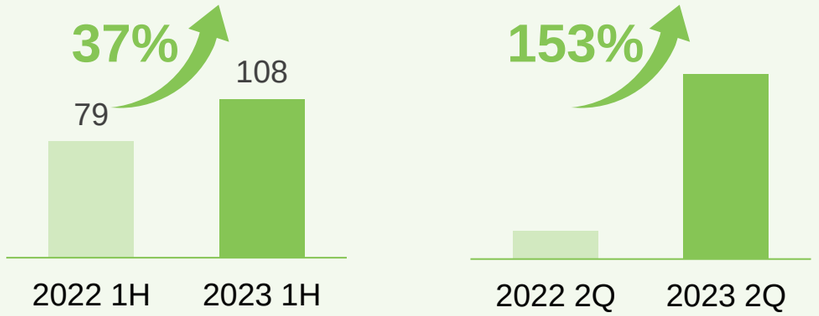
Total revenue[1]
(RMBm)



2023年 1H

Product sales	License fees income	Service income
130m	12.08m	1.09m

Olverembatinib Revenue
(RMBm)



Cash Amount

RMB 1.49Bn

As of 2022.6.30

As of June 30, 2023

RMB 1.58Bn

As of 2023.6.30

In January 2023, Ascentage Pharma successfully raised c. HK$550m through equity placement

Cash Flow from Operations

RMB 130m

vs same period last year

Increased 50%

Source: Company financial data

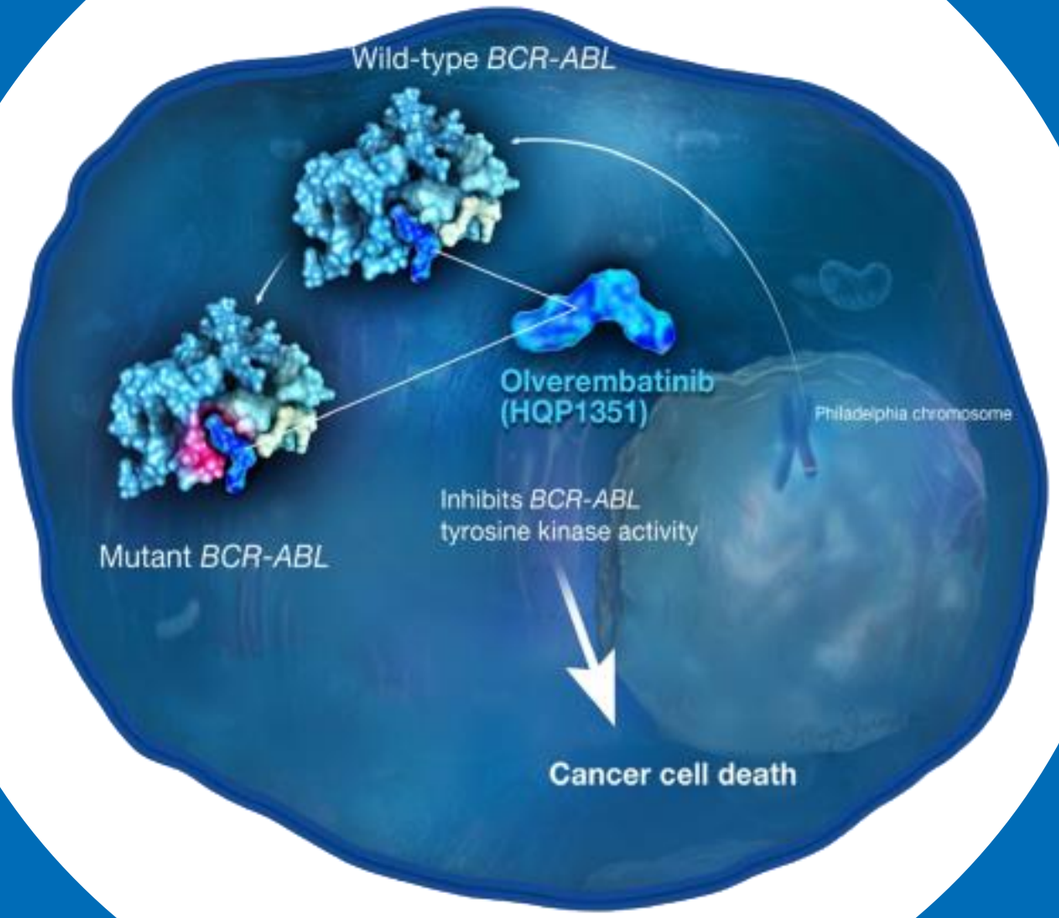
Olverembatinib (HQP1351)

Overview

The first and the only approved and commercialized third generation BCR-ABL inhibitor in China

National Major Pharmaceutical Innovation Project

Global best-in-class



Olverembatinib: Global best-in-class 3rd generation BCR-ABL TKI [1]

Effective in other 3G TKI failed patients

- Effective in CML patients who are **resistant to ponatinib and asciminib** - **83%**[2] CCyR in ponatinib-failed CML patients
- **Stronger inhibition of kinase activity of many mutations or compound mutations other TKIs not sensitive to**[3]

Efficacy

- **Effective and durable anti-leukemic effects** in CML and Ph+ ALL patients including those **harboring T315I mutation**
- **80%** of CML-CP patients achieved MCyR[4]
- Excellent efficacy and safety data in **adult and pediatric Ph+ ALL** patients with potential to be first-line treatment

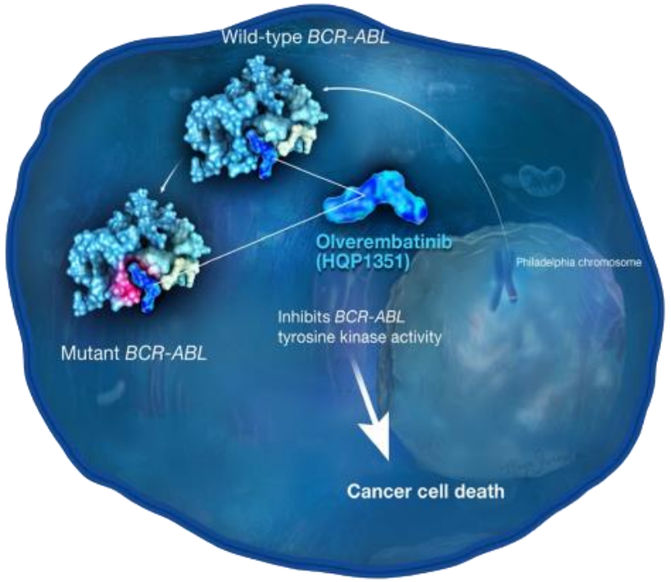
Safety

- **80%** of patient continue treatment after 5 years of treatment
- TRAE decreases over time
- **Hematologic adverse events were mostly mild** and manageable

Global annual sales of 2G and 3G BCR-ABL TKI exceeds US$5bn

[1] Analysis based on published data, not head-to-head comparison trials; [2] Based on preliminary data (Jabbour E et al. ASH (2022) Olverembatinib (HQP1351) Overcomes Ponatinib Resistance in Patients with Heavily Pretreated/Refractory Chronic Myeloid Leukemia (CML) and Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia (Ph+ ALL) 64th ASH annual meeting) ; [3] Based on the results of in vitro studies; [4] Jiang Q et al. (2022) A Five-Year Follow-up on Safety and Efficacy of Olverembatinib (HQP1351), a Novel Third-Generation BCR-ABL Tyrosine Kinase Inhibitor (TKI), in Patients with TKI-Resistant Chronic Myeloid Leukemia (CML) in China
Data Source: Company Data, Released Data

Olverembatinib: The first and the only commercialized 3rd generation BCR-ABL inhibitor in China



CML	**Approved (China)**	For adult patients with TKI-resistant CML-CP or CML-AP harboring T315I mutation
	Soon to be approved (China)	For patients with CML-CP resistant to 1st and 2nd generation TKIs
Ph+ ALL	**Global Ph III pivotal registrational study**	Combo with chemo vs imatinib combo with chemo in newly diagnosed Ph+ ALL patients, potential first-line treatment
	Phase II (China)	In combination with APG-2575 for patients with r/r Ph+ ALL
CML / Ph+ ALL	Global Phase 1b bridging study	For patients with CML or Ph+ ALL who are resistant to 2 TKIs (including ponatinib and asciminib)
GIST	Phase Ib/II (China)	Monotherapy for GIST
		Recommended by CDE for Breakthrough Therapy Designation (BTD) for SDH-deficient GIST

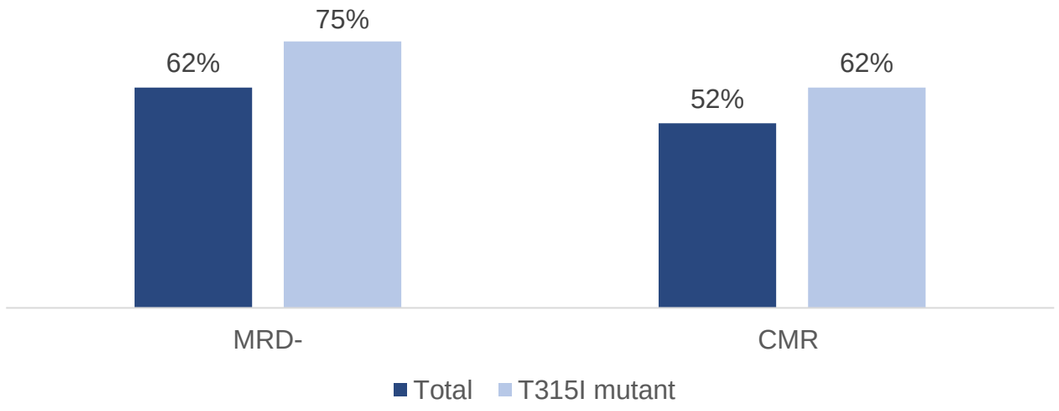
Olverembatinib in patients with Ph+ Acute Lymphoblastic Leukemia

Olverembatinib monotherapy or combo with VP-based low intensive chemotherapy

- 21 pts with Ph/BCR-ABL1+ ALL treated with olverembatinib due to T315I mutation or R/R diseases. T315I mutation detected in 16 pts, including 6 with additional mutations
- MRD- and CMR rates for the entire cohort were 62% and 52%. **In pts with T315I mutation, MRD- and CMR rates were 75% and 62%, respectively**

Conclusion

- Olverembatinib is effective and safe in Chinese adult Ph/BCR-ABL1+ ALL with molecular or hematological R/R disease, **especially in pts with T315I mutation.**

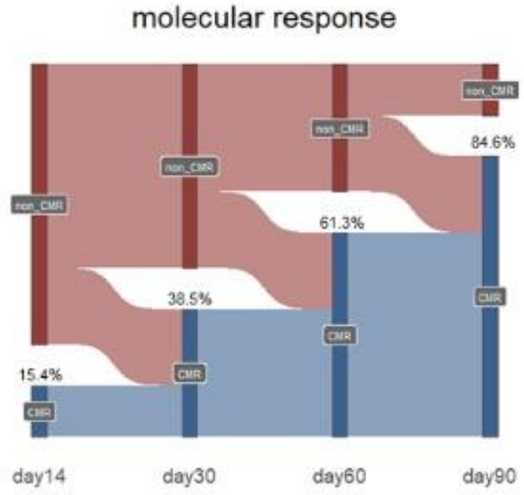


Olverembatinib combo with chemo (Protocol PDT-ALL-2016)

- All 13 enrolled patients had a median follow-up of 8.967 months (range 6.422~11.511) and **achieved Complete Remission, representing an ORR of 100%**
- CMR was achieved in 2/13 (15.4%), 5/13 (38.5%), 8/13 (61.3%), 11/13 (84.6%) on day 14, 30, 60, 90, respectively

Conclusion

- The results of olverembatinib clinical trials demonstrated promising efficacy results and acceptable safety data, indicating that this strategy may become another treatment option in frontline Ph-positive ALL.



Sources:
Kaibo Zhu, et al.(2023), Frontline Combination of Olverembatinib and PDT-ALL-2016 Pediatric Inspired Protocol in Philadelphia Chromosome- Positive Acute Lymphoblastic Leukemia
Weiyang Liu, et al(2023) Efficacy and Safety of the Third-generation TKI Olverembatinib in Adults PH/BCR-ABL1-POSITIVE Acute Lymphoblastic Leukemia with T315I mutation and Relapsed/Refractory Disease

Olverembatinib in pediatric Ph+ ALL patients

Treatment outcomes for children with Ph + ALL remained poor despite the use of intensive chemotherapy, TKI, and consolidative allogeneic hematopoietic cell transplantation.

The 5-year event-free survival rate after first- and second-generation TKI treatment is only 60%. There are limited treatment options and unmet medical needs for r/r Ph+ALL patients.

Efficacy

- 7 patients (age 5.0 to 17.6 years) included in the study, all of whom previously received dasatinib or intolerant to dasatinib
- In monotherapy, **2 out of 3 achieved complete response with negative minimal residual disease (MRD) (<0.01%)**
- Of the 2 evaluable patients treated with olverembatinib in combination with other treatments, **both patients attained remission with negative MRD (<0.01%)**
- Olverembatinib also appeared to contribute to **leukemia control in the CNS**

Safety

- **Excellent safety profile among the 6 evaluable patients.**
- The most frequent complaint was grade 2 extremity pain in 2 patients and grade 2 myopathy of lower extremities in 1 patient. 1 patient had a grade 3 fever and 1 episode of pneumonia, which were relieved by symptomatic therapy or a reduction in drug dose
- **Hematological toxicity was not observed** in the 3 patients treated with olverembatinib monotherapy
- **Hypertriglyceridemia, electrolyte disturbances or cardiac toxicity were not observed**

Olverembatinib exhibits good safety profile in pediatric patients irrespective of their disease status and combinations with other treatments.

Promising efficacy in children with relapsed Ph + ALL, not only in bone marrow but also in CNS.

Source: Xiaolan Li, et al (2023), Olverembatinib Treatment in Pediatric Patients With Relapsed Philadelphia-Chromosome-Positive Acute Lymphoblastic Leukemia

Olverembatinib in patients with TKI-resistant SDH-deficient gastrointestinal stromal tumors (GIST)

Clinical Results

20 evaluable pts with SDH-deficient GIST

Efficacy

- >65% GIST patients failed at least 2 TKI therapies
- The median treatment duration was 7.8 months
- The **longest treatment duration achieved was 42 months**
- **5 PRs were reported**
- **93.8% CBR[1]**

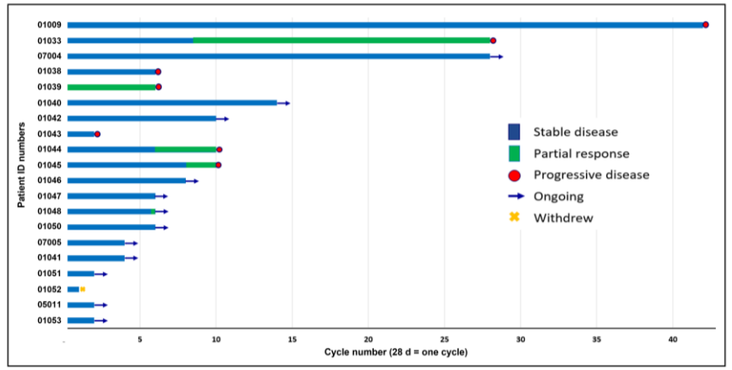
Safety

- Most adverse events were grade 1 or 2; 2 pts experienced grade 3 AEs (9%)
- A total of 15 (75%) pts experienced treatment-related AEs (grade 3 neutropenia [n = 1]). **No serious TRAEs were reported**

Conclusion

- **Olverembatinib was well tolerated**
- **Olverembatinib showed antitumor activity in pts with TKI-resistant, SDH-deficient GIST**

Efficacy



Safety

Treatment-emergent AEs (all grades ≥10%)	
	N = 20
Any AE, no. (%)	20 (100.0)
Anemia	11 (55.5)
Pyrexia	11 (55.5)
Hyperuricemia	10 (50.0)
Increased ALT	10 (50.0)
Increased AST	9 (45.0)
Headache	6 (30.0)
Constipation	5 (25.0)
Pantalgia	4 (20.0)
Fatigue	2 (10.0)
Chest pain	2 (10.0)
Dizziness	2 (10.0)
Infection	2 (10.0)
Proteinuria	2 (10.0)
Myalgia	2 (10.0)

[1] CBR (Clinical benefit rate)=CR+PR+SD>16 weeks

Source：Haibo Qiu et al.(2023), Antitumor activity of olverembatinib (HQP1351) in patients (pts) with tyrosine kinase inhibitor- (TKI-) resistant succinate dehydrogenase- (SDH-) deficient gastrointestinal stromal tumor (GIST)

Lisaftoclax (APG-2575) Overview

Novel, orally administered Bcl-2 selective inhibitor

The 2nd drug entered into pivotal phase II study globally

Best in class potential

Lisaftoclax (APG-2575): Clinically proven, differentiated advantage with best-in-class potential

2nd globally and 1st in China Bcl-2 selective inhibitor entering global registrational clinical trial

Clinically validated

- **700+ subjects** enrolled into lisaftoclax studies, including CLL, AML, MM, MCL, T-PLL, WM, MDS patients
- **300+ CLL patients** treated with lisaftoclax demonstrating promising safety and efficacy data

Efficacy

- Reached **98% ORR** in combination with BTKi in r/r CLL/SLL patients
- Reached **100% ORR** in combination with BTKi in TN CLL/SLL patients
- **Effective in venetoclax-failed and BTKi-resistant patients**

Safety

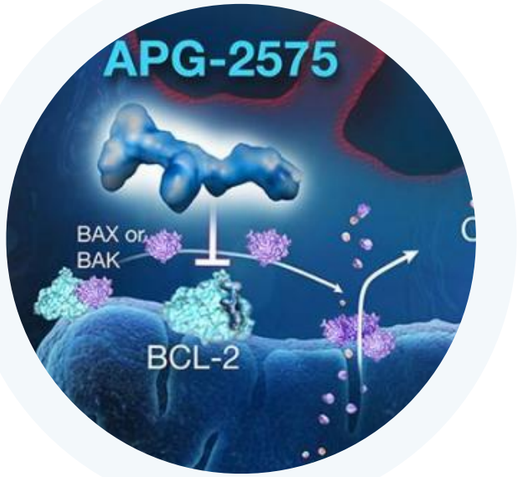
- **Very low clinical TLS**
- No DLTs observed, MTD not reached
- Less neutropenia and thrombocytopenia
- **No DDI observed** in combination with BTK

Unique clinical design

- **Daily dose ramp-up** vs. weekly dose ramp-up
- More convenient to patients and HCPs
- Unique **BTKi combination therapy**

Source: Company data

Lisaftoclax(APG-2575): 700+ patients have been treated, covering multiple diseases

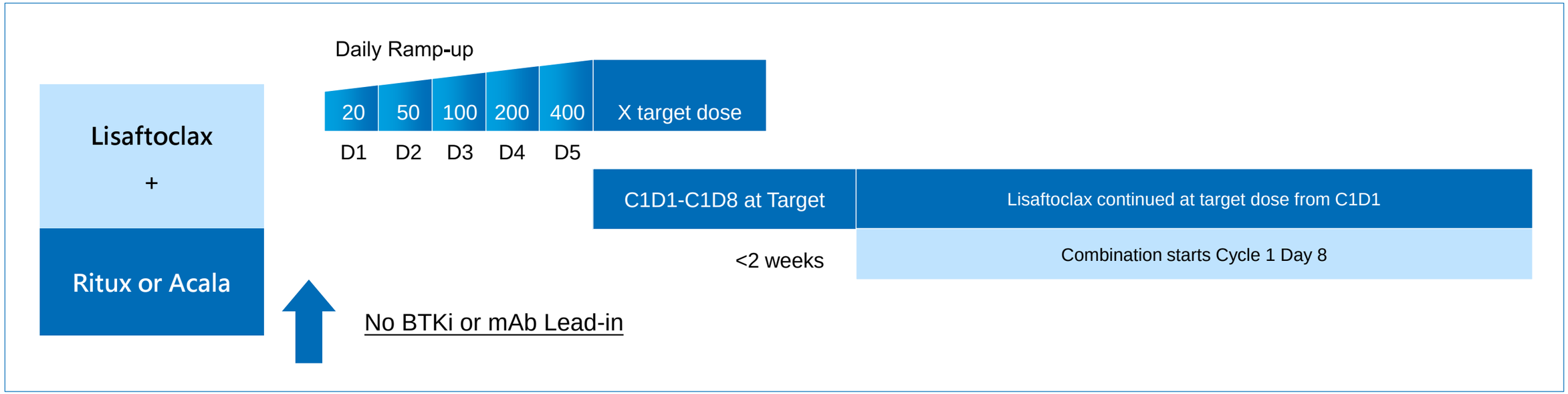


CLL/SLL	**Registrational Phase II study (China)** **Registrational Phase III (Global)**	**Monotherapy for r/r CLL/SLL** **In combination with BTK inhibitors for previously treated CLL/SLL patients**
AML	Phase Ib/II(Global)	Monotherapy/Combination therapy
MDS	Phase Ib/II(Global)	Monotherapy/Combination therapy
WM	Phase Ib/II(Global)	Monotherapy or in combination with ibrutinib/rituximab
MM	Phase Ib/II(Global)	Combination therapy
T-PLL	Phase I(Global)	Combination therapy
MCL	Phase Ib/II(China)	Combination therapy

Unique and differentiated clinical design; global best-in-class potential

★Daily Dose Ramp-up: More convenient to HCPs & patients, lower TLS risks and faster to achieve therapeutic dose

★ Lisaftoclax and BTKi combination therapy can begin quickly (Cycle 1 Day 8)



Source: Davids M et al.(2022) Lisaftoclax (APG-2575) Safety and Activity As Monotherapy or Combined with Acalabrutinib or Rituximab in Patients (pts) with Treatment-Naïve, Relapsed or Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (R/R CLL/SLL): Initial Data from a Phase 2 Global Study, 64th ASH annual meeting

Lisaftoclax (APG-2575) combined with ibrutinib or rituximab in patients with Waldenström macroglobulinemia (WM)

Clinical results

Among the 46 dosed patients, 42 were efficacy-evaluable. Lisaftoclax doses were escalated to 1000, 1200, and 800 mg in Arms A, B and C, respectively.

Efficacy

- 2 VGPRs were reported in Arm B at 800 and 1200 mg. Median (range) time to VGPR was 3.1 (1.8-4.4) months.

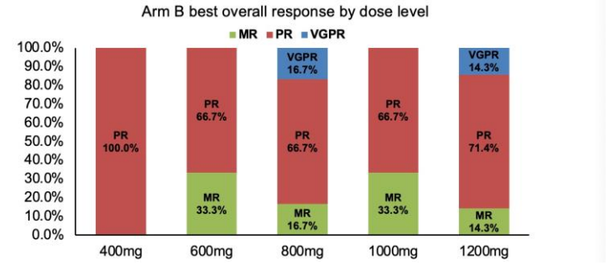
Safety

- Maximum tolerated dose has not been reached. One DLT (grade 3 clinical TLS) was reported in Arm B at 1200 mg, and 1 laboratory TLS in Arm B at 1000 mg. No ventricular arrhythmias reported.
- Lisaftoclax related ≥ grade 3+ AEs included neutropenia (19.5%), leukopenia (4.3%), and 2.2% for anemia, weight loss, sepsis, and TLS (each).

Conclusion

- Lisaftoclax is well tolerated at dose levels of up to 1200 and 1000 mg in patients with naïve and r/r WM, respectively
- Lisaftoclax combined with ibrutinib demonstrated a promising efficacy in treatment-naïve WM patients
- No observable DDI between lisaftoclax and ibrutinib

Best response for Arm B.



le 3. Best overall response by investigator

	Arm A (n = 12)	Arm B (n = 22)	Arm C (n = 8)
Major response rate, n (%)	4 (33.3)	19 (86.4)	3 (37.5)
VGPR		2 (9.1)	
PR	4 (33.3)	17 (77.3)	3 (37.5)
MR	2 (16.7)	3 (13.6)	2 (25)
Time to (TT) response, mo., median (range)			
TT minor response	4.6 (1-9)	1.0 (1-5)	4.4 (1-10)
TT major response	5.9 (1-9)	2.0 (1-21)	4.6 (1-23)

CR: complete response; VGPR: very good partial response; PR: Partial response; MR: minor response; major response: PR+VGPR+CR

Overall safety summary

Category, n (%)	Arm A (n = 14)	Arm B (n = 24)	Arm C (n = 8)
AE ≥ Grade 3	6 (42.9)	12 (50.0)	4 (50.0)
Lisaftoclax-related AE ≥ grade 3	3 (21.4)	6 (25.0)	2 (25.0)
Serious AE	4 (28.6)	12 (50.0)	2 (25.0)
AE leading to death	1 (7.1)[a]	1 (4.2)[b]	
AE leading to lisaftoclax discontinuation		2 (8.3)[c]	
AE leading to lisaftoclax reduction		1 (4.2)[d]	
AE leading to lisaftoclax being withheld	4 (28.6)	17 (70.8)	3 (37.5)
COVID-19 related AE	2 (14.3)	8 (33.3)	3 (37.5)

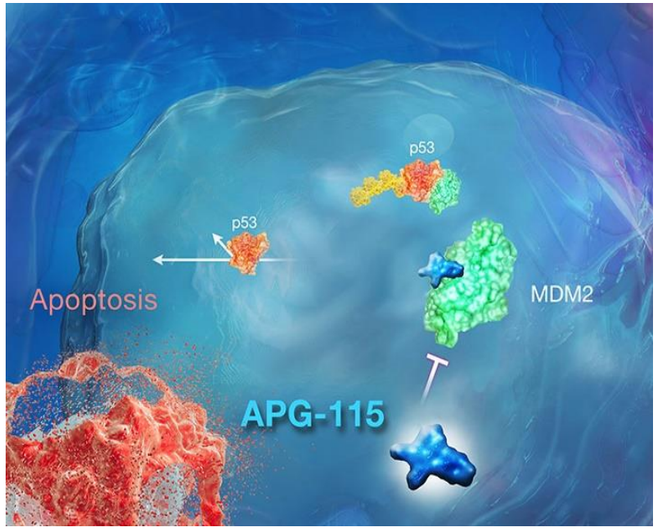
[a]Cerebrovascular accident; [b]Capnocytophaga sepsis; [c]Skin infection and metastatic prostate cancer; [d]neutropenia

Data Source：Sikander Ailawadhi, et al.(2023), Preliminary data of a phase 1b/2 study of BCL-2 inhibitor lisaftoclax (APG-2575) alone or combined with ibrutinib or rituximab in patients (pts) with Waldenström macroglobulinemia (WM)

Alrizomadlin (APG-115)

MDM2-p53 inhibitor

First-in-Class potential



Product highlights

- Orally bioavailable, highly selective, small molecule inhibitor targeting MDM2-p53. Designed to restore the activation of p53 tumor suppressor activity by blocking the MDM2-p53 interaction PPI (protein-protein interaction)
- 6 orphan drug designations (ODDs) from FDA
- 2 rare pediatric disease designations (RPDs) from FDA

Indications targeted by Clinical Development

- Melanomas
- Malignant Peripheral Nerve Sheath Tumor (MPNST)
- AML
- Chronic myelomonocytic leukemia (CMML)
- MDS
- Salivary gland cancer
- Liposarcoma (LPS)
- Neuroblastoma or other solid tumors

Alrizomadlin (APG-115) in combination with Lisaftoclax (APG-2575) has promising potential in the treatment of pediatric tumors

Targeting the MDM2-P53 and BCL-2 apoptosis pathways simultaneously is highly synergic and can achieve "**synthetic lethality**"

Clinical Needs

- Pediatric tumors are the leading cause of death in children
- **The prognosis for these tumors is poor, especially in patients with recurrence and metastasis**
- New therapies are needed to address the unmet clinical needs

Mechanism and Theory

- Compared with adult tumors, pediatric solid tumors are characterized by **low TP53 mutation frequency and high MDM2 amplification frequency,** suggesting that the use of MDM2 inhibitors to restore P53 tumor suppression function is a potential effective treatment strategy
- Multiple preclinical studies suggest that MDM2 inhibitor demonstrates potent activities in multiple pediatric tumor models
- APG-115 in combination with APG-2575 can simultaneously target BCL-2, BCL-xL and MCL-1 and **synergistically trigger apoptosis in cancer cells**

Progress Update

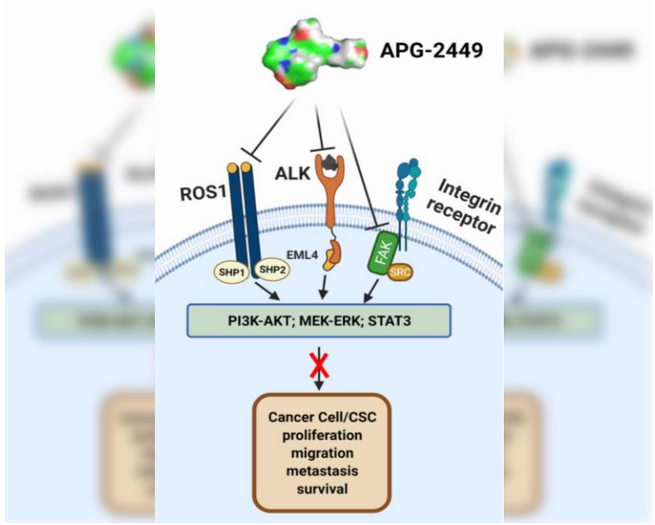
- Phase 1 clinical study of the safety, tolerability, PK and efficacy of APG-115 alone or in combination with Lisaftoclax (APG-2575) is ongoing
- The first dose cohort of APG-115 monotherapy for children with solid tumors did not reach DLT and was **well tolerated**

Source: company data

APG-2449

ALK/FAK/ROS1

triple ligase kinase inhibitor



Potentially the 1st ALK/FAK/ROS1 triple inhibitor globally

- Innovative drug aiming at high FAK-expressing tumors and ALK/ROS1 fusion mutant NSCLC
- Through (1) effective ALK/ROS1 inhibitor and (2) FAK inhibitor in combination with chemotherapy or targeted therapies, effectively coming resistance
- Simultaneous blocking of FAK and ALK can significantly improve efficacy and overcome resistance to ALK single-target inhibitors
- Effective for intracranial lesions in patients with brain metastases
- Well tolerated; no obvious neurotoxicity occurs

Indications targeted in clinical development

NSCLC

ovarian cancer

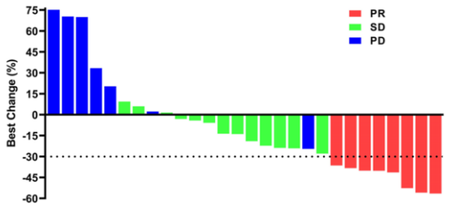
Selected for poster discussion at 2023 ASCO

Source: Fang, D.D., Tao, R., Wang, G. et al. Discovery of a novel ALK/ROS1/FAK inhibitor, APG-2449, in preclinical non-small cell lung cancer and ovarian cancer models. BMC Cancer 22, 752 (2022). https://doi.org/10.1186/s12885-022-09799-4

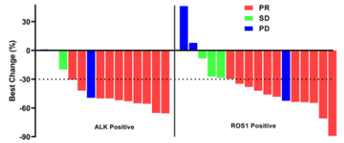
FAK inhibition with novel FAK/ALK inhibitor APG-2449 could overcome resistance to second-generation ALK inhibitors in NSCLC patients

Efficacy

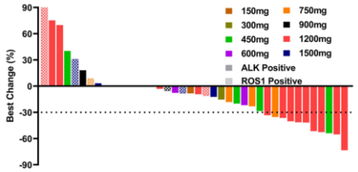
Best tumor response (%) in patients with 2nd gen TKI resistant ALK+ NSCLC



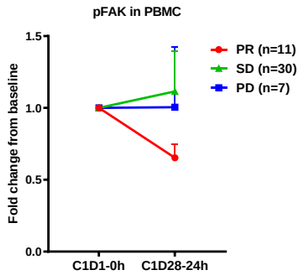
Best tumor response (%) in patients with TKI-naïve ALK/ROS1+ NSCLC



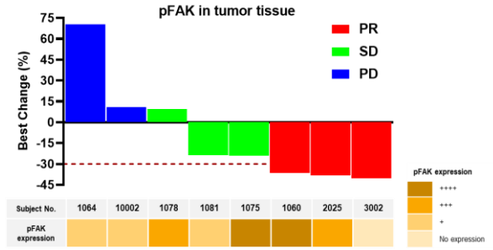
Best tumor response (%) of brain metastases observed in patients with 2nd gen TKI resistant ALK+ NSCLC



pFAK fold change from baseline in PBMCs collected from pts with NSCLC post treatment with APG-2449 at different doses.



Best tumor response vs. pFAK expression at the tumor tissues collected from ALK-TKI resistant 8 pts with NSCLC, who treated with APG-2449 at RP2D.



Clinical results

- In TKI-naïve NSCLC and ROS1+ treatment-naïve patients, ORR was 78.6% and 70.6%, respectively
- Among 28 ALK + NSCLC patients resistant to 2G ALK TKI, 8 achieved PR, ORR 28.6%
- In 13 brain metastases patients resistant to 2G ALK TKI, 8 achieved intracranial PRs, intracranial ORR is 61.5%
- Compared to baseline, those who experienced PR showed greater reduction in phosphorylated FAK (pFAK) levels, patients with higher FAK expression at baseline were likely to achieve deeper clinical responses to APG-2449
- APG-2449 was well tolerated. There was no neurotoxicity in 136 NSCLC patients receiving APG-2449

Conclusion

- APG-2449 showed a favorable preliminary safety profile and antitumor activity in patients with NSCLC
- FAK inhibition may be a novel approach to overcome ALK resistance in NSCLC patients resistant to 2G ALK inhibitors

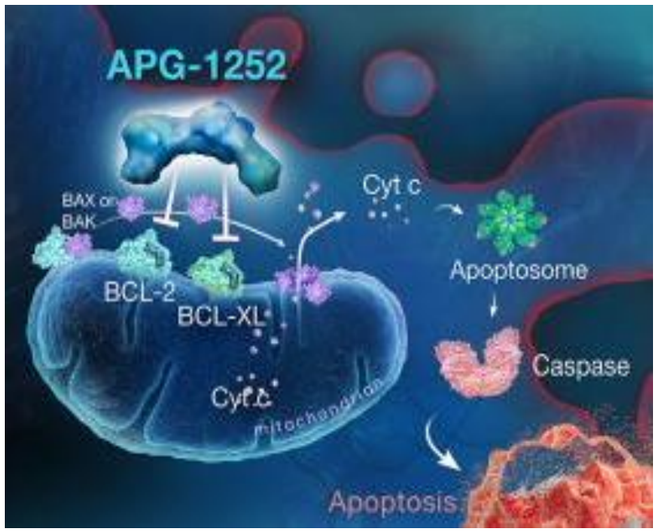
Safety

	Any grade	≥ Grade 3
Population	136	136
Subjects with at least one TRAE, n (%)	123 (90.4)	19 (14.0)
Preferred term, n (%)		
Increased blood creatinine	63 (46.3)	0
Increased ALT	55 (40.4)	4 (2.9)
Increased AST	45 (33.1)	1 (0.7)
Nausea	37 (27.2)	1 (0.7)
Vomiting	31 (22.8)	2 (1.5)
Decreased leukocyte count	30 (22.1)	1 (0.7)
Diarrhea	29 (21.3)	0
Decreased neutrophil count	24 (17.6)	1 (0.7)
Rash	17 (12.5)	0

Source：Yuxiang Ma, et al.(2023), FAK inhibition with novel FAK/ALK inhibitor APG-2449 could overcome resistance in NSCLC patients who are resistant to second-generation ALK inhibitors

Pelcitoclax (APG-1252)

Bcl-2/Bcl-xL inhibitor



Product highlights

- Restore apoptosis through dual inhibition of the Bcl-2 and Bcl-xL proteins
- Novel combination in solid tumors and hematologic malignancies
- ODD received from FDA for the treatment of SCLC
- A total of 205 patients have been treated with pelcitoclax as monotherapy or in combination with other anti-tumor agents

Indications targeted in clinical development

SCLC
NSCLC

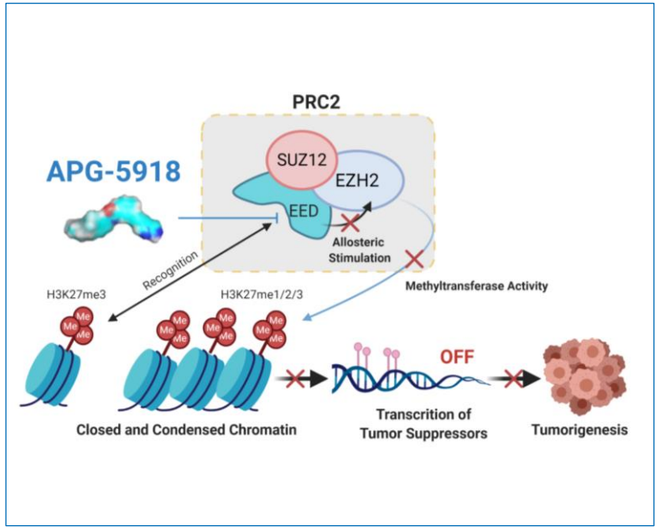
Neuroendocrine tumor (NET)

Non-Hodgkin's lymphoma (NHL)

To release latest clinical results at 2023 ESMO

APG-5918

EED inhibitor



China's first EED inhibitor to enter clinical trials

- APG-5918 binds to the H3K27me3-interacting EED domain, resulting in a conformational change in the EED H3K27me3 binding pocket, and prevents EED from interacting with histone methyltransferase EZH2
- APG-5918 has potent in vitro and in vivo targeted pharmacological activity in cancer cell lines and xenograft models

Indications targeted in clinical development

Solid tumors and hematologic malignancies

Anemia

Addressing patient needs through innovative therapeutics to create massive global market opportunities

China sales

Global sales

First proprietary product approved

Olverembatinib approved in China, validating R&D capabilities

2021

Successfully built out commercial infrastructure

RMB200m sales in the first year of launch. Included in NRDL at favorable rate

Suzhou R&D HQ and manufacturing facilities operational

2022

Clinical development accelerates: more indications approved

Olverembatinib full approval for CML in China. Initiate global Phase III registrational trial for Ph+ ALL

Initiate lisaftoclax (APG-2575) global registrational trial for CLL/SLL

2023

Twin product engines driving sales

Lisaftoclax (APG-2575) approved in China. Global registrational trial completes

Olverembatinib global registrational trials for further indications commence

More pipeline products entering late-stage clinical trials

2024-25

Leading international biopharma with multiple blockbuster products

Lisaftoclax (APG-2575) and olverembatinib enter global markets, continue to expand indications to cover all major hematological malignancies

Fund future product development with ample cash flows

2026 - beyond

Data source: Company data

Patient-Centric Innovation | Global Breakthrough Therapies

Products strategically target the US$10bn+ global blood cancer market

- Products cover all major hematological malignancies, with each product facing billion-dollar market

Focus on global FIC and BIC products with unique and valuable advantages

- Unique clinical advantages establish commercial value, driving global market penetration
- Cross-product combination create significant synergies

Olverembatinib commercialized; APG-2575 entered in global registrational Phase III study

- Key products have begun global pivotal trials. International sales to be generated in the foreseeable future

468 issued patents and 1,200+ applications globally, providing multi-layered, all-round protection for products and core technologies

Global leading R&D team possesses comprehensive capabilities, seamlessly executing the entire R&D lifecycle from discovery to registration

Accelerating growth of olverembatinib sales propelled by increasing prescriptions under NRDL coverage

IR@ASCENTAGE.COM

Ascentage Pharma Group International

68 Xinqing Road, Suzhou Industrial Park,
Suzhou, Jiangsu, PRC

亞 盛 醫 藥
Ascentage Pharma