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Ascentage Pharma
(Ticker: 6855.HK)

2023 Annual Results & Business Updates

March 28, 2024

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Ascentage Pharma

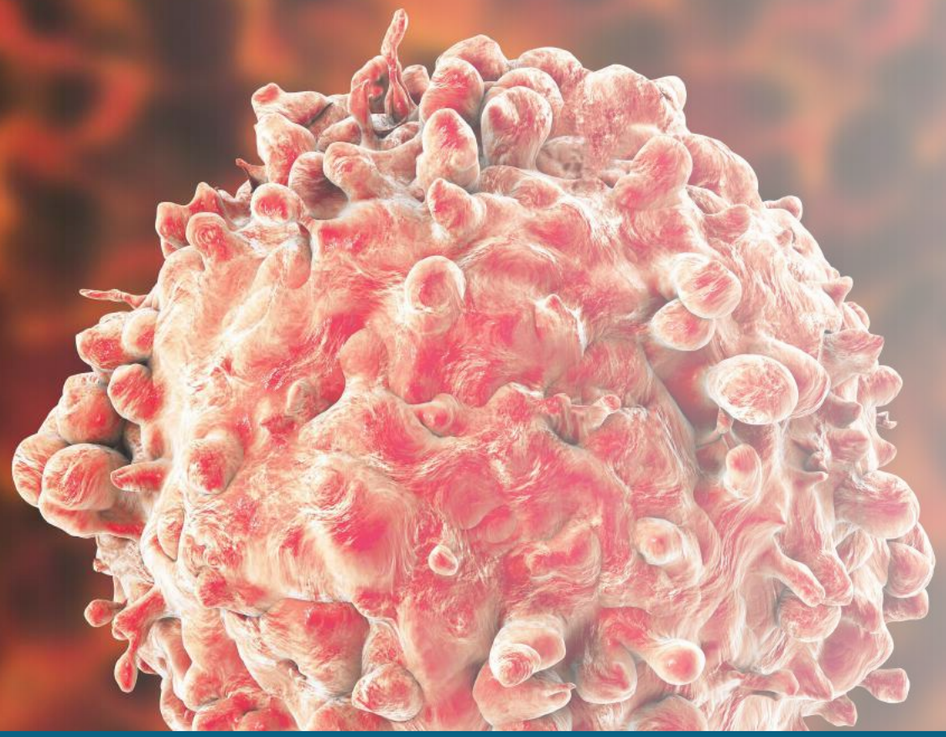
Patient-Centric Innovation | Global Breakthrough Therapies

VISION To become a global leading integrated biopharmaceutical company

MISSION To address global unmet medical needs

VALUE Patients first; Science-based; Data-driven

Blood cancer market at a glance



1.24 million

Global blood cancer annual incidence

US$90bn

Global hematological malignancy treatment market (2028E)

6%

of all cancer cases

30%

of total cancer therapy market

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

With proper treatments keeping the disease at bay, patients with certain blood cancers such as chronic myeloid leukemia (CML) can expect to have a normal length of life

Source: American Cancer Society, Mordor Intelligence, Leukemia and Lymphoma Society, Company forecast and data

Key milestones since beginning of 2023 – executing global registrational trials

CLEARANCE FROM FDA AND CDE FOR GLOBAL REGISTRATIONAL TRIALS

Olverembatinib

FDA

- CML
- Monotherapy
- r/r patients

CDE

- Ph+ ALL
- Combination with chemo
- 1L

Lisaftoclax

FDA

- CLL/SLL
- Combination with BTKi
- Patients previously treated with BTKi

CDE

- AML
- Combination with azacitidine
- 1L unfit/elderly patients

CDE

- CLL/SLL
- Combination with acalabrutinib
- 1L

CDE

★ To submit NDA in China in 2024 ★

- CLL/SLL
- Monotherapy
- r/r patients

Global registrational trial clearance received since 2023

Source: company data

Key milestones since beginning of 2023 – continuing to lead global innovation

40+ PUBLICATIONS AT INTERNATIONAL CONGRESSES AND LITERATURES; 498 ISSUED PATENTS GLOBALLY

20+ publications

Oral report on olverembatinib for 6 years in row,
Data release on Lisaftoclax MM, AML, etc

4 publications

Olverembatinib, lisaftoclax, APG-115, APG-2449

2 publications

Oral report on APG-1252

2 publications

Olverembatinib

3 publications

Olverembatinib, lisaftoclax, APG-115

Clinical Cancer Research

Neoplasia Research

cancers

Annals of Hematology

EXPERT OPINION ON THERAPEUTIC PATENTS

FUNCTIONAL & INTEGRATIVE GENOMICS

Blood Cancer Journal

JPBA Journal of Pharmaceutical and Biomedical Analysis

CLINICAL LYMPHOMA, MYELOMA & LEUKEMIA

Source: company data

Key milestones since beginning of 2023 – Olverembatinib new indicationa approval & NRDL inclusion

OLVEREMBATINIB APPROVED FOR NEW INDICATION, BENEFITING MORE PATIENTS

Full approval in November 2023

- Approved for CML-CP adult patients who are resistant and/or intolerant to 1G and 2G TKIs
- 1st and only marketed 3G BCR-ABL TKI in China

Expanding market potential in China

200K+ Existing CML patient pool in China

20-30k Annual new cases

Resistance to 1G and 2G TKIs is common

NRDL coverage since March 2023

- Favorable price under NRDL while significantly improving access and affordability
- 10,000+ patient treatment cycles since NRDL coverage
- Entered 526 hospital listings and DTP pharmacies

Recognized by NCCN

Included in Emerging Treatment Options for CML

NCCN National Comprehensive Cancer Network®

Source: Company data

Accumulated sales revenue of olverembatinib reached RMB362 million[1]
Commercial breakeven for olverembatinib achieved in 2023

Since NRDL inclusion, affordability significantly increased

Sales volume increased ↑ 259%

Number of hospitals listed increased ↑ 567%

Total patients treated increased ↑ 123%

As sales and marketing efficiency improved, olverembatinib achieved commercial breakeven in 2023

Total revenue in 2023 ▶ 222m RMB

Product sales revenue in 2023 ▶ 194m RMB

Cash inflow from operations ▶ 263m RMB

Through accelerating hospital entry, accumulating patients on treatment and lengthening DoT, sales in 2024 is expected to continue to grow, providing sustainable operating cash flows for Ascentage

[1] since NMPA approval in November 2021, as of year end 2023, including VAT

Best-in-class product portfolio: targeting US$10bn+ global markets

Olverembatinib

Global best-in-class 3rd gen BCR-ABL TKI

Commercialized

- Effective in 1G/2G/3G TKI (including ponatinib and asciminib) resistant/intolerant CML patients
- Safety profile suitable for long duration of treatment (DoT)
- Commercialized in China for CML; NRDL[1] covered
- Global phase 3 registrational trial for Ph+ ALL
- **Global registrational phase 3 trial for CML, cleared by FDA**

US$6bn global market[2]

Lisaftoclax

2nd Bcl-2 inhibitor globally

China launch in 2025

- Best-in-class potential with better safety profile and dose ramp-up schedule than venetoclax[4]
- 100% and 98% ORR in combination with BTKi in treatment-naïve and R/R CLL/SLL patients, respectively
- **Global registrational phase 3 trial for CLL, cleared by FDA**

US$4bn global market[3]

[1] National Reimbursement Drug List, [2] Represents 2G TKI 2022 sales, ponatinib 2025 forecast sales and asciminib 2028 forecast sales. [3] Represents venetoclax 2029 forecast sales; [4] Not head-to-head clinical results ; based on released data analysis
Source: Company data, published clinical data

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** - **53%**[2] CCyR in ponatinib-failed CML patients
- **Stronger inhibition than other TKIs of kinase activity of many mutations or compound mutations** [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]
- Demonstrated efficacy and safety profile in **adult and pediatric Ph+ ALL** patients with potential to be first-line treatment

Safety

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

Global peak sales for 2G and 3G BCR-ABL TKI at US$6bn

[1] Analysis based on published data, not head-to-head comparison trials; [2] Jabbour E, et al. (ASH 2023) Update of olverembatinib (HQP1351) overcoming ponatinib and/or asciminib resistance in patients (pts) with heavily pretreated/refractory chronic myeloid leukemia (CML) and Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) ; [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
Source: company data and public literature

Next steps: Execute global registrational trial for Ph+ ALL and CML

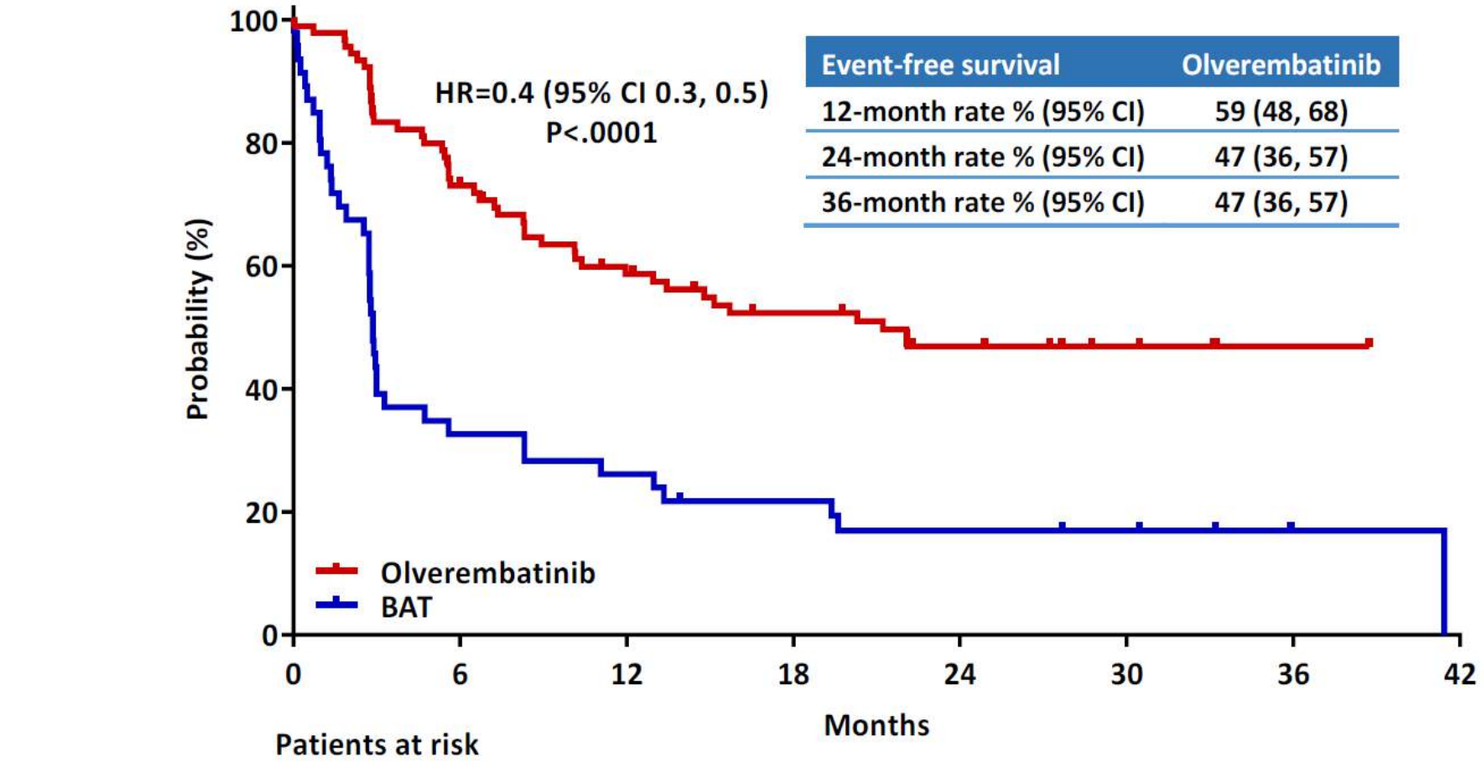
	Phase 1 and 2	Registrational	Approved
CML	For patients with TKI-resistant CML-CP or CML-AP harboring T315I mutation		✓ Approved in China
	For adult patients with CML-CP resistant and/or intolerant to 1st and 2nd generation TKIs		✓ Approved in China
	r/r CML	Cleared by FDA to commence global registrational phase 3 clinical trial	
Ph+ ALL	Combo with chemo in newly diagnosed patients (first-line treatment)	Patient enrollment begun	
	Combo with APG-2575 for patients with r/r Ph+ ALL	Strong synergistic therapeutic value	
GIST	Monotherapy for SDH-deficient GIST	Large unmet medical needs	

Source: Company data

Registrational phase 2 study: Efficacy versus Best Available Treatment (BAT)[1] in TKI-resistant CML-CP patients

Olverembatinib significantly improved event-free survival (EFS) at 21.22 months, compared with BAT arm EFS at 2.86 months

Olverembatinib reduced the event risk 65%, compared with the BAT control arm



Event-free survival	Olverembatinib
12-month rate % (95% CI)	59 (48, 68)
24-month rate % (95% CI)	47 (36, 57)
36-month rate % (95% CI)	47 (36, 57)

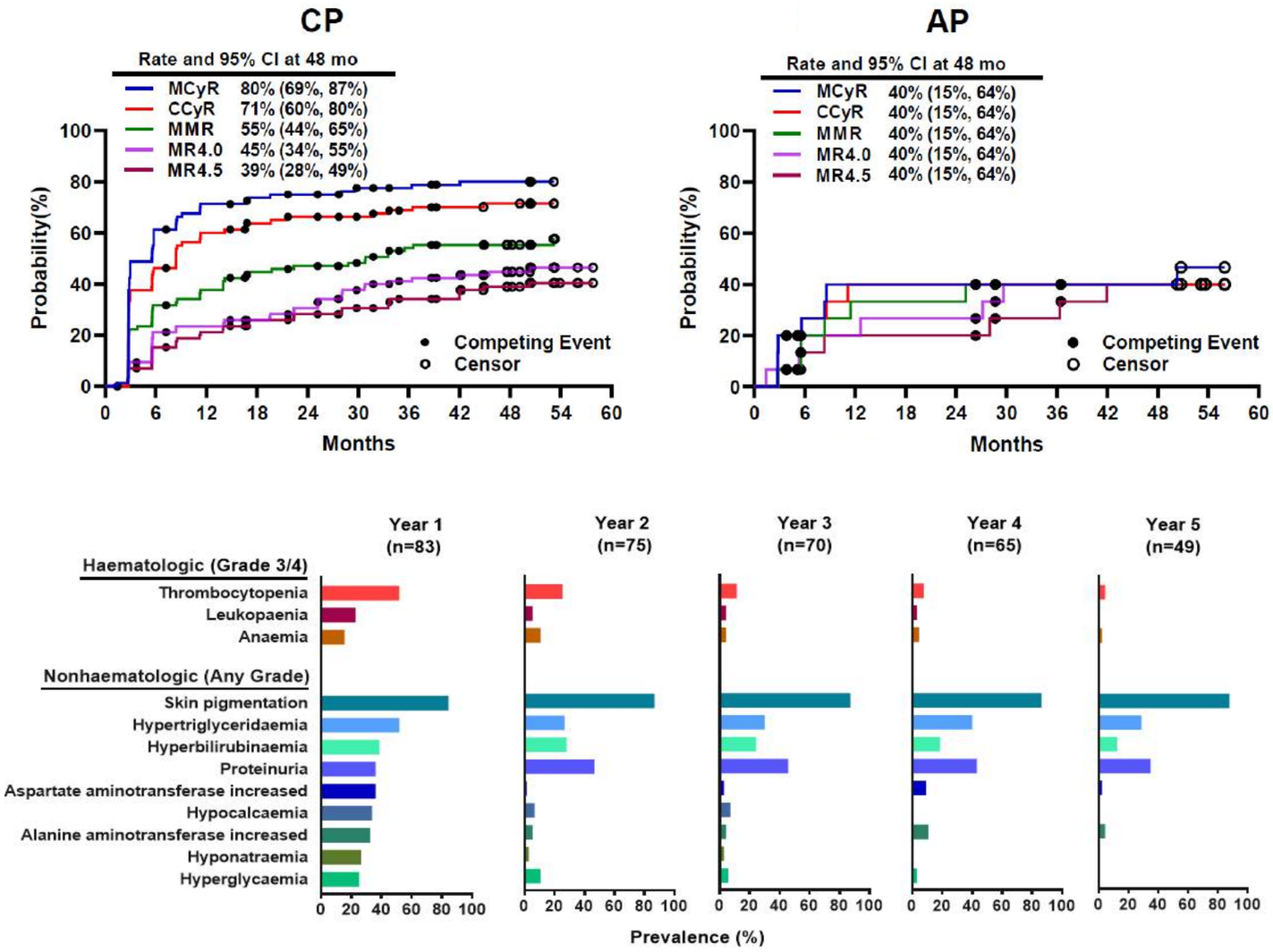
Patients at risk

Olverembatinib	96	63	48	40	32	17	6	0
BAT	48	15	12	9	7	5	1	0

[1] BAT includes interferon, hydroxyurea, and homoharringtonine or TKIs (imatinib, dasatinib, and nilotinib) and combinations

Source: Jiang Q, et al. (ASH 2023) Olverembatinib Demonstrates Efficacy versus Best Available Therapy in Patients with Tyrosine Kinase Inhibitor-Resistant Chronic Myeloid Leukemia in Chronic-Phase in a Registrational Randomized Phase 2 Study

5-year data on R/R CML from phase 1 study: Durable efficacy and differentiated safety profile



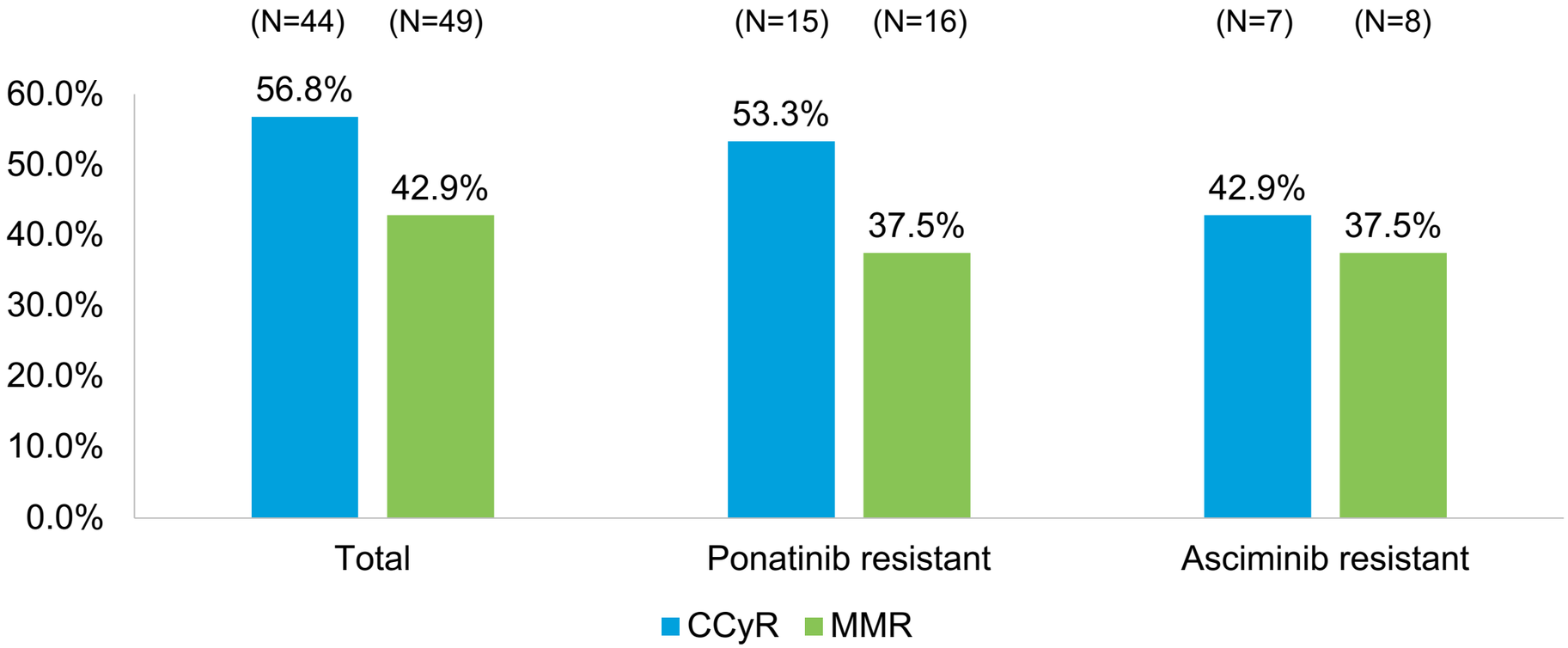
- ✓ 80% and 71% of CML-CP patients achieved MCyR and CCyR, respectively
- ✓ Therapy responses increased over time and correlated with favorable long-term outcomes
- ✓ 80% of patients remain on therapy for more than 5 years
- ✓ Prevalence of most TRAEs decreased over time

MCyR = major cytogenetic responses, CCyR = complete cytogenetic responses, MMR = major molecular responses

Source: 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

Global phase 2 study: Favorable clinical benefit and tolerability in heavily pretreated, particularly ponatinib- or asciminib-failed patients

Olverembatinib monotherapy in heavily pre-treated CML-CP patients



Olverembatinib monotherapy is efficacious and well tolerated in patients with TKI-refractory CML and Ph+ ALL patients

In ponatinib resistant CML patients, 53.3% of the patients achieved CCyR and 37.5% of patients achieved MMR

Source: Jabbour E, et al. (ASH 2023) Update of olverembatinib (HQP1351) overcoming ponatinib and/or asciminib resistance in patients (pts) with heavily pretreated/refractory chronic myeloid leukemia (CML) and Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL)

Potentially constitute the cornerstone treatment for 1L therapy for Ph+ ALL

Olverembatinib combination therapies as 1L treatment for Ph+ ALL demonstrated deep response in real world data, and may potentially offer a “chemo-free” treatment option

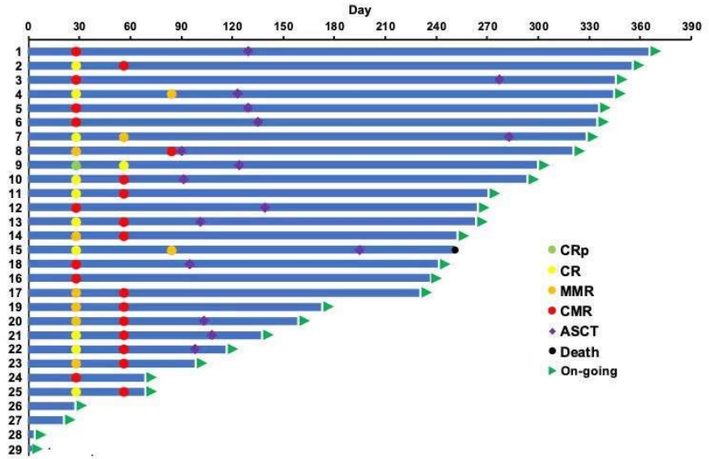
Olverembatinib + venetoclax and reduced-intensity chemo as 1L treatment

Response	n/N (%)
CR/CRi	45/45 (100)
CR	43 (95.6)
CRi	2 (4.4)
Early death	0/45 (0)
CMR*	
after cycle 1	24/45 (53.3)
after cycle 2	27/45 (60.0)
after cycle 3	28/45 (62.2)

At the end of cycle 1, 100% pts achieved CR

53.3% of patients achieved CMR

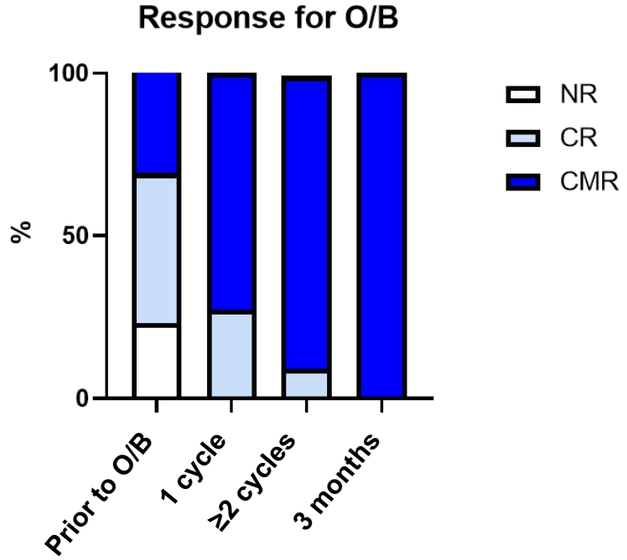
Olverembatinib + VP for 1L Ph+ ALL



100% ORR

83% CMR at 12 weeks

Olverembatinib + blinatumomab (Chemo-free)



100% CMR at 3 months

Source: Gong X, et al. (ASH 2023) Olverembatinib Combined With Venetoclax and Reduced-Intensity Chemotherapy for Patients with Newly Diagnosed Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia: Early results from a phase II study; G. Xu, et al. (ASH2023), Combination of Olverembatinib and VP Regimen As First-Line Therapy for Adult Patients with Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia; Zhang T, et al. (ASH 2023) Frontline combination of 3rd generation TKI olverembatinib and blinatumomab for Ph+/Ph-like ALL patients

Lisaftoclax to launch in China in 2025
FDA clearance for phase 3 registrational trial

Globally the 2nd Bcl-2 selective inhibitor entering global registrational clinical trial

China launch in 2025 for r/r CLL

To submit NDA in 2024 and to be approved in 2025

Global registrational Ph3 for CLL

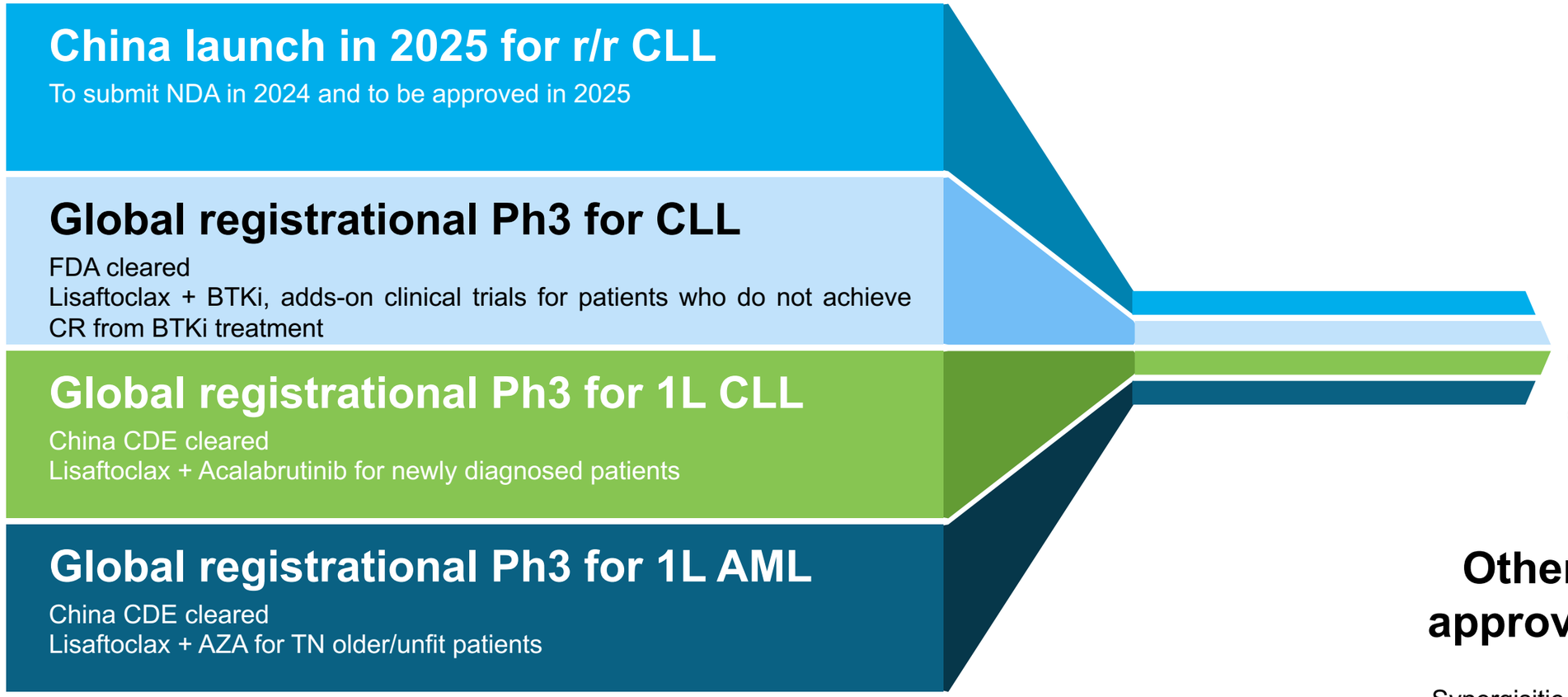
FDA cleared
Lisaftoclax + BTKi, adds-on clinical trials for patients who do not achieve CR from BTKi treatment

Global registrational Ph3 for 1L CLL

China CDE cleared
Lisaftoclax + Acalabrutinib for newly diagnosed patients

Global registrational Ph3 for 1L AML

China CDE cleared
Lisaftoclax + AZA for TN older/unfit patients



US$4bn+

Global market opportunity[1]

Other indications not approved for Venetoclax

MM, MDS, WM, etc.
Synergisitic combination with olverembatinib and APG-115

Source: Company data
[1] Venetoclax 2029 forecast sales

Lisaftoclax: potential best-in-class Bcl-2 inhibitor globally

Improved benefit-risk and superior overall convenience

Clinical validation

- **800+ subjects** enrolled into lisaftoclax studies, including CLL, AML, MM, MCL, T-PLL, WM, MDS patients
- **~400 CLL subjects** treated with lisaftoclax demonstrating safety and efficacy
- Favorable efficacy and safety results in **MM and AML** patients

Efficacy

- **Clinical benefit shown in subjects who progressed on venetoclax and BTKi-resistant patients**
- **100% ORR** in combination with BTKi in treatment-naïve CLL/SLL patients
- **98% ORR** in combination with BTKi in r/r CLL/SLL patients

Safety

- Lower incidence of neutropenia and thrombocytopenia and less infections vs venetoclax[1]
- **No DDI observed** with BTKi
- **Much lower clinical TLS** vs venetoclax[1]
- Well tolerated - No DLTs observed, MTD not reached

Unique clinical profile

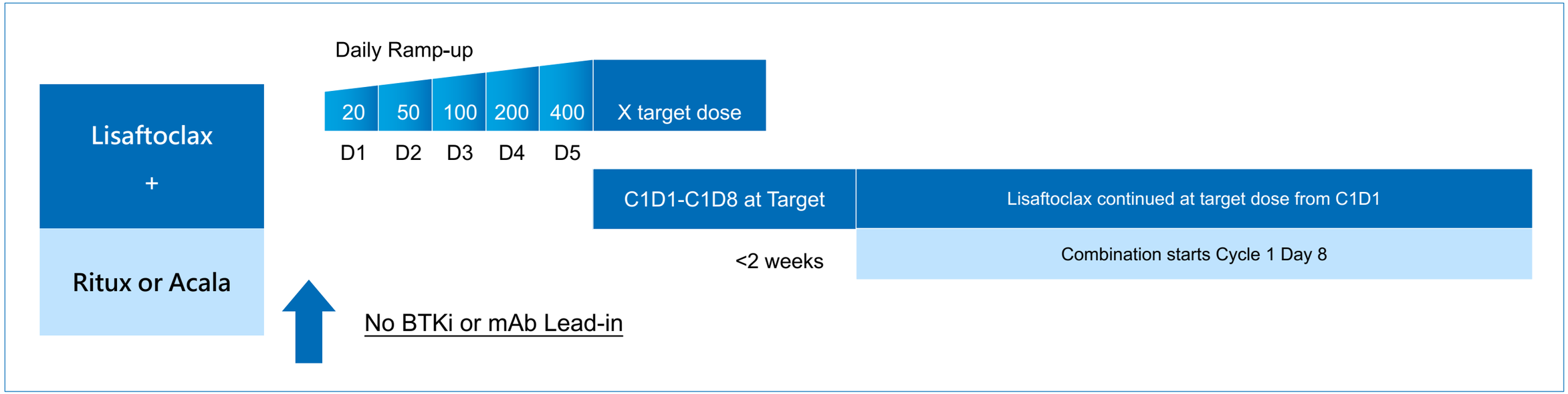
- Highly convenient to patients and healthcare system
- **Daily dose ramp-up** vs weekly dose ramp-up required by venetoclax
- Achieving target treatment dose and BTK combination in as quickly as ~1 week

Source: Company data; 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
Note: [1] analysis based on published data, not head-to-head comparison trials

Unique and differentiated clinical design

★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

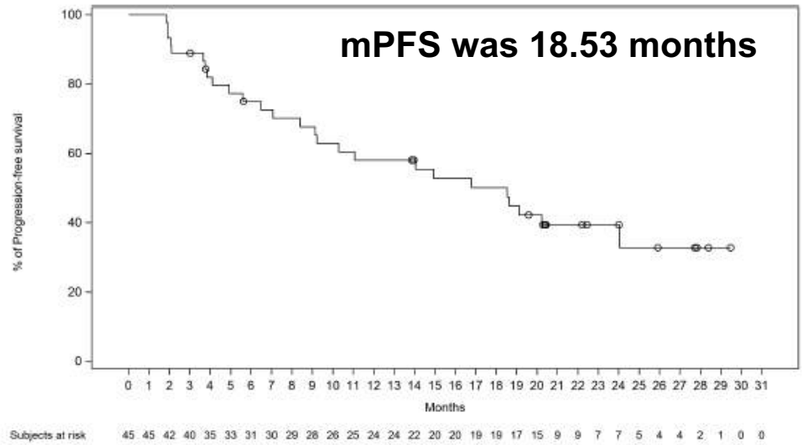
Updated data from 14-month follow-up in R/R CLL patients

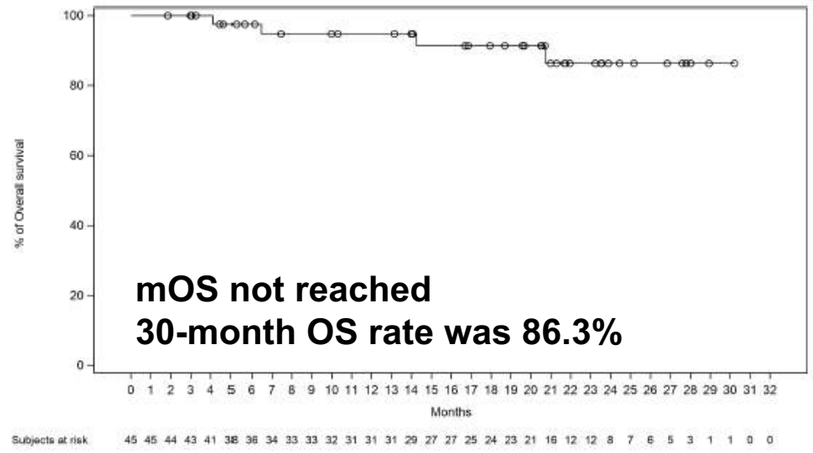
Favorable tolerability and efficacy in R/R CLL patients, including heavily pretreated and BTKi-treated patients
No significant new or unmanageable safety findings were observed

Best overall responses

	Lisaftoclax dosage, mg					Total
	100	200[a]	400[b]	600	800	—
Efficacy assessment, n	3	2	12	13	15	45
Response, n (%)						
ORR	0	2 (100.0)	10 (83.3)	9 (69.2)	12 (80.0)	33 (73.3)
CR/CRi	0	1 (50.0)	2 (16.7)	3 (23.1)	5 (33.3)	11 (24.4)
PR	0	1 (50.0)	8 (66.7)	6 (46.2)	7 (46.7)	22 (48.9)
SD	3 (100.0)	0	2 (16.7)	2 (15.4)	0	7 (15.6)
PD	0	0	0	2 (15.4)	3 (20.0)	5 (11.1)
MRD in PB assessment, n	—	—	6	7	5	18
Response, n (%)						
MRD	—	—	2 (33.3)	2 (28.6)	3 (60.0)	7 (38.9)
[c]MRD			2 (16.7)	2 (15.4)	3 (20.0)	7 (15.6)
MRD in BM assessment, n	—	—	2	1	3	6
Response, n (%)						
MRD	—	—	2 (100.0)	0	2 (66.7)	4 (66.7)
[c]MRD			2 (16.7)		2 (13.3)	4 (8.9)

- Median time to first response: 2.07 months





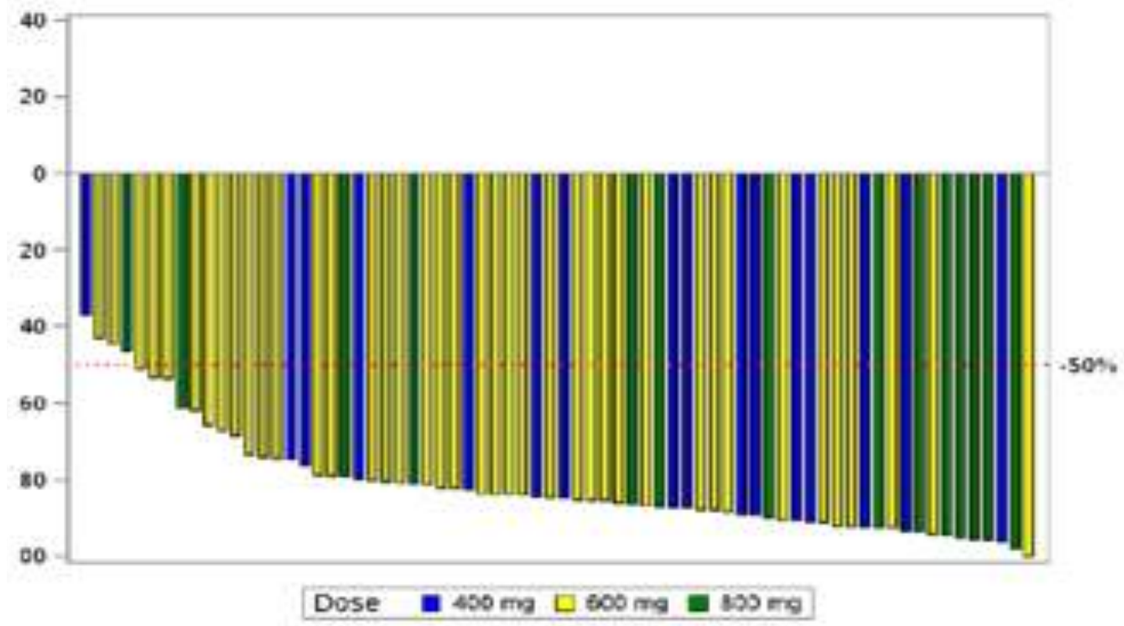
Source: Updated Efficacy and Safety Results of Lisaftoclax (APG-2575) in Patients (pts) with Heavily Pretreated Chronic Lymphocytic Leukemia (CLL): Pooled Analyses of Two Clinical Trials

Global phase 2 study: Lisaftoclax efficacy on CLL

	ORR
Monotherapy (n=43)	67%
Lisaftoclax + Rituximab (n=34)	79%
Lisaftoclax + Acalabrutinib (TN) (n=16)	**100%**
Lisaftoclax + Acalabrutinib (R/R) (n=57)	**98%**
Lisaftoclax + Acalabrutinib (R/R) - BTKi naïve (n=46)	100%
Lisaftoclax + Acalabrutinib (R/R) - venetoclax resistant (n=4)	75%

Lisaftoclax + Acalabrutinib (N=74)

%ΔSPD lymph node

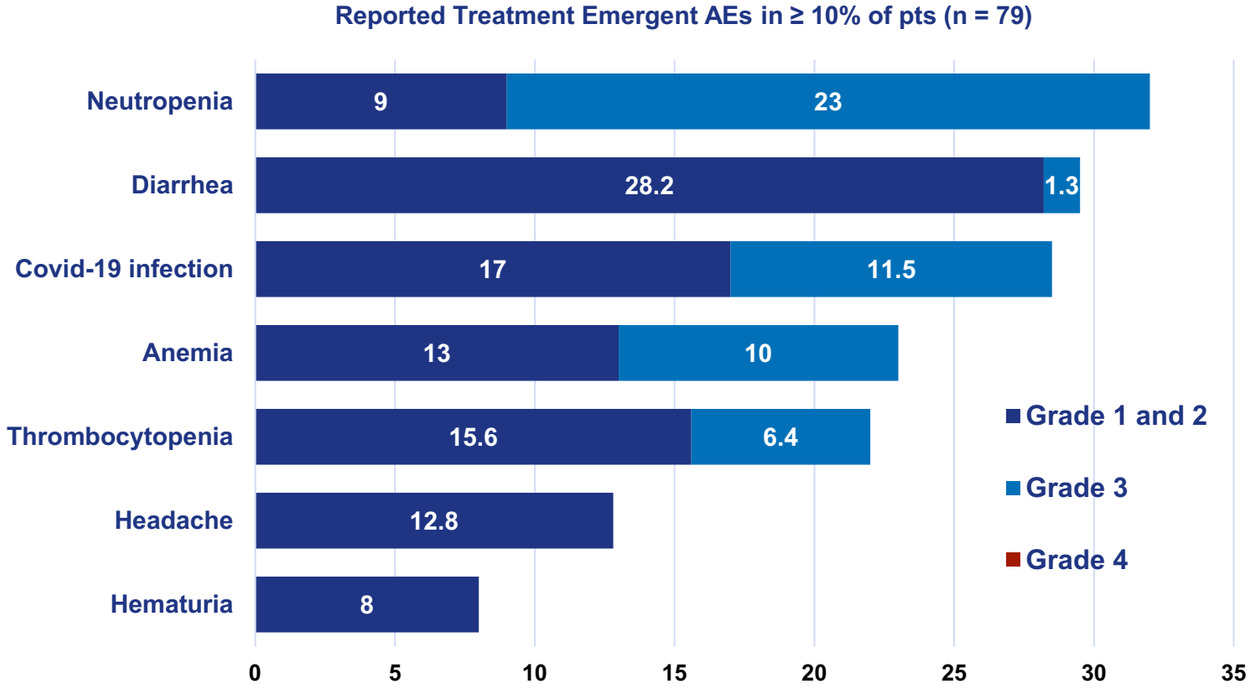


Lisaftoclax alone or combined with acalabrutinib or rituximab had favorable clinical activity in treatment-naïve patients and patients with R/R CLL/SLL

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

Global phase 2 study: Lisaftoclax safety profile in CLL patients

Lisaftoclax + acalabrutinib



- No DLTs observed
- MTD has not been reached
- No DDI in combination with BTKi
- Low TLS (n = 4; 2 clinical/2 laboratory)
- No treatment-related discontinuation or deaths

Manageable safety profile as a single agent or in combination with rituximab or with acalabrutinib with initial daily dose ramp-up of Lisaftoclax

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

Demonstrated preliminary anti-tumor activity and favorable safety profile in R/R MM or AL amyloidosis patients

30 patients (with a median of 4 lines of prior therapy) were enrolled in this multi-center trial

Best overall response, n (%)	Arm A N=21	Arm B N=2	Arm C N=5
Patients	R/R MM	R/R MM	AL amyloidosis
Treatment	Lisaftoclax + pomalidomide & dexamethasone	Lisaftoclax + daratumumab, lenalidomide & dexamethasone	Lisaftoclax + pomalidomide & dexamethasone
VGPR	**6 (28.6)**	1 (50.0)	3 (60.0)
PR	**8 (38.1)**	1 (50.0)	0
SD	7 (33.3)	0	1 (20.0)
ORR (VGPR + PR)	**14 (66.7)**	2 (100.0)	3 (60.0)
NR	0	0	1 (20.0)

VGPR, very good partial response, PR, partial response, SD, stable disease, ORR, overall response rate, NR, no response

Favorable safety profile; grade 3 or 4 AEs were minimal and tolerated

- A total of 7 patients experienced grade ≥3 lisaftoclax-related TEAEs, including:
  - **neutropenia (10.0%)**
  - **febrile neutropenia (3.3%)**
  - iron deficiency anemia (3.3%)
  - thrombocytopenia (3.3%)
  - prolonged electrocardiogram QT interval (3.3%)
  - acute kidney injury (3.3%)
- Two patients experienced lisaftoclax-related serious TEAEs, including 1 acute kidney injury and 1 febrile neutropenia (3.3% each).

Source: Ailawadhi S, et al. (ASH 2023) First Report on the Effects of Lisaftoclax (APG-2575) in Combination with Novel Therapeutic Regimens in Patients with Relapsed or Refractory Multiple Myeloma (R/R MM) or Immunoglobulin Light-Chain (Amyloid Light-Chain [AL]) Amyloidosis

Encouraging clinical efficacy and tolerability in AML and MDS patients

Lisaftoclax + azacitidine (AZA) resulted in 75% and 71% ORR in R/R AML and TN older/unfit AML patients, respectively

As of July 19, 2023, 115 pts were enrolled.

	Therapy	Diagnosis	# evaluable pts	ORR[1], n (%)	CR/CRi, n (%)
A	Lisaftoclax + LD-HHT	R/R AML	3	0.0%	0.0%
B	Lisaftoclax + SD-HHT	R/R AML	8	75.0%	75.0%
C	Lisaftoclax + AZA	R/R AML [2]	36	75.0%	44.4%
E	Lisaftoclax + AZA	TN, older/unfit AML	21	71.4%	47.6%
D	Lisaftoclax + AZA	HR-MDS	10	70.0%	60.0%

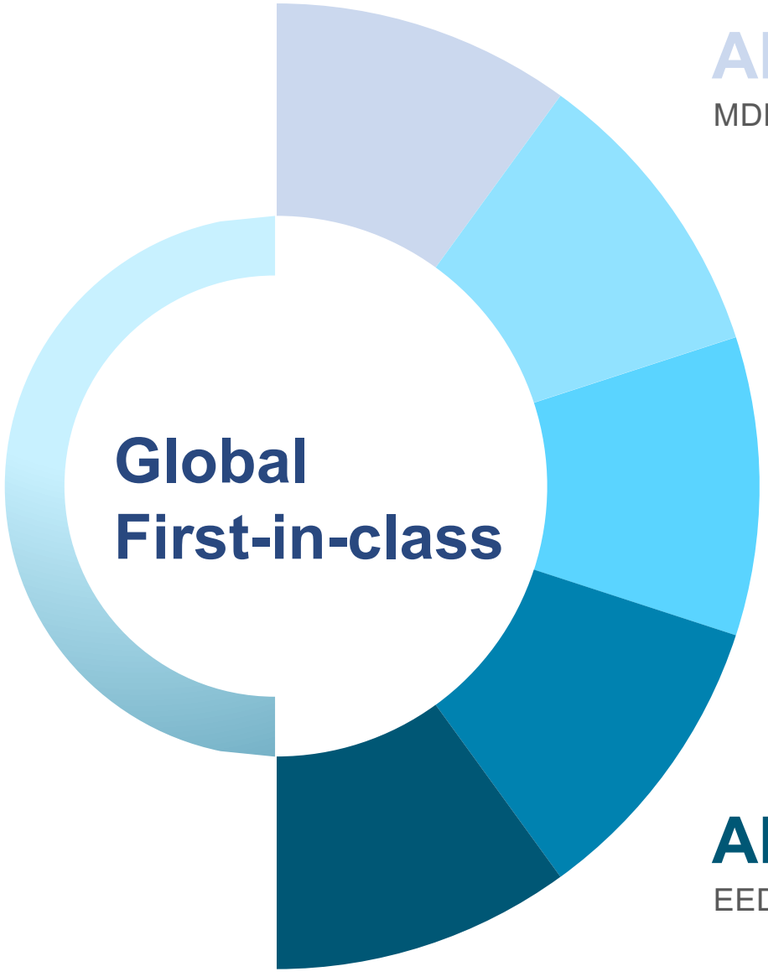
Favorable tolerability as monotherapy and when combined with AZA or HHT

- No TLS was reported during the study, and dose-limiting toxicities were observed in 1 patient
- All 13 patients who received lisaftoclax monotherapy experienced TEAEs, of which all were grade ≥3; 4 (30.8%) patients experienced SAEs.
- In patients treated with lisaftoclax combined with HHT, 12 (85.7%) experienced TEAEs, of which all were grade ≥3; 2 (14.3%) were SAEs.
- Of the 75 evaluable patients treated with lisaftoclax combined with AZA, 100% experienced TEAEs, including 55 (73.3%) who experienced grade ≥3 TEAEs and 18 (24.0%) SAEs.

In R/R AML patients treated with lisaftoclax and azacitidine, the median time to CR/CRi/MLFS was 1.25 months; and median PFS was 10.22 months

[1] In AML, ORR= CR+ CRi + MLFS + PR; in MDS, ORR= CR+ mCR + PR.
[2] Including 1 CMML, 2 MPAL, and 1 BPDCN
Source: Wang H, et al. (ASH 2023) Safety and Efficacy of Lisaftoclax (APG-2575), a Novel BCL-2 Inhibitor (BCL-2i), in Relapsed or Refractory (R/R) or Treatment-Naïve (TN) Patients (Pts) with Acute Myeloid Leukemia (AML), Myelodysplastic Syndrome (MDS), or Other Myeloid Neoplasms

First-in-class pipeline: multiple shots-on-goal in untapped markets



APG-115

MDM2-P53 inhibitor

- Conducting clinical studies in melanoma, salivary gland cancer, MPNST, AML, CMML, MDS, liposarcoma and pediatric neuroblastoma and solid tumors [1]
- Potential synergies with APG-2575 to achieve “synthetic lethality”

APG-1252

Bcl-2/Bcl-XL inhibitor

- 205 patients treated: SCLC, NSCLC, neuroendocrine tumor, and non-Hodgkin’s lymphoma

APG-2449

ALK/FAK/ROS1 inhibitor

- Good safety and tolerability and preliminary efficacy in ALK-positive NSCLC patients

APG-1387

IAP inhibitor

- 260 patients treated: advanced solid tumors and chronic HBV infection

APG-5918

EED inhibitor

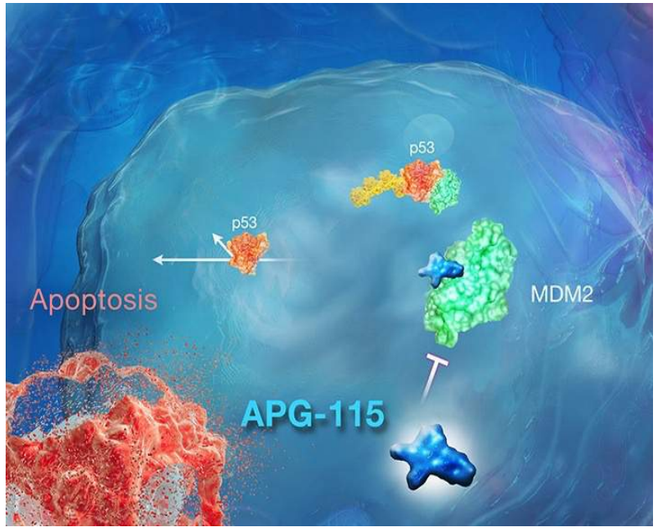
- Potent antiproliferative activity in cancer cell lines
- Potential for treating beta hemoglobinopathy, including sickle cell disease and ß-thalassemia

[1] MPNST: malignant peripheral nerve sheath tumor; CMML: chronic myelomonocytic leukemia
Source: Company data

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

Source: Company data

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

Targeting the MDM2-P53 and BCL-2 apoptosis pathways simultaneously 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**

Mechanism

- Compared with adult tumors, pediatric solid tumors are characterized by **low TP53 mutation frequency and high MDM2 amplification frequency**
- APG-115 in combination with lisaftoclax 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 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

Alrizomadlin (APG-115) demonstrates clinical potential in progressive salivary gland cancer

APG-115 monotherapy demonstrates promising antitumor activity in patients with progressive salivary gland cancer including adenoid cystic carcinoma (ACC) with good tolerability

The phase I/II multicenter, open-label study enrolled 31 patients with metastatic salivary gland cancer refractory to standard therapies

- ORR and DCR at 13% and 94%, respectively
- **Antitumor activity was more pronounced in patients with adenoid cystic carcinoma, with ORR and DCR at 16% and 96%, respectively**
- In the 26 patients with stable disease, more than half had a reduction in tumor size by >10%
- Demonstrated acceptable toxicity profile at the selected dose. Only 2 patients discontinued treatment due to AEs, and no grade 4 toxicity was observed

About metastatic salivary gland cancers and ACC

- Metastatic salivary gland cancers are a rare group of disease, with no approved therapeutics
- For ACC patients, VEGF inhibitors tend to be the standard of care, with 0%-15% response rates and 5-10 months PFS . The mPFS in patients with untreated disease is 2.8 months.
- MDM2 gene amplifications are common, and preclinical evidence supports the activity of MDM2 inhibitors both as monotherapy and in combination with chemotherapy

Efficacy: Adenoid Cystic Carcinoma

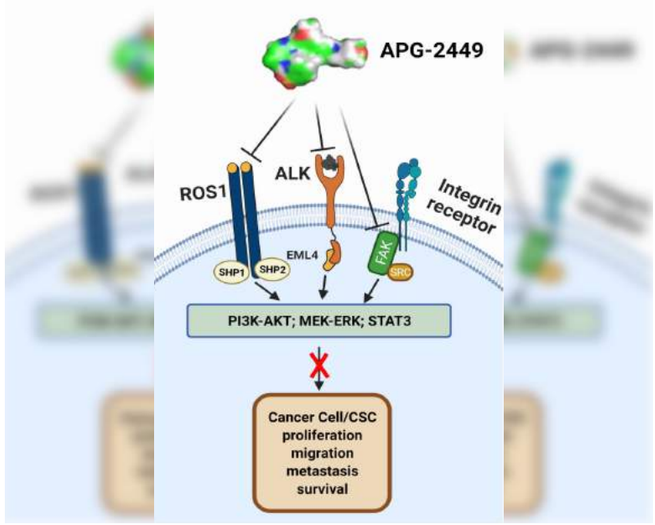
		Adenoid Cystic Carcinoma (ACC)	
		N=25	Duration (months)
Duration on Therapy			7.4
Best Response	PR	4 (16%)	11.7
	SD	20 (80%)	8.1
	PD	1 (4%)	-
Survival Outcomes			
OS	Median	Not reached	
PFS	6 month	84%	
	Median	10.5 months	

Source: Pearson AT, Muzaffar J, Kirtane K, et al. Phase I/II study of a novel MDM-2 inhibitor (APG-115-alrizomadlin) in p53 wild type salivary gland cancers. Presented at: 2024 Multidisciplinary Head and Neck Cancers Symposium; February 29-March 2, 2024; Phoenix, AZ. Abstract 8.

APG-2449

ALK/FAK/ROS1

triple ligase kinase inhibitor



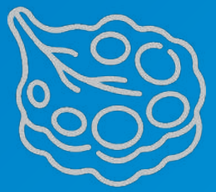
Potentially the 1st ALK/FAK/ROS1 triple inhibitor globally

- 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 overcoming 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



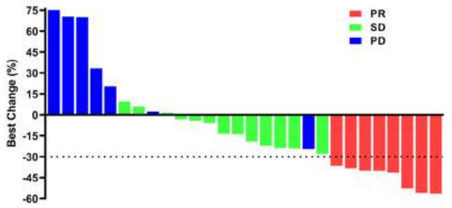
Selected for poster discussion at 2023 ASCO

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

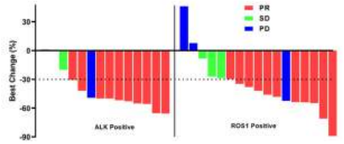
Novel FAK/ALK inhibitor APG-2449 could overcome ALK resistance in NSCLC

Efficacy

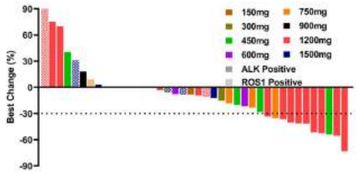
Best tumor response (%) in patients with 2nd gen TKI resistant ALK+ NSCLC



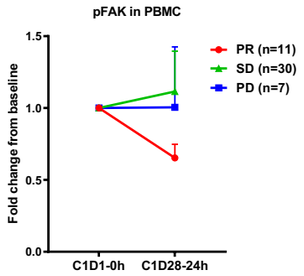
Best tumor response (%) in patients with TKI-naïve ALK/ROS1+ NSCLC



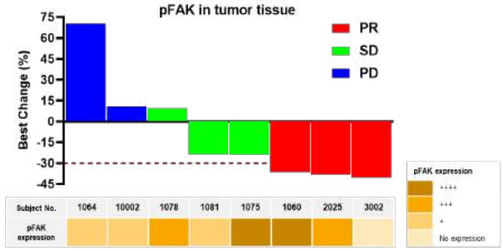
Best tumor response (%) of brain metastases observed in patients with 2nd gen TKI resistant ALK+ NSCLC



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

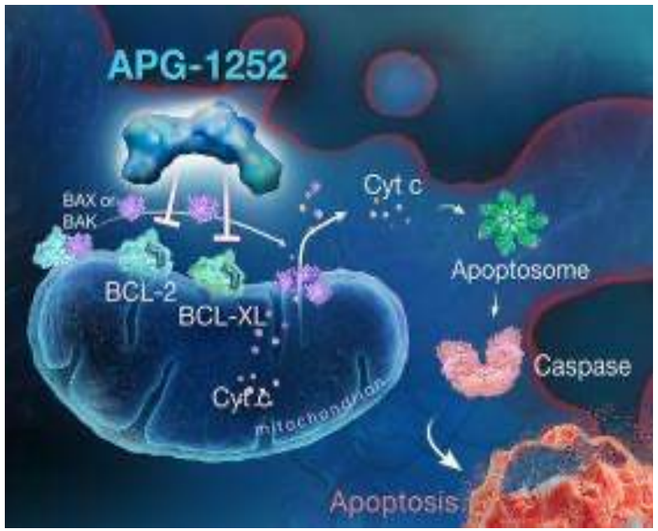
Safety

	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)

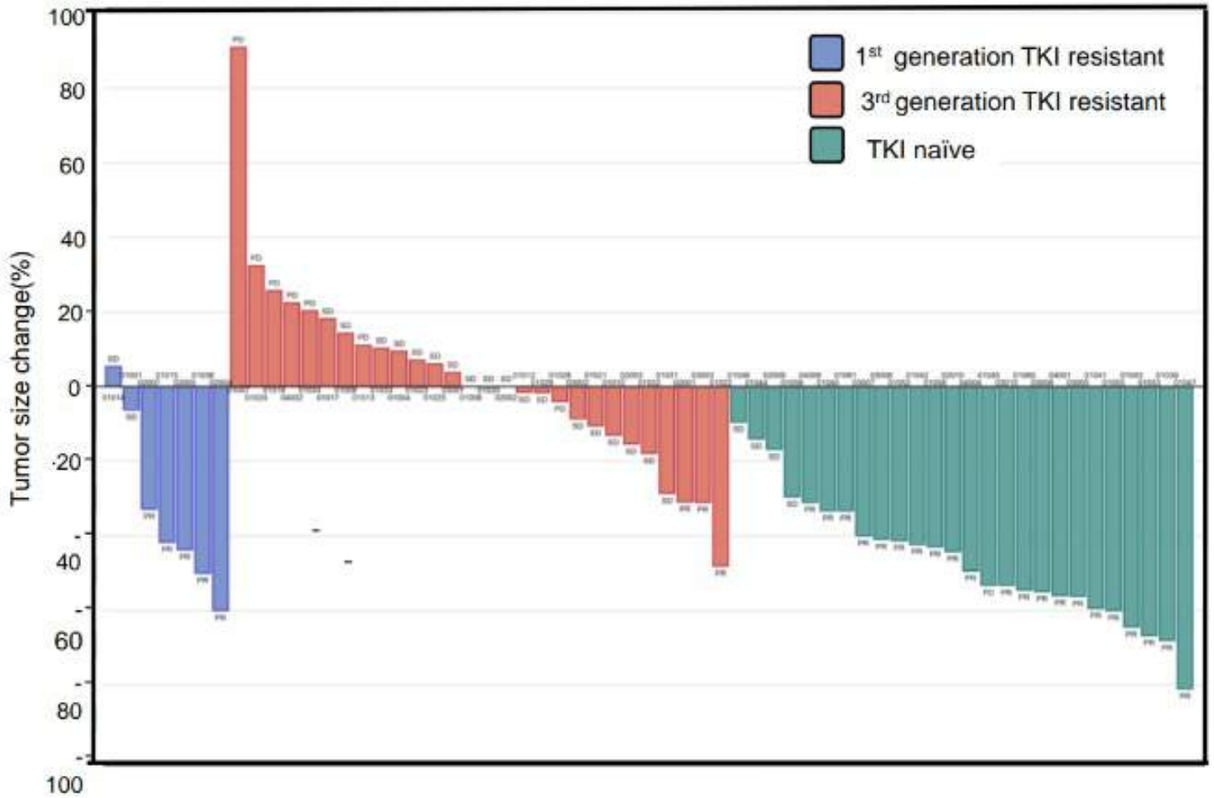
Presented in mini-oral format at 2023 ESMO

Source: Company data

Pelcitoclax plus osimertinib is well tolerated, and preliminary efficacy observed in EGFR-mutant NSCLC patients

Pelcitoclax plus osimertinib may improve clinical outcomes of patients with NSCLC harboring TP53- and EGFR- positive mutations

Best tumor response	1G TKI resistant n=7	3G TKI resistant n=28	TKI-naïve n=26	Overall n=61
ORR	71.4%	10.7%	80.8%	47.5%
PR	71.4%	10.7%	80.8%	47.5%
SD	28.6%	64.3%	15.4%	39.3%
PD	0.0%	25.0%	3.8%	13.1%
DCR	100.0%	75.0%	96.2%	86.9%

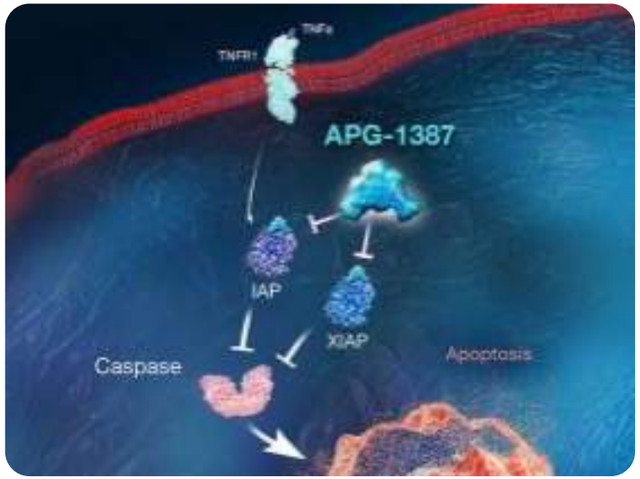


Patients with high Bcl-xL expression experienced better efficacy, with longer PFS, in the 3G TKI resistant group

Source: Y. Ma, et al.(2023 ESMO), Updated study results of pelcitoclax (APG-1252) combined with osimertinib in patients (pts) with EGFR-mutant non-small cell lung cancer (NSCLC)

APG-1387

An Antagonist of IAP/XIAP (SMAC Mimetic) Dimmer



Chronic HBV infection

- Completed phase I study of monotherapy in treatment-naïve CHB patients
- Conducting phase II clinical trial of APG-1387 combined with entecavir in CHB patients, compared to entecavir monotherapy

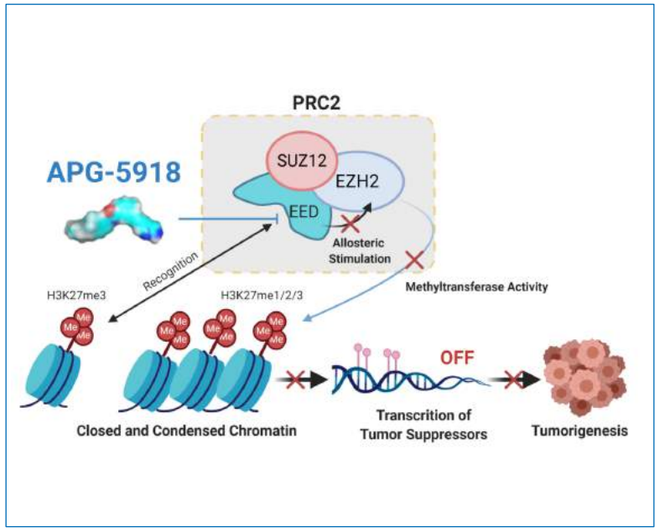
Solid tumors

- Completed a phase I clinical trial in the US for the combination of APG-1387 and pembrolizumab in the treatment of solid tumors
- Conducting phase Ib/II clinical trial of APG-1387 in combination with toripalimab in solid tumors
- Conducting phase I/II study to investigate the combination of APG-1387 with chemotherapy, nab-paclitaxel and gemcitabine in advanced pancreatic cancer patients

Source: Company data

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

SLE

Anemia

Source: Company data

Pipeline summary

Compounds	Target	Indications	Preclinical	Phase I	Phase II	Registration Trial	NDA Approval	Trial Region	Rights Region
Olverembatinib (HQP1351)	BCR-ABL/KIT	Resistant CML							
		Resistant CML(Global-FDA)			(cleared by US FDA)		耐立克 奥雷巴替尼 olverembatinib		
		TN Ph+ ALL							
		GIST							
Lisaftoclax (APG-2575)	Bcl-2 Selective	BTKi treated CLL/SLL (Global-FDA)			(cleared by US FDA)				
		r/r CLL/SLL (China)							
		TN CLL/SLL (Global)							
		AML							
		WM							
		MDS							
		MM							
		T-PLL							
		MCL							
		ER+/HER2-BC and Solid Tumors							
Alrizomadlin (APG-115)	MDM2-p53	Melanoma and Solid Tumors							
		ACC							
		AML,MDS							
APG-1387	IAP/XIAP	Solid tumors (IO Combo)							
		PDAC+ Chemo							
		CHB							
Pelcitoclax (APG-1252)	Bcl-2/Bcl-xL	NSCLC+ TKI							
		SCLC+ Chemo							
		NET							
		NHL							
APG-2449	FAK/ALK/ROS1	NSCLC/ Solid tumors							
APG-5918	EED Selective	Tumors/Hemoglobinopathy							
APG-265	PROTACs MDM2	Tumors							
UBX1967/1325	Bcl Family	DME							

Source: Company data

Addressing clinical needs through innovative therapeutics: Substantial global opportunities

China sales

Global sales

First proprietary product approved

Olverembatinib approved in China

RMB200m sales in the first year of launch

Suzhou R&D HQ and manufacturing facilities operational

Olverembatinib new indication approved and NRDL covered

Olverembatinib full approval for CML in China, NRDL covered

Initiated olverembatinib and lisaftoclax global registrational trials for Ph+ ALL and CLL/SLL

Passed EU QP GMP audit with zero deficiency

Executing global registrational trials

Lisaftoclax to submit NDA in China

Execute multiple global registrational trial (olverembatinib for CML and Ph+ALL; Lisaftoclax for AML/MDS/MM)

Olverembatinib to apply for NRDL for new indication approval

Twin product engines driving sales

Lisaftoclax to be approved in China

Olverembatinib NRDL coverage to be expanded

More pipeline products to enter late-stage clinical trials

Leading international biopharma with multiple blockbuster products

Lisaftoclax and olverembatinib to enter global markets, continue to expand indications to cover all major hematological malignancies

Fund future product development with ample cash flows

2021-2022 | 2023 | 2024 | 2025 | 2026 - beyond

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 entering billion+ USD market

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

- Unique clinical advantages establish commercial value, driving global market penetration

Olverembatinib commercialized; Lisaftoclax in global registrational Phase III trial

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

Strong IP position

- 498 issued patents, including 352 issued overseas

Global leading R&D team possesses comprehensive capabilities

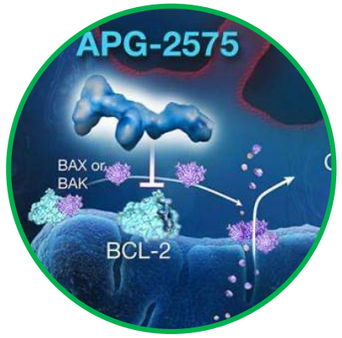
- Seamlessly executing the entire R&D lifecycle from discovery to registration

Accelerating growth of olverembatinib sales

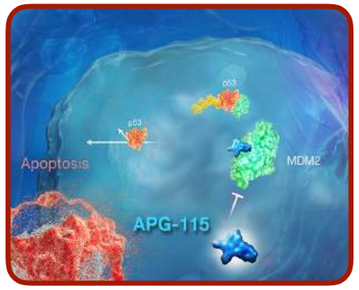
- Propelled by increasing prescriptions under NRDL coverage
- Expansion of indication to benefit more patients

Source: Company data

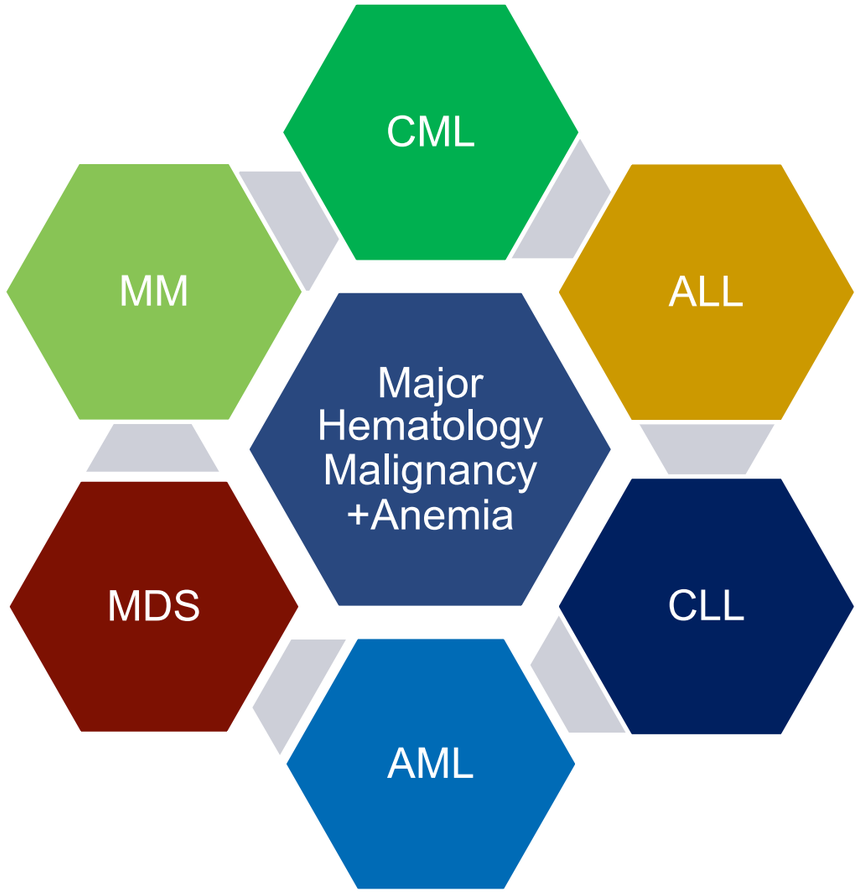
Patient-Centric Innovation; Global Breakthrough Therapies



Lisaftoclax
Bcl-2 Selective Inhibitor



Alrizomadlin
MDM2-p53 Inhibitor



68 Xinqing Road, Suzhou Industrial Park
Suzhou, Jiangsu, P.R.C

ir@ascentage.com

700 King Farm Blvd., Suite 510
Rockville, MD 20850, USA

Suite 30.03, 133 Castlereagh St.,
Sydney NSW 2000 Australia

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Ascentage Pharma

2023 Annual Results & Business Updates

March 28, 2024