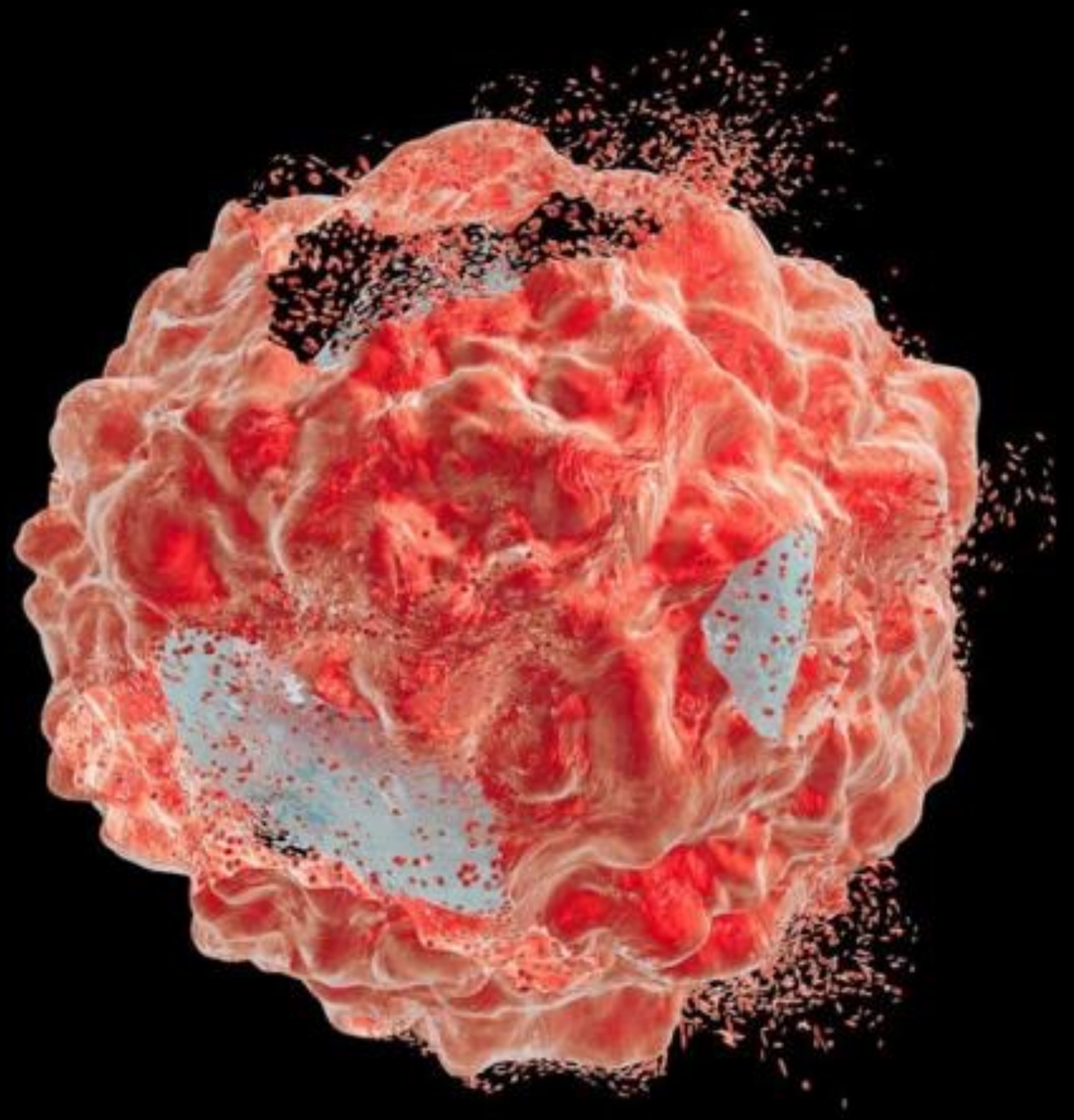

Ascentage Pharma Group

Advancing Therapies That Restore Apoptosis

March, 2022

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Innovative and Proprietary Platform Delivering Potentially First and/or Best-in-Class Drugs

Breakthrough science

178 issued patents

600+ pending applications

100+ publications

Dedicated team

1 vision: building a global biopharmaceutical company

20+ years commitment of executive team

600+ employees

Strong pipeline

1 NDA Approval

10+ indications

12 novel compounds

50+ clinical trials

30+ INDs

Global development

Integrated organization in **China, United States, Europe and Australia**

Major Achievements in 2021

NDA approval of v (HQP1351)

- The **first and the only** approved third generation BCR-ABL inhibitor in China
- Received support from **National Major New Drug Discovery and Manufacturing Program**
- Granted the **"Priority Review" and a "Breakthrough Therapy Designation"** by CDE
- Granted **ODDs and a Fast-Track Designation**

Clinical breakthrough for apoptosis asset APG-2575

- **Registrational pivotal study of APG-2575 for treatment of patients with CLL/SLL initiated in China and the first patient has been dosed**
- **18 global phase Ib/II studies**

Break the record of Chinese biotech companies

- Granted 15 **ODDs** by FDA and 1 **ODD** by EC
- Granted 2 **Fast-Track Designation**
- Granted 2 **Rare Pediatric Disease** Designations

Data releases in International Academic Conference

- HQP1351：The positive data for patients with long-term follow-up was presented and it's the fourth consecutive time where Olveremabatinib was selected for oral presentation at the ASH.
- APG-2575: The promising data from the phase I Study in China and US was released in ASH and ASCO. The data release was selected for oral presentation at the ASCO
- APG-115：The data from the phase II Study combination with Pembrolizumab was selected for oral presentation at the ASCO

6 clinical and commercial collaborations

- with AstraZeneca, MSD, Pfizer, and Innovent, etc.

Expected Milestones in 2022

NDA submission: We expect to submit a full-approval NDA application of Olverembatinib for the treatment of CML patients who are resistant/intolerant to first and second generation TKIs

We will continue to promote the sales of Olverembatinib and actively promote the Olverembatinib to enter in thw National Reimbursement Drug List

Key asset clinical development and data release expectation

HQP1351

- A phase Ib study for treatment of patients with CML and Ph + ALL is ongoing in the US. We will continue to consult with the FDA on global pivotal phase II registration study.
- Release data of GIST

APG-2575

- Release the partial data of APG-2575 in combination with the BTK inhibitor in 2022
- Release clinical data of AML in 2022Q4 or 2023Q1
- Consult with FDA and CDE on proposed pivotal phase II studies.
- Complete the enrollment for pivotal phase II trial of APG-2575 for the treatment of patients with r/r CLL/SLL in China in 1H 2023

APG-115

- Release the data of APG-115 monotherapy and in combination with azacytidine/cytarabine in AML/MDS in 2022
- Consult with FDA on proposed pivotal phase II study

APG-2449

- Release the data of Phase I study and consult with CDE on proposed pivotal phase II study

APG-5918

- Submit IND in 2022 Q2

Olverembatinib: the only approved and commercialized third generation BCR-ABL inhibitor in China

耐立克®
奥雷巴替尼 olverembatinib

- The first commercialized product of **Ascentage Pharma**
- The **only** approved and commercialized third generation BCR-ABL inhibitor in China

Received NDA Approval
2021.11

The first prescription
2021.12

Entered into the list of the first commercial insurance
2021.12

Co-promote with Innovent Biologics in China
innovent 信达生物制药

Accelerate the market coverage
国药集团 SINOPHARM | 国药控股 SINOPHARM GROUP | SPH 上药控股 SHAPHAR | 华润医药 CR PHARMA

National coverage scope

80% CML Market in China

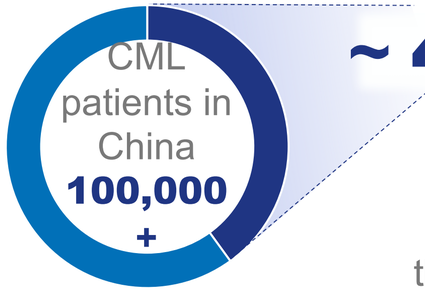
~800 hospitals

Commercial insurances in **10** cities

A commercialization team of **100** with rich experience in hematologic malignancies field

Commercialization

Market potential - Maximize market value of Olverembatinib

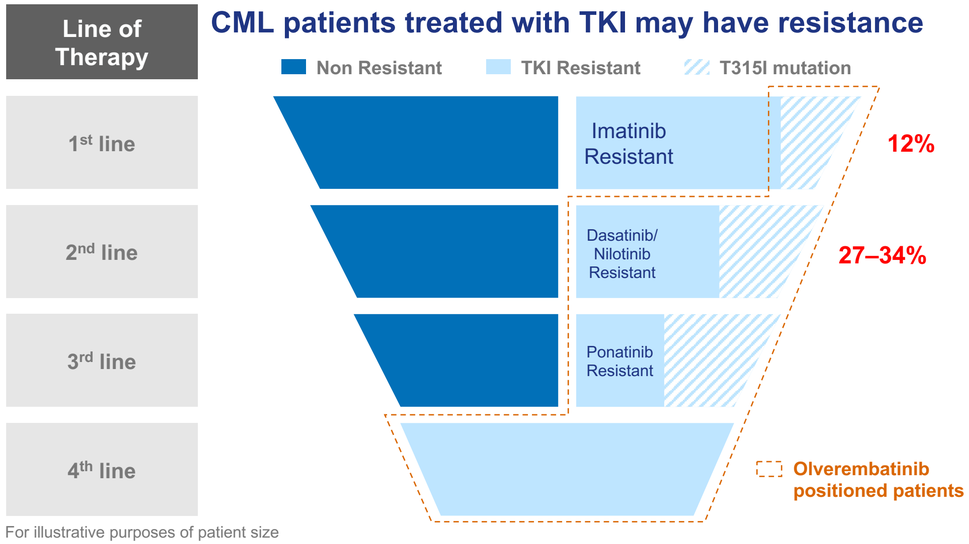


~ 40% received 2nd+ line therapy

Along with the increase of 2nd generation TKI treatment,

the number of **T315I mutation** patients will increase

- **Annual Sale of Global CML Market is $6 Bn**
- **Annual sale of 2 2nd generation** TKI (Dasatinib, Nilotinib) in 2020, 2021 **> $4 Bn**



For illustrative purposes of patient size

- T315I mutation was the most frequent mutation detected in imatinib-, nilotinib-, and dasatinib resistant cases, accounting for 12.3%, 27.3%, and 34.1%[1]

Strategic Alliance

Sales Distribution Collaboration

国药控股 SINOPHARM

SPH 上药集团 Shanghai Pharma

華潤医药 CR PHARMA

- Formed **strategic alliance relationships** with Sinopharma Group, Shanghai Pharmaceuticals Holding Co., Ltd and China Resources Pharmaceutical Group Limited.
- **Leveraging the sales distribution networks of various companies,** we delivered the drugs across China as soon as the supply of Olverembatinib was production released.

- Source:1. Chin J Hematol, 2020,41(06): 469-476

Multiple Ongoing Strategic Alliances

BCL-xL
UNITY BIOTECHNOLOGY

BCR-ABL & BCL-2
Innovent

BCL-2
AstraZeneca

MDM2-p53
MSD

BCL-2
Pfizer

IAP
Clover Biopharmaceuticals

Constant Improvement in Cash Flow

The first commercialized product and realized revenue

耐立克®
奥雷巴替尼 olverembatinib

Issuance and placement of additional shares and raised **1.3Bn** rmb

Cash& Cash Equivalent **1.74Bn** rmb

Year-on-year Increase **70.3%** ↑

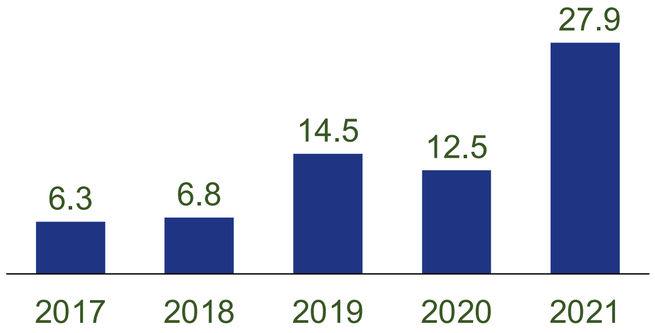
Revenue **27.91M** rmb

Year-on-year Increase **123.2%** ↑

Key Financial Highlights

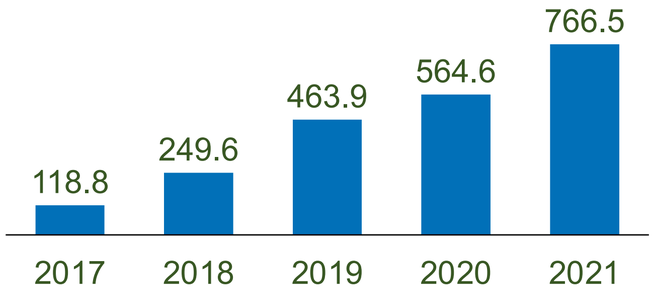
Revenue[1]

(RMB mm)



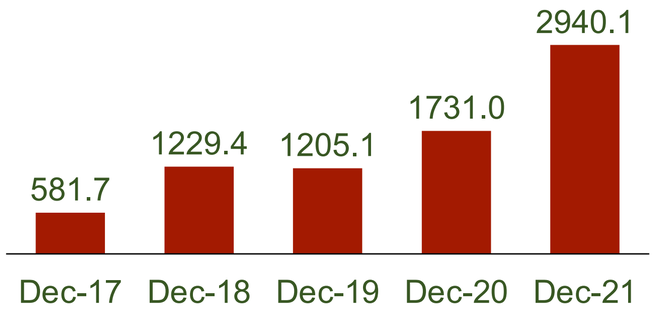
R&D Expense

(RMB mm)



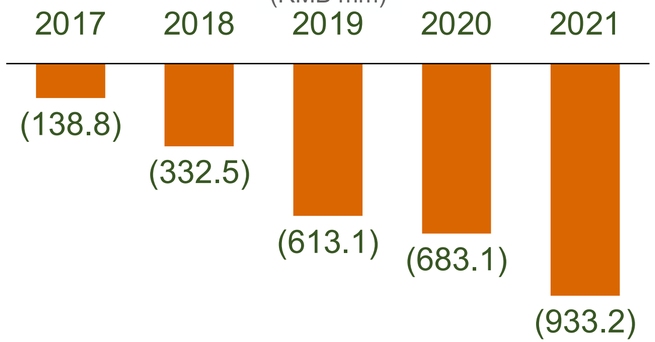
Total Assets

(RMB mm)



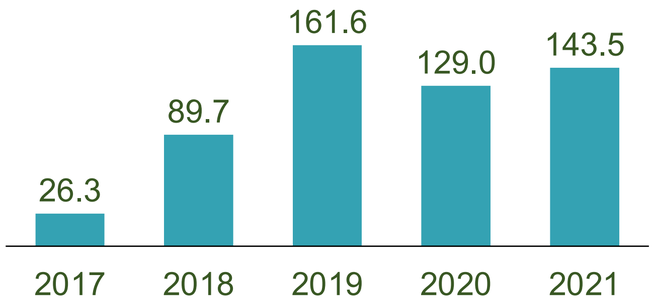
EBIT[2]

(RMB mm)



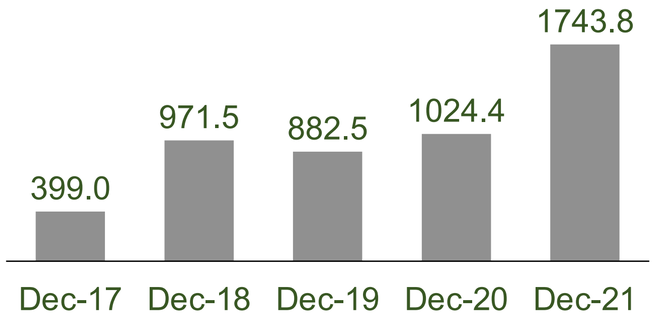
OPEX

(RMB mm)



Cash & Equivalents[3]

(RMB mm)



1) Revenue from provision of research and development services, and compounds library and intellectual property license fee income; 2) EBIT = Gross Profit – R&D Expense – Other OPEX 3) Cash & Equivalents include cash and bank balances, and other financial assets, which represent mainly investment in short-term financial products

Our Experienced Executives Team

Dajun Yang, M.D., Ph.D.

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CHAIRMAN &
CHIEF EXECUTIVE OFFICER

GEORGETOWN UNIVERSITY

UNIVERSITY OF MICHIGAN

ASCENTA THERAPEUTICS

Yifan Zhai, M.D., Ph.D.

CHIEF MEDICAL OFFICER

NATIONAL CANCER INSTITUTE

gsk

EXELIXIS

BAYER

Gang Zhu.

CHIEF COMMERCIAL OFFICER

Celgene

SANOFI

NOVARTIS

Yiqing Chen

CHIEF FINANCIAL OFFICER

EY Building a better working world

华大基因 BGI

东方·花旗 citi ORIENT

Shaomeng Wang Ph.D.

Co-Founder

Professor in Medicine, University of Michigan

Former Editor-in-chief, Journal of Medicinal Chemistry

UNIVERSITY OF MICHIGAN

Journal of Medicinal Chemistry

Thomas Knapp

SVP, GENERAL COUNSEL

BOEING

PAUL HASTINGS

SUCAMPO The Science of Innovation

ΣELLAS LIFE SCIENCES GROUP

Jeff Kmetz

CHIEF BUSINESS OFFICER

pharmacyclics An AbbVie Company

Pulse Biosciences

ALEXION

BAYER

Chongdong Fu, Ph.D.

CMC HEAD

復旦大學 FUDAN UNIVERSITY

和黄医药 HUTCHMED

Rich Pipeline With Significant Global Opportunities

Product	Target	Indications	Preclinical	Ph I	Ph II	Registration Trial	NDA Approval	Trial Region	Rights Regions
HQP1351	BCR-ABL/KIT	Resistant CML					耐立克 奧雷巴替尼 olverembatinib		
		Resistant CML · Ph+ ALL							
		GIST							
		Ph+ ALL							
APG-2575	Bcl-2 Selective	r/r CLL/SLL							
		r/r CLL/SLL							
		WM							
		AML							
		MDS							
		MM							
		T-PLL							
		MCL							
		ER+/HER2- BC and solid tumors							
APG-115	MDM2-p53	Melanoma and Solid Tumors(IO Combo)							
		ACC							
		AML,MDS							
APG-1387	IAP/XIAP	Solid tumors(IO Combo)							
		PDAC+ Chemo							
		CHB							
APG-1252	Bcl-2/Bcl-xL	NSCLC+ TKI							
		SCLC+ Chemo							
		NET							
APG-2449	FAK/ALK/ROS1	NSCLC/ Solid tumors							
APG-5918	EED Selective	Tumors/Hemoglobinopathy							
APG-265	PROTACs MDM2	Tumors							
UBX1967/1325	Bcl Family	DME							

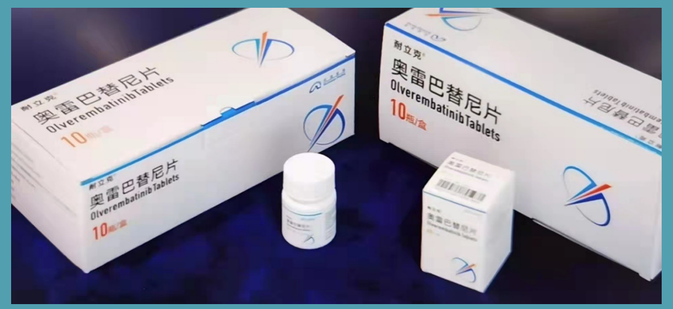
◆ POC ◆ POC in progress

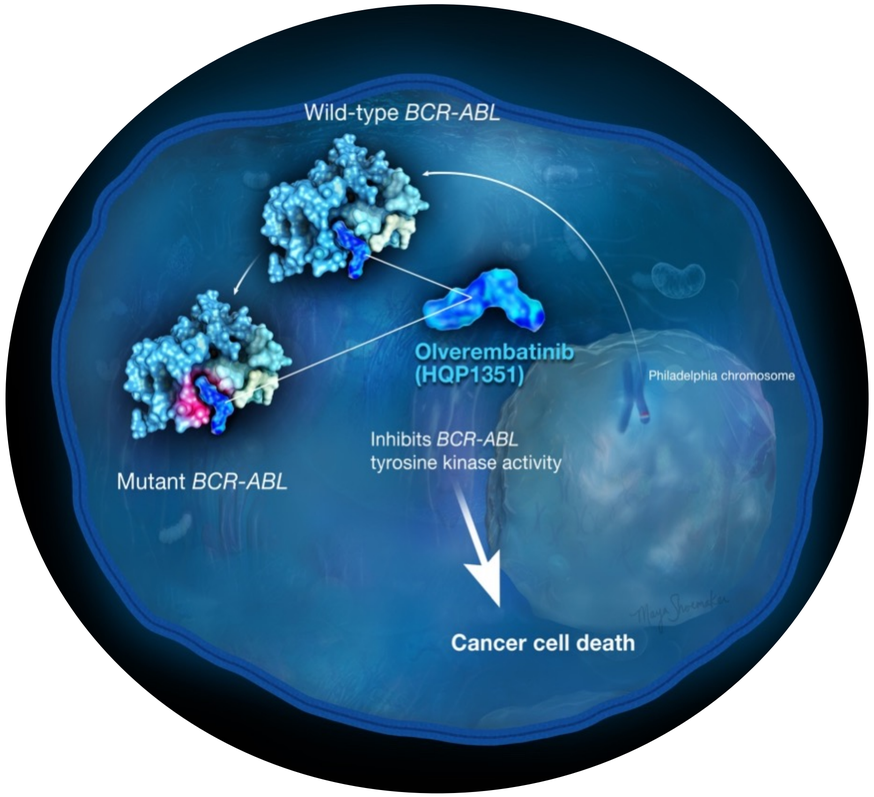
HQP1351 Olverembatinib Overview

The only approved and commercialized third generation BCR-ABL inhibitor in China,
targeting BCR-ABL mutants, including those with the T315I mutation

Received support from National Major New Drug Discovery and Manufacturing Program

Best-in-class drug potential globally





Development Milestone: From IND Clearance to NDA Approval in 4 Years

- 2020.04: granted **Orphan Drug Designation(CML)** and **Fast Track Designation** by FDA
- 2020.06: submitted **NDA** to the CDE for T315I-mutant CP-CML and AP-CML in China
- 2020.10: HQP1351 has granted **"Priority Review"**

2021

- 2021.03: received **" Breakthrough Therapy Designation "**
- 2021.11: received **NDA Approval**
- 2021.11: granted **Orphan Drug Designation (CML) by European Commission**
- 2021.12 granted **Orphan Drug Designation (AML)**
- 2022.03: granted **Orphan Drug Designation (ALL)**

2020

2019

- 2019.01: awarded "National Major Innovative Drug Project"
- 2019.07: entered Phase Ib clinical study for TKI rCML in US
- 2019.09: finished enrollment of 2 pivotal Phase II trials in China
- Clinical results of HQP1351 in CP|AP TKI resistant / intolerant CML **were orally presented at ASH 2018, 2019 , 2020 and 2021**， nominated as "Best of ASH" in 2019

2018

- 2018.07: held a pivotal Phase II clinical trial kick-off meeting with PI

2016

- 2016.02: NMPA issued a **"one-time umbrella approval"** for r/r CML

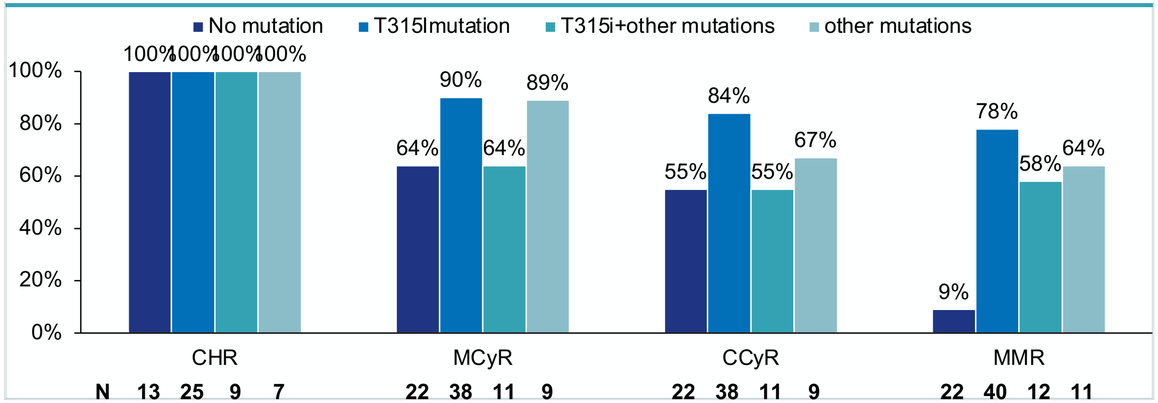
2015

- 2015.04: submitted an IND TKI resistant CML in China

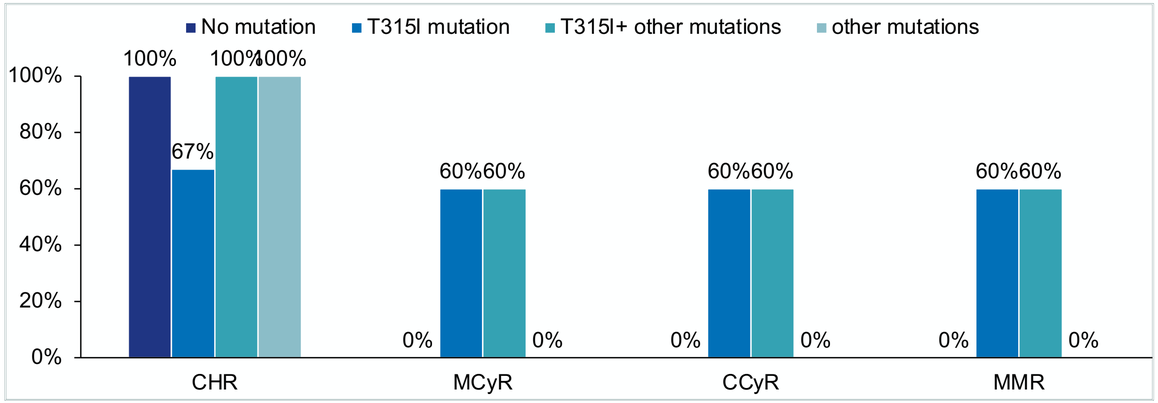
Phase I Study Summary: Efficacy

Highly Efficacious in TKI Resistant CML Patients

CP

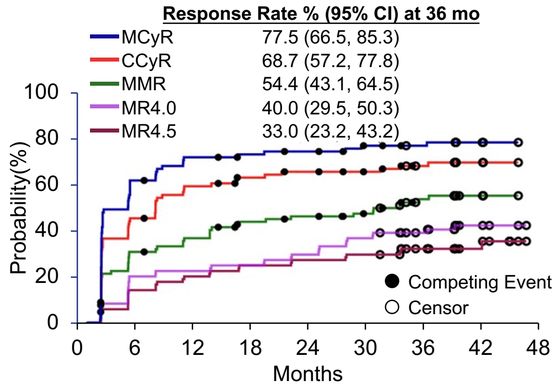


AP



Cumulative Incidence of Achieving Responses (≥30mg)

CP



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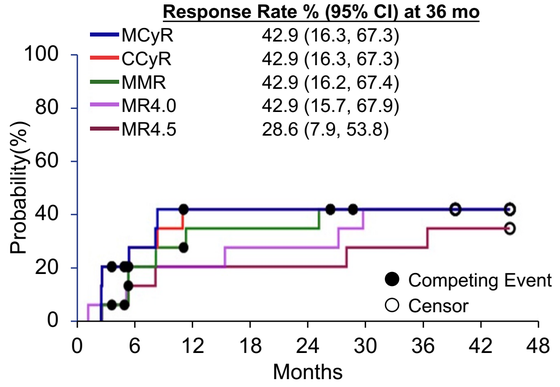
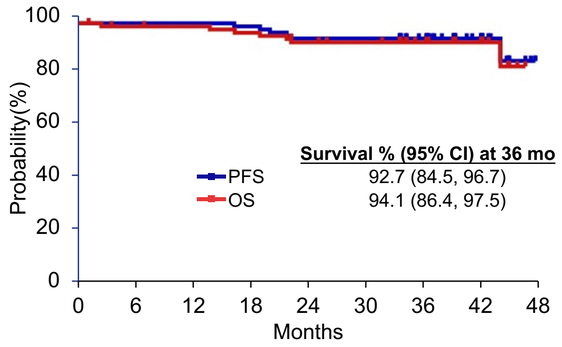
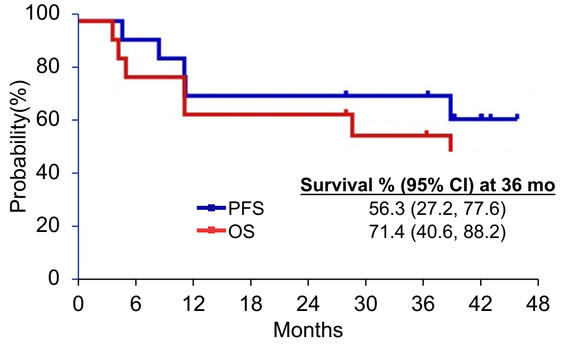


Progression-free Survival & Overall Survival (≥ 30mg)

CP



AP

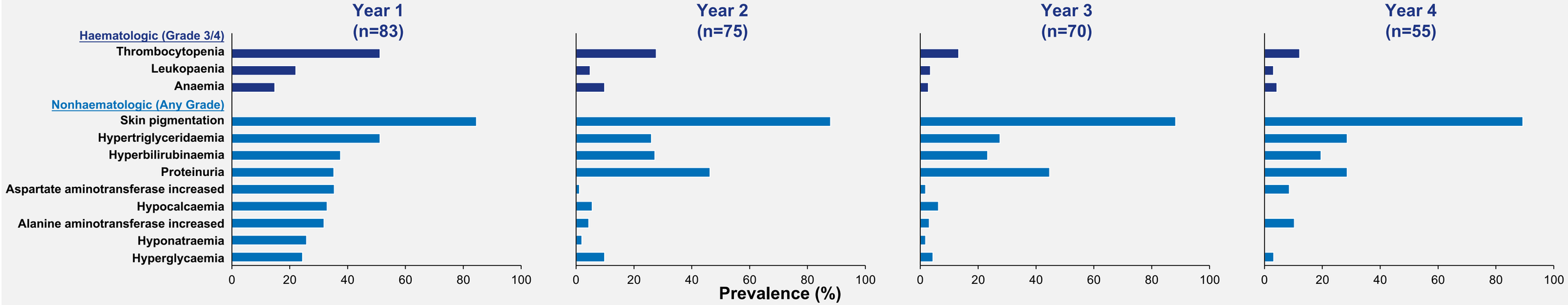


CML Response Criteria: Complete Hematological Response (CHR), Bone Marrow; Major Cytogenic Response (MCyR*)
Complete Cytogenic Response (CCyR), Major Molecular Response (MMR^)

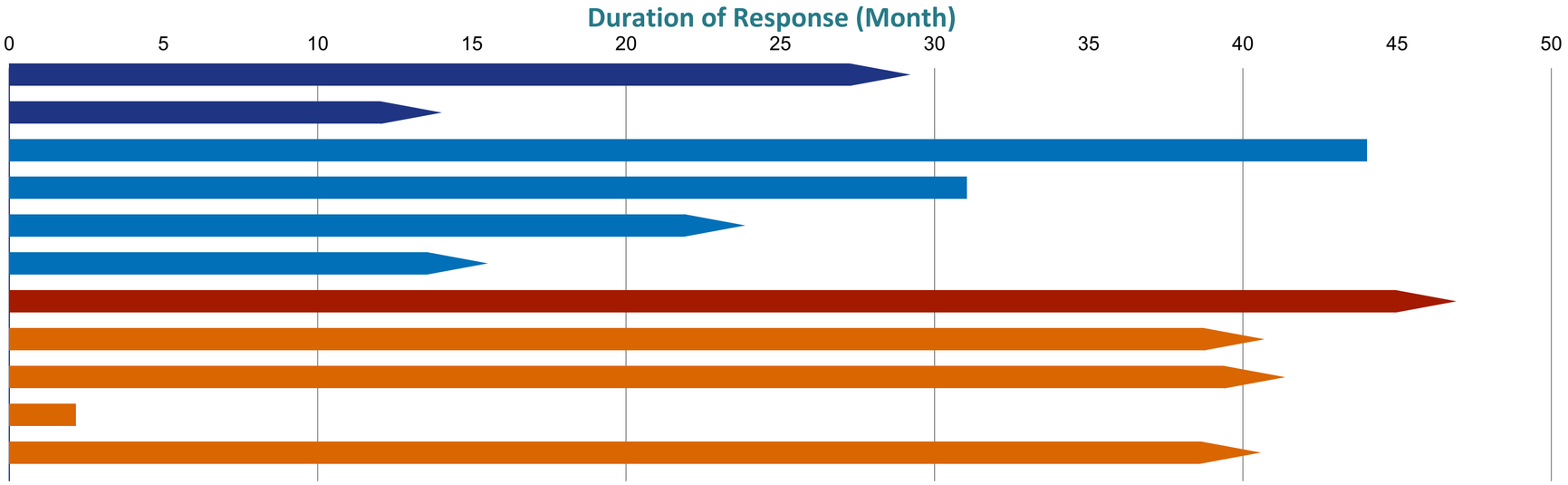
Source: Qian Jiang et al.(2021), Updated Safety and Efficacy Results of Phase 1 Study of Olverembatinib (HQP1351), a Novel Third-Generation BCR-ABL Tyrosine Kinase Inhibitor (TKI), in Patients with TKI-Resistant Chronic Myeloid Leukemia (CML) , 2021 ASH Annual Meeting and Exposition

Phase I Study Summary： Safety Profile and Compound Mutation

Prevalence of Treatment-related Adverse Events over Time (≥30mg), Well-Tolerated With Minimal Dose Interruptions



CP/AP	Mutation	Best response
CP	SS: G250E, F317L, T315I NGS: G250E, F317L, T3151	MR4.5
AP	SS: F359C, T315I NGS: F359C, T,315I	MR4.5
AP	SS: E255K, E279A, T315I, F317L NGS: E255K, E279A, T315I, F317L, F359C	MMR
CP	SS: T315I, E459K NGS: T315I, E459K	MMR
CP	SS: E459K, T315I, L248V, F359C NGS: E459K, T315I, L248V, F359C	MMR
CP	SS: T315I, F359V NGS: T315I, F359V	MMR
CP	SS: F359V, V299L, F317L NGS: F359V, V299L, F317L	CCyR
CP	SS: K247R, Y253F, T315I, F359I, ,G250E NGS: K247R, Y253F, T315I, F359I, ,G250E	CHR
CP	SS: F359V, M351T, T315I NGS: F359V, M351T, Y253H, T315I	CHR
AP	SS: T315I, E255K NGS: T315I, E255K	CHR
AP	SS: M244V, H396R NGS: M244V, H396R	CHR



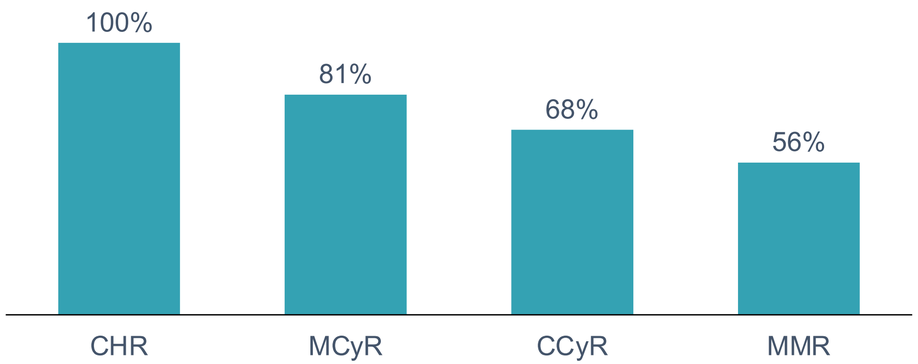
Source: Qian Jiang et al.(2021), Updated Safety and Efficacy Results of Phase 1 Study of Olverembatinib (HQP1351), a Novel Third-Generation BCR-ABL Tyrosine Kinase Inhibitor (TKI), in Patients with TKI-Resistant Chronic Myeloid Leukemia (CML) ,2021 ASH Annual Meeting and Exposition

Pivotal Phase 2 Study Summary

Highly Efficacious in T315I-Mutated CML Patients

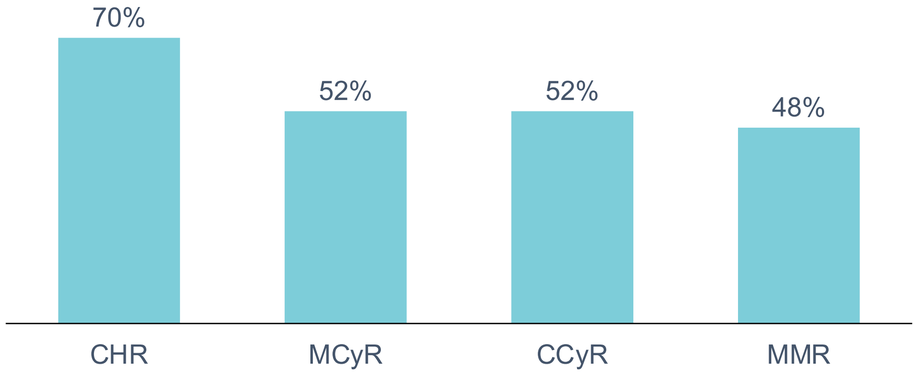
CP

T315I + n = 41



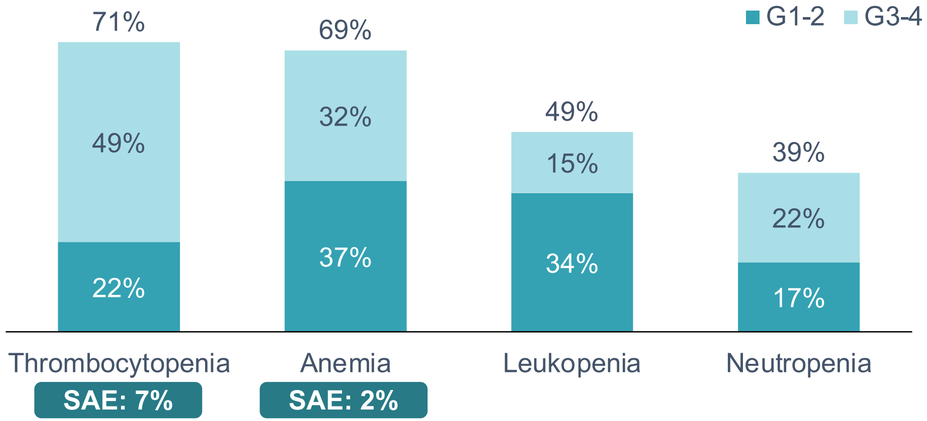
AP

T315I + n = 23



Treatment-related Hematologic Adverse Events

CP



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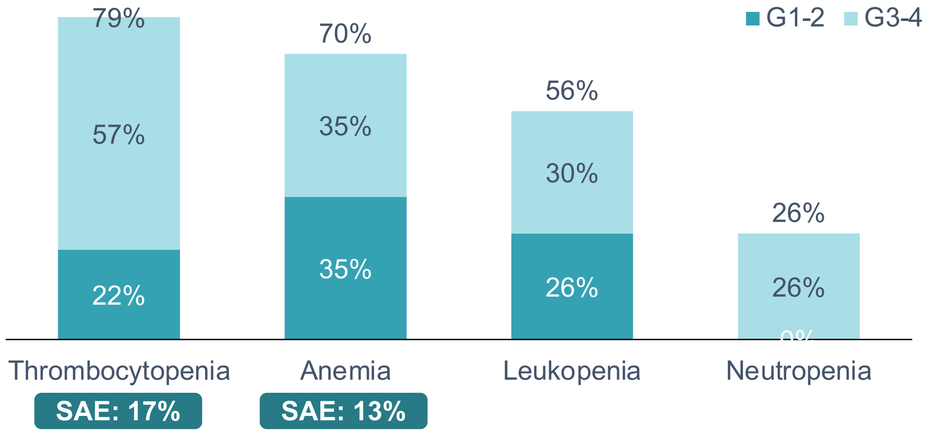


CML Response Criteria: Complete Hematological Response (CHR), Bone Marrow; Major Cytogenic Response (MCyR*) Complete Cytogenic Response (CCyR), Major Molecular Response (MMR^)

* MCyR is a validated End Point, ^ MMR defined by PCR (<1/1000)

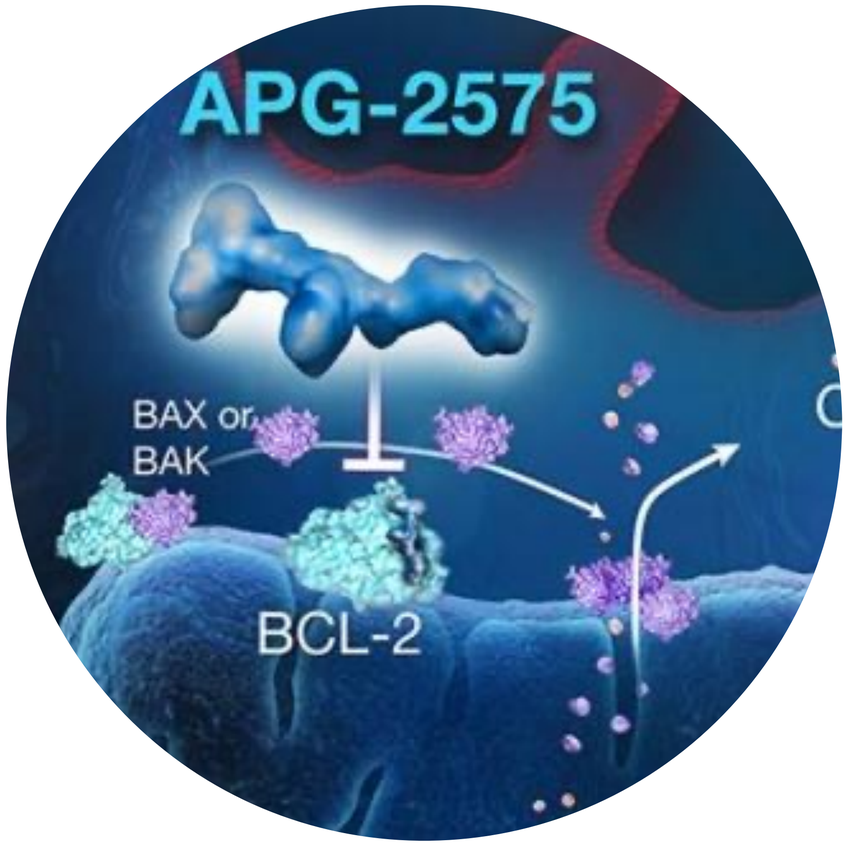
Source: Qian Jiang et al.(2021), Updated results of pivotal phase 2 trials of olverembatinib (HQP1351) in patients (pts) with tyrosine kinase inhibitor (TKI)-resistant BCR-ABL1 T315I-mutated chronic- and accelerated-phase chronic myeloid leukemia (CML-CP and CML-AP) , 2021 ASH Annual Meeting and Exposition

APG-2575 Overview

Novel, orally administered Bcl-2 selective inhibitor, follow to Venclexta®

The second drug entered into pivotal phase II study globally

Best in class potential



Clinical POC Established With Best-in-Class Safety Potential

1

More than **300** subjects enrolled into the APG-2575 studies, including r/r CLL, FL, MCL, MZL, DLBCL, WM, MM, AML, MDS and HCL patients, dosed ranging from 20mg to 1200mg

2

More than 190 patients with relapsed/refractory CLL (r/r CLL) have been treated with APG-2575 and POC achieved

- **80% PR** in Evaluable R/R CLL/SLL Patients in Phase I Study in the US
- Demonstrated **100% ORR** in Evaluable r/r CLL/SLL Patients at Dose ≥ 200 mg in Phase I Study in China

3

Potential Best-in-Class with well tolerated safety profile, no DLT, no MTD reported

4

5 Orphan Drug Designations (ODD):
CLL, WM, MM, AML, FL

5

IND clearance for ER+ breast cancer and other solid tumors by FDA

6

Initiated registrational pivotal Phase II study for treatment of r/r CLL/SLL and **the first patient has been dosed**

Source: Sikander Ailawadhi, et al.(2021), First-in-human study of lisaftoclax (APG-2575), a novel BCL-2 inhibitor (BCL-2i), in patients (pts) with relapsed/refractory (R/R) CLL and other hematologic malignancies (HMs)., 2021 ASCO Annual Meeting and Exposition ； Mingyuan Sun, et al.(2021), A Phase 1 Study to Evaluate the Safety, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Lisaftoclax (APG-2575), a Novel BCL-2 Inhibitor (BCL-2i), in Patients (pts) with Certain Relapsed or Refractory (R/R) Hematologic Malignancies (HMs) , 2021 ASH Annual Meeting and Exposition

Phase I Study in the US: Safety+ 80%ORR

Treatment-related adverse events with APG-2575 (N = 36)

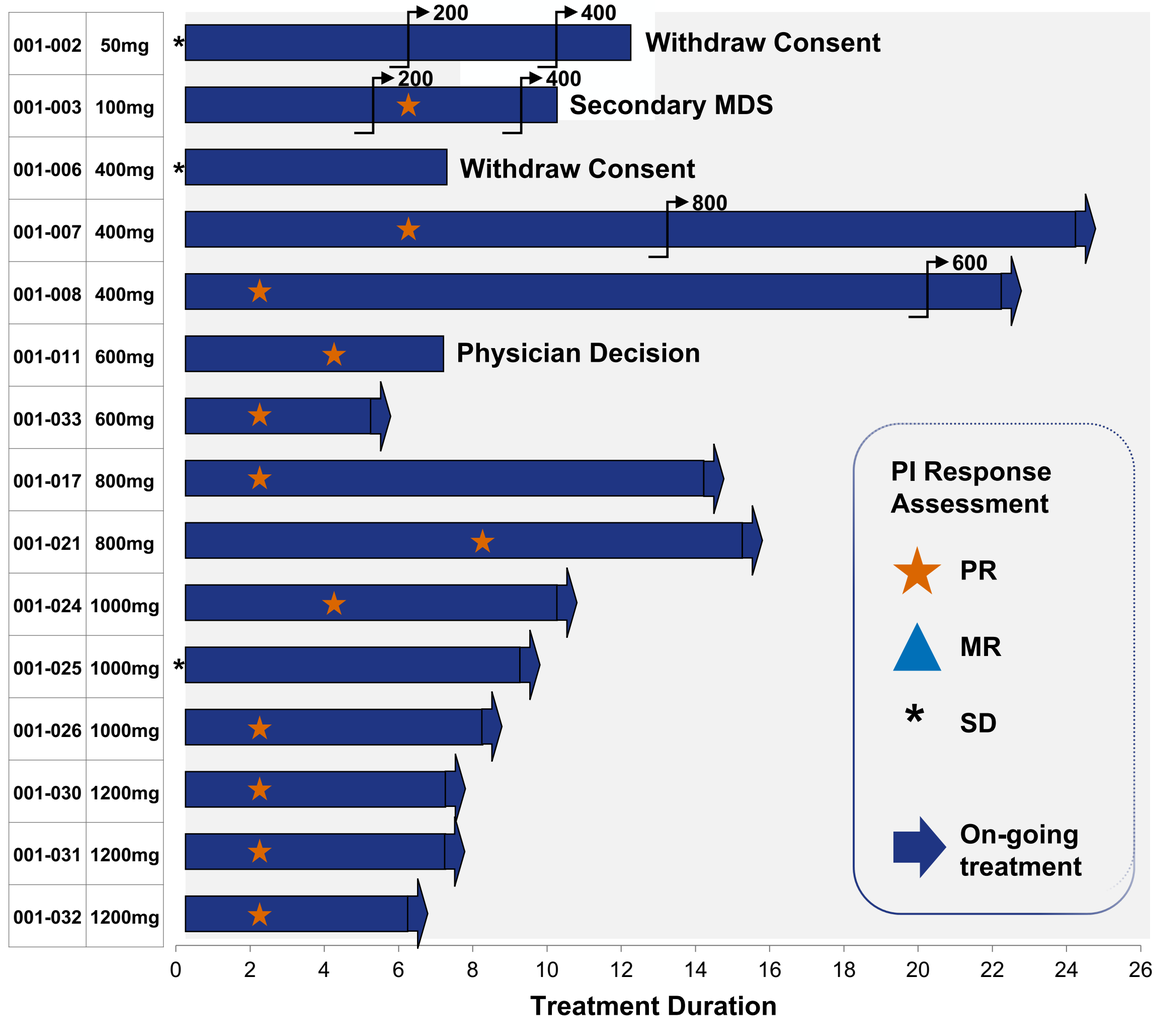
Any grade AE (≥ 10%)	No. (%)
Any APG-2575-related AE[a]:	27 (75.0)
Fatigue	10 (27.8)
Neutropenia	8 (22.2)
Diarrhea	7 (19.4)
Anemia	6 (16.7)
Constipation	4 (11.1)
Nausea	4 (11.1)

≥ Grade 3 AE (≥ 5%)	No. (%)
Any ≥ grade 3 APG-2575-related AE:	9 (25.0)
Neutropenia	5 (13.9)
Nausea	2 (5.6)
Platelet count decreased	2 (5.6)
–	–
–	–
–	–

- No DLTs observed at APG-2575 doses of up to 1,200 mg.
- The MTD has not been reached.
- No laboratory or clinical TLS has been reported during this study.
- The median (range) treatment duration is 6 (1-24) cycles.
- APG-2575 at 600 mg daily has been selected as the RP2D for monotherapy.
- In all, one patient (1/36, 2.8%) discontinued APG-2575 because of TRAEs (grade 2 pruritus, skin sensitivity).
- No grade 5 TRAEs noted.

CLL/SLL Swimmer Plot

80% PR in Evaluable R/R CLL/SLL Patients



a A patient with more than one AE is counted once.

Source: Sikander Ailawadhi, et al.(2021), First-in-human study of lisaftoclax (APG-2575), a novel BCL-2 inhibitor (BCL-2i), in patients (pts) with relapsed/refractory (R/R) CLL and other hematologic malignancies (HMs)., 2021 ASCO Annual Meeting and Exposition

Phase I Study in China: Safety/Efficacy+100%ORR

Lisaftoclax is well tolerated

No DLT observed, MTD not reached

Extremely low lab and clinical TLS

Treatment-related adverse events with APG-2575 (TRAEs; ≥10%)

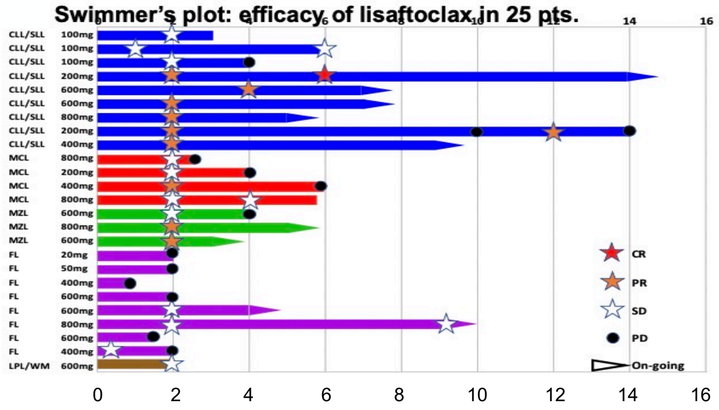
	20 mg	50 mg	100 mg	200 mg	400 mg	600 mg	800 mg	Total
Population	2	1	3	3	6	9	7	31
Any TRAE, n (%)	2 (100%)	1 (100%)	3 (100%)	3 (100%)	4 (66.7%)	7 (77.8%)	8 (100%)	28 (87.5%)
System Organ Class/Preferred term, n (%)								
Platelet count decreased	1 (50.0%)	0	2 (66.7%)	1 (33.3%)	2 (33.3%)	2 (22.2%)	3 (37.5%)	11 (34.4%)
Anemia	1 (50.0%)	1 (100%)	2 (66.7%)	0	0	2 (22.2%)	3 (37.5%)	9 (28.1%)
Neutrophil count decreased	0	0	2 (66.7%)	2 (66.7%)	1 (16.7%)	1 (11.1%)	1 (12.5%)	7 (21.9%)
White blood cell count decreased	0	0	1 (33.3%)	1 (33.3%)	1 (16.7%)	0	4 (50.0%)	7 (21.9%)
Hyperuricemia	0	0	1 (33.3%)	0	0	2 (22.2%)	2 (25.0%)	5 (15.6%)
Diarrhea	0	0	0	1 (33.3%)	1 (16.7%)	2 (22.2%)	1 (12.5%)	5 (15.6%)
Hyperphosphatemia	0	0	0	0	0	2 (22.2%)	2 (25.0%)	4 (12.5%)
Hypertriglyceridemia	0	0	1 (33.3%)	1 (33.3%)	0	1 (11.1%)	1 (12.5%)	4 (12.5%)

TRAEs ≥ Grade 3 and SAE

	≥Grade 3, n (%)	SAE, n (%)
Population	31	31
Any TRAE, n (%)	7 (21.9)	1 (3.2)
System Organ Class/Preferred term, n (%)		
Platelet count decreased	4 (12.5)	1 (3.2)
Neutrophil count decreased	3 (9.4)	0
White blood cell count decreased	1 (3.1)	0
Anemia	2 (6.3)	1 (3.2)

All TRAE SAEs were observed in 1 patient at the 100-mg dose level

APG-2575 Swimmer's plot (25pts)



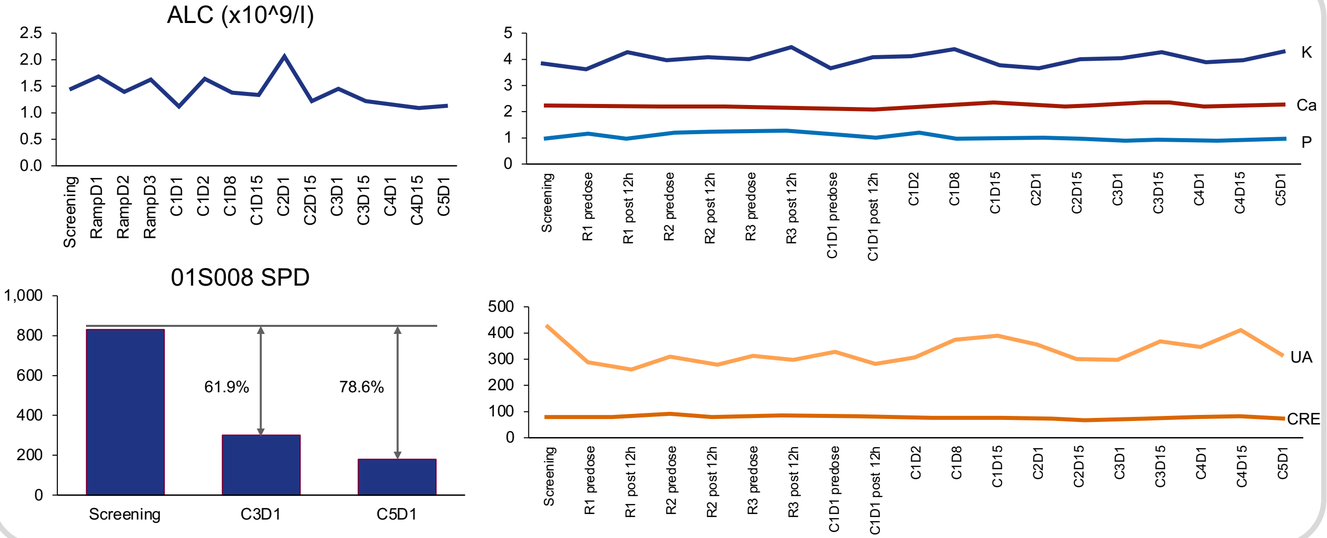
100% ORR in Evaluable R/R CLL/SLL Patients at Dose ≥ 200 mg in China Phase I Study

- With a median treatment of 4 cycles, 9/25 evaluable pts achieved at least a PR
- The highest response rates were seen in pts with CLL (66.7%). At doses of ≥ 200 mg, all 6 pts with CLL experienced a PR or CR.

Source: Mingyuan Sun, et al.(2021), A Phase 1 Study to Evaluate the Safety, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Lisaftoclax (APG-2575), a Novel BCL-2 Inhibitor (BCL-2i), in Patients (pts) with Certain Relapsed or Refractory (R/R) Hematologic Malignancies (HMs) , 2021 ASH Annual Meeting and Exposition

APG-2575-CN-001 Phase I Interim Data I Efficacy

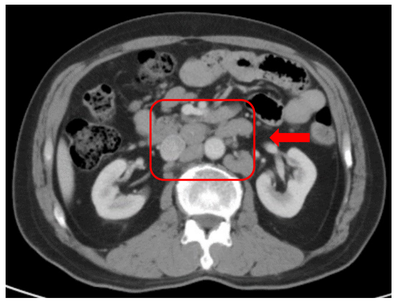
Ibrutinib Resistant High Risk Patient; Rapid and Deep Response



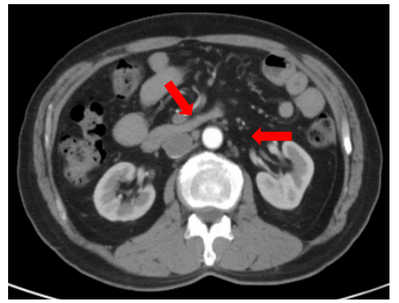
Patient 01S008: Complete Response

CR in r/r CLL (IGVH mutation, No TP53)

Before APG-2575



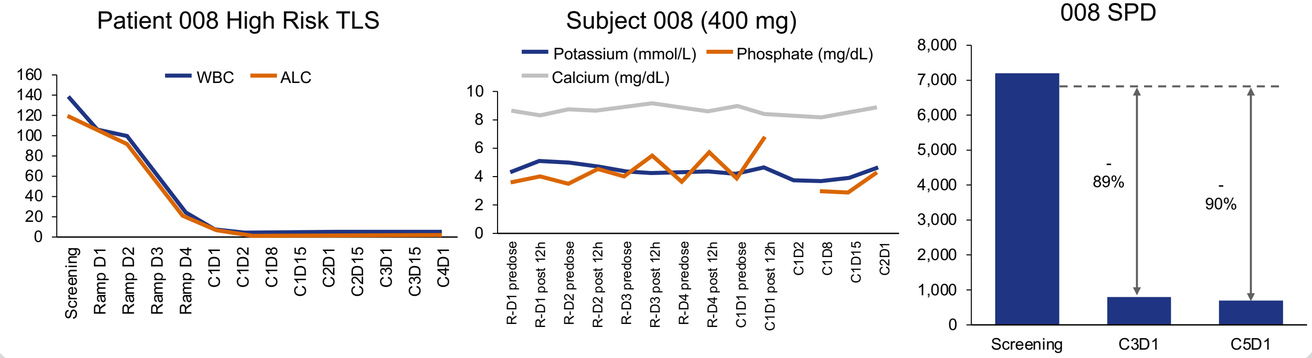
After APG-2575



Lymph Node Response: C3D1 **-62%;** C5D1 **-78.6%;** C7D1 **All lymph nodes normal**

Del17p CLL Patient at High Risk of TLS: Rapid & Deep Response

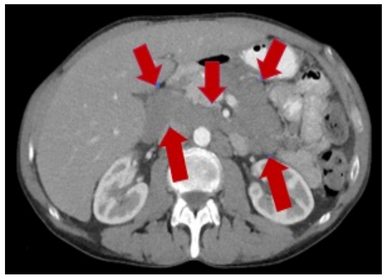
Patient 008: PR parameters



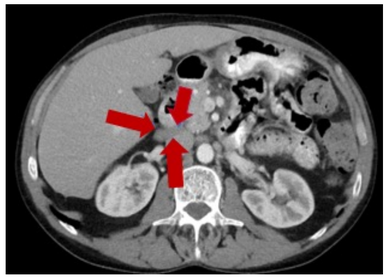
Durable PR in a patient with r/r CLL

Patient 008: -90% Nodal Response

Before APG-2575



After APG-2575



Nodal Response: C3D1-89% | C5D1-90%

Source: Mingyuan Sun, et al.(2021), A Phase 1 Study to Evaluate the Safety, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Lisaftoclax (APG-2575), a Novel BCL-2 Inhibitor (BCL-2i), in Patients (pts) with Certain Relapsed or Refractory (R/R) Hematologic Malignancies (HMs) , 63rd ASH Annual Meeting and Exposition

Strong Differentiation From Venetoclax

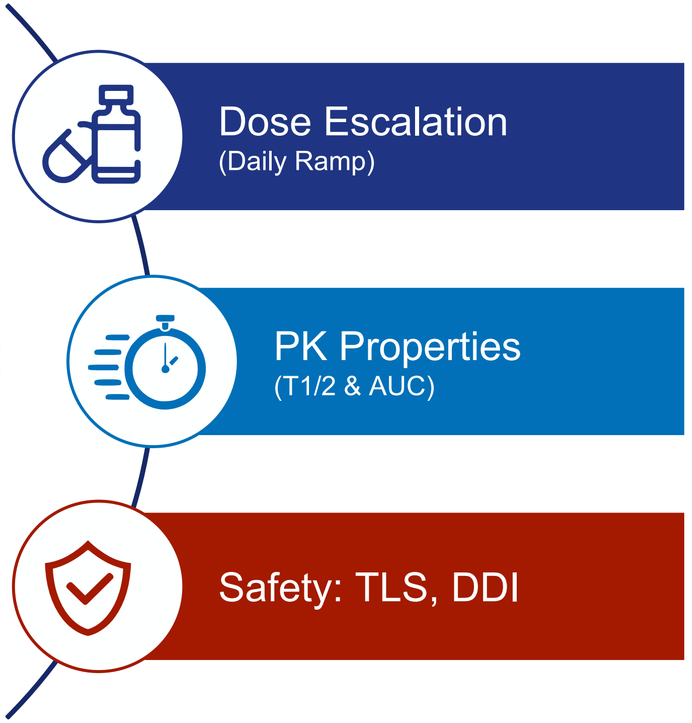
APG-2575 Compared to Venetoclax

- Efficacious in BTK resistant WM PDX model in which Venetoclax shows no effect
- Daily ramp-up verse weekly ramp up
- Extremely low lab and clinical TLS
- Less neutropenia and thrombocytopenia
- Short T1/2 & exposure--potentially lower risk with better safety profile
- Second BCL-2 registration clinical trial globally
  First BCL-2 registration clinical trial for CLL in China

Product, Patient, Provider Attributes

When Selectively Targeting BCL-2

Less is more



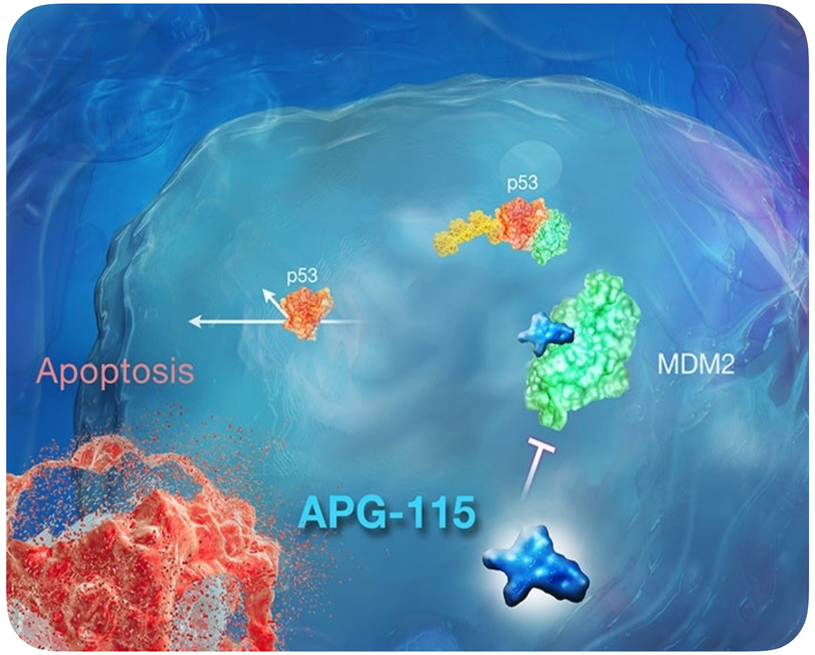
Source: Company data

APG-115

MDM2-p53 Inhibitor

Activates p53 tumor suppression via MDM2-p53 PPI

Potential First-in-Class Drug



APG-115 : Mechanism

APG-115 Delivers Anti-tumor Activity by Multiple MOAs

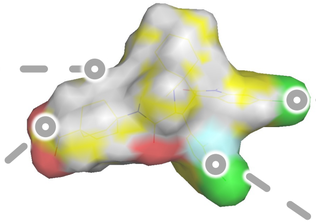
Tumor Cells Apoptosis

Activates WT p53-dependent intrinsic apoptosis.

T-Cell Mediated Anti-tumor Immunity

MDM2 protein expression is upregulated in T-cell and is essential in enhancing T-cell function via stabilization of STAT5 protein

(*Zhou et al. Nature 2021)*



APG-115
Inhibition of MDM2-p53 interaction

Tumor microenvironment

Activates innate immunity by reprograming macrophages M2 to M1 to suppress tumorigenesis (Fang et al. 2019).

Synthetic Lethality

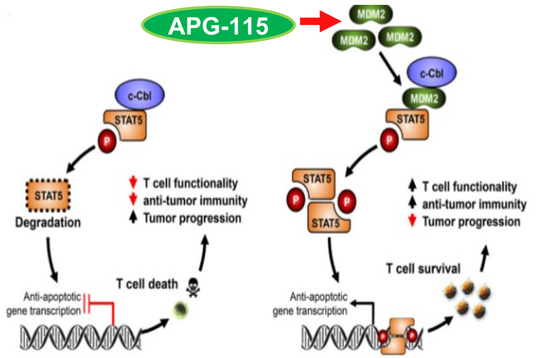
+ Bcl-2: AML, DLBCL *(Luo et al. 2020)*

+ BET: AML *(Li et al. 2020; Latif et al. 2021)*

+ ATM / + MET: Lung, CRC *(Sullivan et al. 2012)*

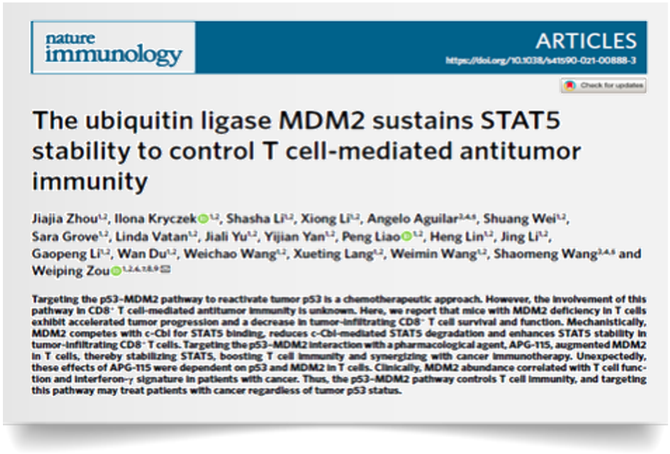
Host immunomodulator

- STAT5 activation is important for CD8$^+$ T-cell survival and function.
- MDM2 competes with c-Cbl and prevents c-Cbl-mediated STAT5 degradation.
- APG-115 synergizes with IO and enhances T-cell mediated antitumor immunity.



Zhou J et al. Nat Immunol 2021;22:460-470.

STAT5, signal transducer and activator of transcription 5.
5. Tolcher AW et al. Molec Cancer Ther 2019;18:A086.


nature immunology ARTICLES

The ubiquitin ligase MDM2 sustains STAT5 stability to control T cell-mediated antitumor immunity

Jiajia Zhou, Ilona Kryczek, Shasha Li, Xiong Li, Angelo Aguilar, Shuang Wei, Sara Grove, Linda Vatan, Jiali Yu, Yijian Yan, Peng Liao, Heng Lin, Jing Li, Gaopeng Li, Wan Du, Weichao Wang, Xueting Lang, Weimin Wang, Shaomeng Wang and Weiping Zou

Targeting the p53–MDM2 pathway to reactivate tumor p53 is a chemotherapeutic approach. However, the involvement of this pathway in CD8$^+$ T cell-mediated antitumor immunity is unknown. Here, we report that mice with MDM2 deficiency in T cells exhibit accelerated tumor progression and a decrease in tumor-infiltrating CD8$^+$ T cell survival and function. Mechanistically, MDM2 competes with c-Cbl for STAT5 binding, reduces c-Cbl-mediated STAT5 degradation and enhances STAT5 stability in tumor-infiltrating CD8$^+$ T cells. Targeting the p53–MDM2 interaction with a pharmacological agent, APG-115, augmented MDM2 in T cells, thereby stabilizing STAT5, boosting T cell immunity and synergizing with cancer immunotherapy. Unexpectedly, these effects of APG-115 were dependent on p53 and MDM2 in T cells. Clinically, MDM2 abundance correlated with T cell function and interferon-γ signature in patients with cancer. Thus, the p53–MDM2 pathway controls T cell immunity, and targeting this pathway may treat patients with cancer regardless of tumor p53 status.

APG-115 ：Clinical Development and Progress

First-in-class potential
Achieved Clinical POC

The FDA has granted **six ODDs** to APG-115 for the treatment of soft tissue sarcoma, gastric cancer (GC), AML, Retinoblastoma, stage IIB-IV melanoma as well Neuroblastoma.

Granted **2 Rare Pediatric Disease (RPD)** designation for the treatment of Retinoblastoma and Neuroblastoma

Granted a **Fast Track Designation** (FTD) by the FDA for the treatment of patients with unresectable or metastatic melanoma, relapsed/refractory to prior immuno-oncologic agent (IO) treatments.

Clinical Development in the US

- Combination with KEYTRUDA®
  - Phase Ib clinical trial completed the patient enrollment
  - The results of a phase II clinical study of APG-115 in combination with pembrolizumab demonstrated promising antitumor activity and good tolerability, and specifically in the PD-1/PD-L1 inhibitor-resistant melanoma cohort reported 1 patient with complete response (CR), an objective response rate (ORR) of 24.1%, and a disease control rate (DCR) of 55.2%.
  - A phase Ib/II study of APG-115 alone or in combination with azacytidine in AML/MDS/CMML (chronic myelomonocytic leukemia).
- An investigator-initiated monotherapy phase I/II study for treatment of salivary gland cancer.

Clinical Development in China

- In May 2021, we initiated a trial of APG-115 in combination with PD-1 Inhibitor in patients with advanced liposarcoma or advanced solid tumors. First patient has been dosed for this trial.
- A phase Ib monotherapy study followed by a combination study with azacytidine or cytarabine in R/R MDS or AML.

APG-115 Plus Pembrolizumab: Efficacy

Efficacy in all Cohorts

Response	Melanoma (n = 32)	NSCLC (n = 19)	STK-11 (n = 5)	ATM (n = 11)	Liposarcoma (n = 17)	UC (n = 12)	MPNST (n = 6)
ORR *(CR + PR)*	24.1% *(7/29)*	6.7% *(1/15)*	0	0	6.2% *(1/16)*	12.5% *(1/8)*	16.7% *(1/6)*
DCR *(CR + PR + SD)*	55.2% *(16/29)*	46.7% *(7/15)*	25% *(1/4)*	44.4% *(4/9)*	81.2% *(13/16)*	12.5% *(1/8)*	66.7% *(4/6)*
Best overall RECIST or iRECIST response							
CR	1	0	0	0	0	0	0
PR	6 *(2 unconfirmed)*	1	0	0	1 *(unconfirmed)*	1	1 *(unconfirmed)*
SD	9	6	1	4	12	0	3

ORR and **DCR** are based on efficacy evaluable population; stable disease (**SD**) requires a minimum duration of 2 cycles. **CR**, complete response; **DCR** disease control rate; **PR**, partial response; **RECIST**, Response Evaluation Criteria in Solid Tumors; **UC**, urothelial carcinoma.

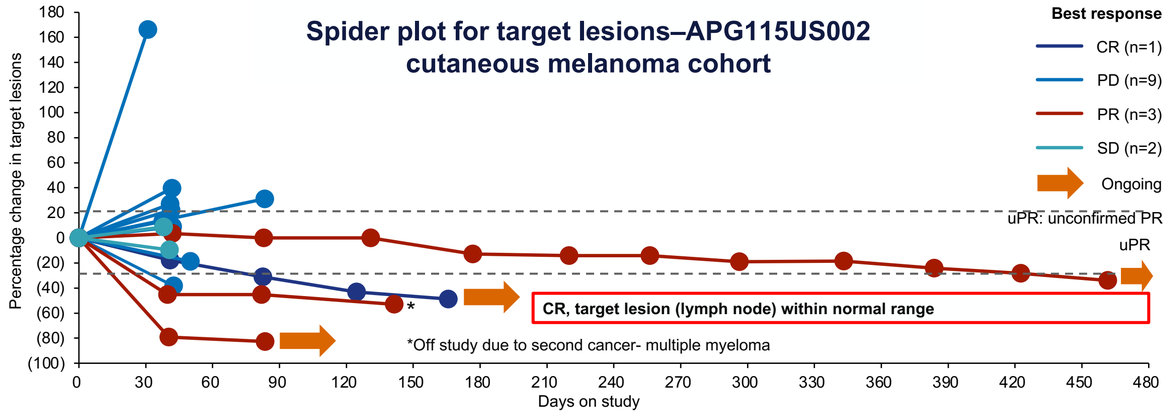
Efficacy in Patients with IO Resistant Melanoma

Response	Uveal (n = 8)	Mucosal (n = 5)	Cutaneous (n = 16)	Unknown primary (n = 3)	Total (N = 32)
ORR *(CR + PR)*	14.3% *(1/7)*	40% *(2/5)*	26.7% *(4/15)*	0	**24.1%** *(7/29*)*
DCR *(CR + PR + SD)*	71.4% *(5/7)*	40% *(2/5)*	46.7% *(7/15)*	100% *(2/2)*	**55.2%** *(16/29)*
Best overall RECIST or iRECIST response					
CR	0	0	1	0	**1**
PR	1	2 *(1 unconfirmed)*	3 *(1 unconfirmed)*	0	**6**
SD	4	0	3	2	**9**

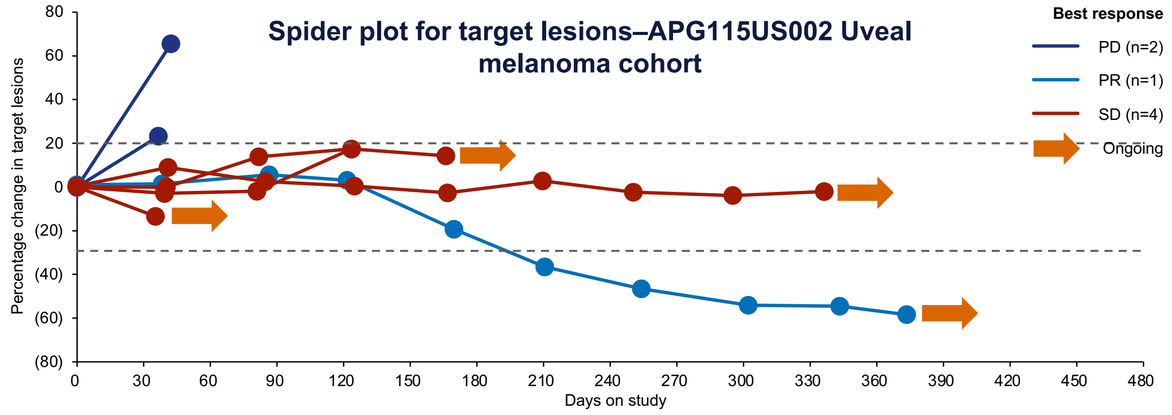
Data cutoff: April 15, 2021.

* Total evaluable patient N: 29

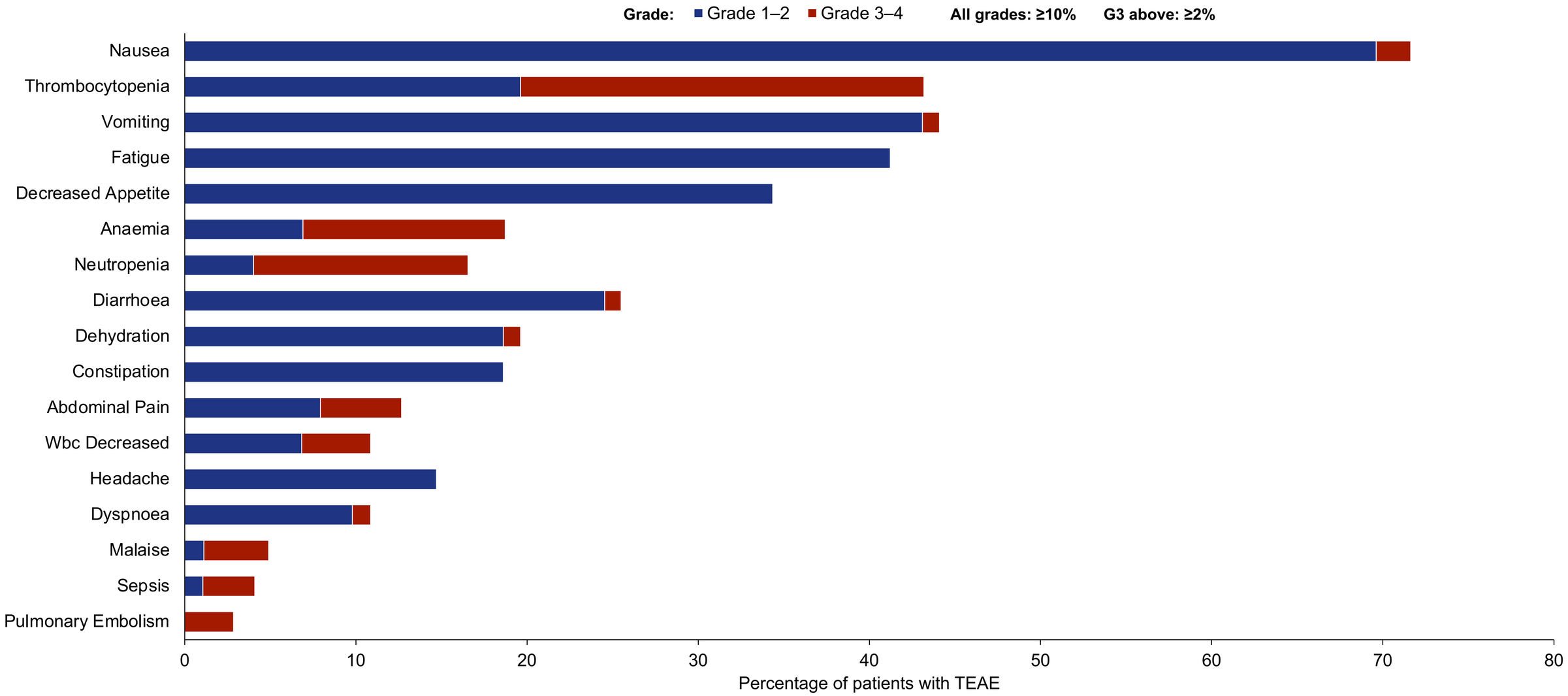
Efficacy in Patients with IO Resistant Cutaneous Melanoma Treated with APG-115 Plus Pembrolizumab



Efficacy in Patients with IO Resistant Uveal Melanoma Treated with APG-115 Plus Pembrolizumab

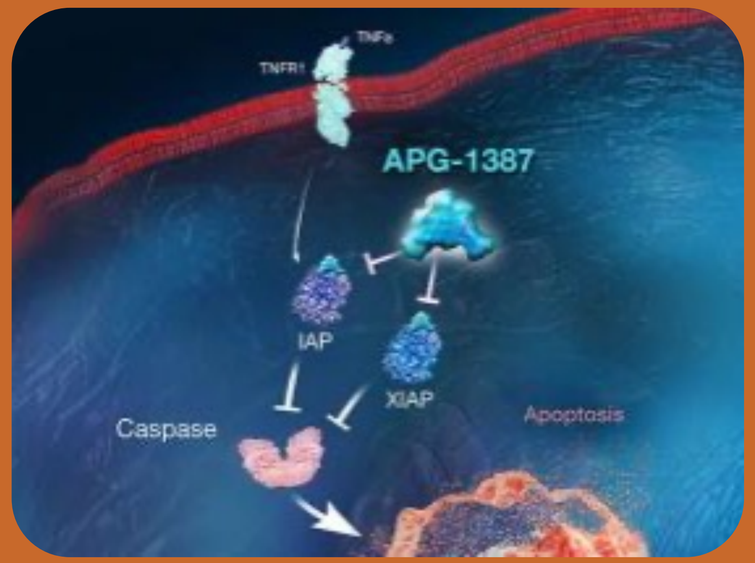


Safety: Treatment Emergent AEs (TEAEs)



APG-1387

An Antagonist of IAP/XIAP
(SMAC Mimetic) Dimmer



Milestones & Clinical Developments

CHB Development

- We have already completed a phase I study for the treatment of patients with CHB.
- The stage 1 safety evaluation of APG-1387 in combination with Entecavir (ETV) for a phase II study has completed. With well-tolerated safety data, the study moved forward to stage 2, efficacy evaluation of APG-1387 in combination with ETV compared to ETV monotherapy.

Immuno-Oncology Development

- A phase I clinical trial in the United States, testing combination of APG-1387 with pembrolizumab, an anti-PD-1 mAb in solid tumors is ongoing. The patient enrollment is expected to be completed in 2022.
- In China, a phase Ib/II clinical trial testing the combination of APG-1387 with toripalimab (拓益), another anti-PD-1 mAb, in solid tumors, is ongoing as well. The phase Ib patient enrollment has been completed and the trial has entered into phase II.
- A phase I/II study that aims to investigate the combination of APG-1387 with chemotherapy, Nab-paclitaxel and Gemcitabine for treating advanced pancreatic cancer. First patient has been dosed in March 2021.

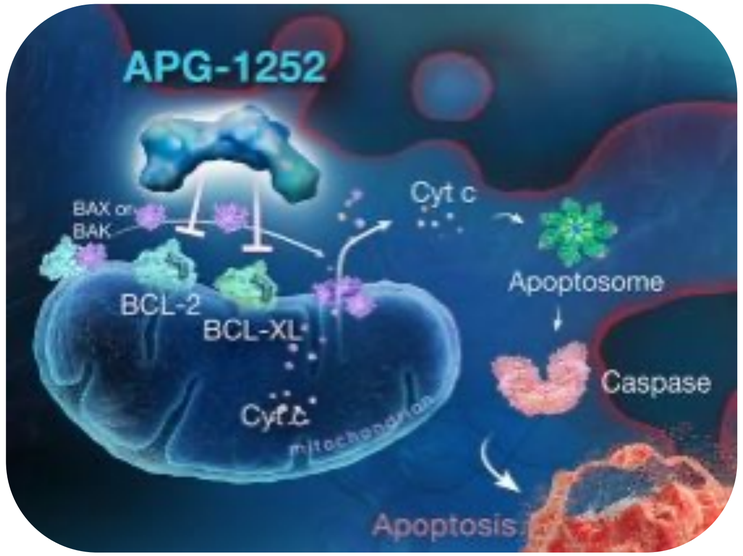
APG-1252

Bcl-2/Bcl-xL inhibitor

Combination use for the treatment of
solid tumors and hematologic malignancies

Granted an ODD
for the treatment of SCLC

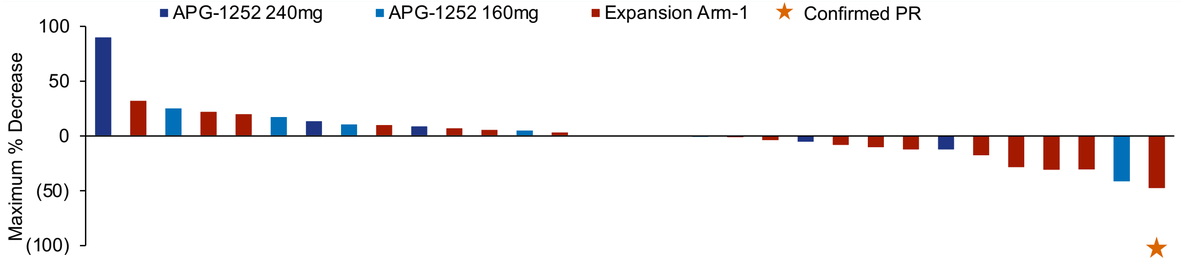
Potential Best-in-Class Drug



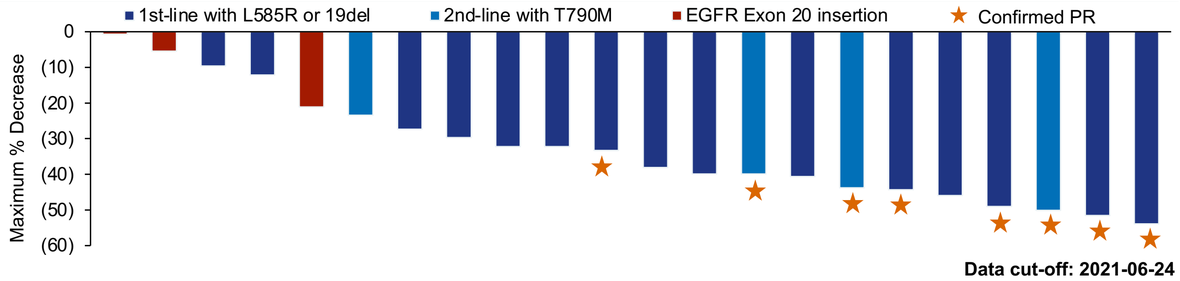
APG-1252 plus Osimertinib：Efficacy

Best response, n (%)	Dose determination 240mg (n=6)	Dose determination 160mg (n=5)	Expansion Arm-1 (n=20)	Expansion Arm-2 (n=22)
Partial response (unconfirmed)	0 (0.0)	1 (20.0)	3 (15.0)	13 (59.1)
Partial response (confirmed)	0 (0.0)	0 (0.0)	1 (5.0)	8 (36.4)
Stable disease	5 (83.3)	2 (40.0)	13 (65.0)	8 (36.4)
Progressive disease	1 (16.7)	2 (40.0)	4 (20.0)	1 (6.3)
DCR	5 (83.3)	3 (60.0)	16 (80.0)	21 (95.5)

Dose determination and expansion Arm-1 N=31



Expansion Arm-2 N=22



Data cut-off: 2021-06-24

- In dose-escalation: 1 PR in 11 evaluable TKI resistant patients
- In arm 1 of dose-expansion phase: 3 PRs and 13 SDs in 20 evaluable patients with ORR of 15% and DCR of 80%
- In arm 2 of dose-expansion phase, 13 PRs and 8 SDs in 22 evaluable patients, including 3 patients harboring EGFR Exon 20 insertion with ORR of 59.1% and DCR of 95.5%.

Combination treatment with APG-1252 and osimertinib at RP2D was safe and feasible.

Preliminary synergy and efficacy of both APG-1252 and osimertinib were also observed in some patients with EGFR TKI osimertinib-resistant and naïve NSCLC.

In treatment-naive and second-line patients with the EGFR T790M mutation or Exon 20 insertion, APG-1252 showed similar efficacy compared with navitoclax when combined with osimertinib

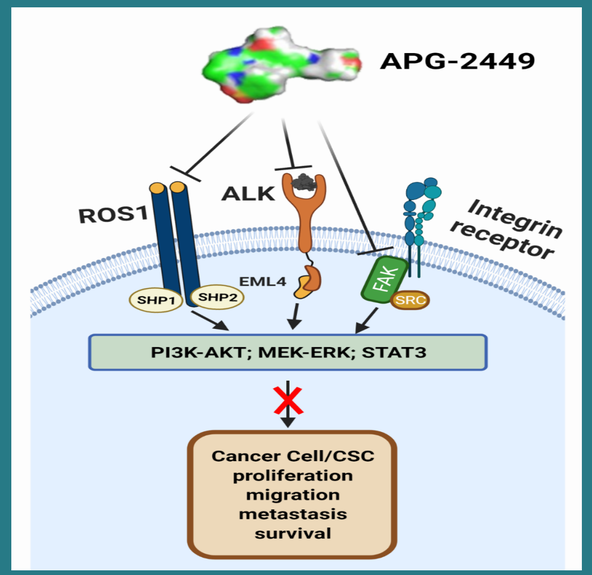
No significant difference in PK profiles of APG-1252 and osimertinib observed in combination treatment when compared to monotherapy.

IASLC 2021 World Conference on Lung Cancer
SEPTEMBER 8 - 14, 2021 I WORLDWIDE VIRTUAL EVENT

Source: Li Zhang et al.(2021), Phase 1b Study of Pelcitoclax (APG-1252) in Combination With Osimertinib in Patients With EGFR TKI-Resistant NSCLC , 2021 World Conference on Lung Cancer (WCLC)

APG-2449

ALK/FAK/ROS1



Milestones & Clinical Developments

APG-2449

- APG-2449 is a novel, orally active, small molecule FAK/ALK/ROS1 triple ligase kinase inhibitor designed and developed by us. It is the first third-generation ALK inhibitor being developed in China.
- Pre-clinical data indicated that It is a very potential novel anticancer drug targeting FAK-expressing tumors and/or ALK/ROS1 fusion gene-positive non-small cell lung cancer.
- APG-2449 dose-dependently inhibited the expression of phosphorylated ALK protein (P-ALK) and its downstream proteins in Ba/F3 cells harboring ALK WT or EML4-ALK L1196M mutation.

Clinical development of APG-2449 in 2021

- Dose Escalation study was completed for phase I study in which patients with ALK+ NSCLC or other solid tumor were enrolled. Enrollment is ongoing for Dose Expansion Cohorts for efficacy assessment in different patient population. The clinical result of the phase I study will be published in the coming medical conference. Based on the preliminary efficacy result of phase I study, the engagement with CDE for pivotal phase II registration study design is to be kicked off in 2022.

Pre-Clinical Assets

EED Selective

APG-5918

MDM2-p53 Degrader

APG-265

Focused on validated targets with clear biomarker, clinical indications and fast regulatory approval

High unmet medical needs

Transformative new technology

First-in-class or best-in-class potential

IP Portfolio for Key Clinical Assets

Key Clinical Assets	Estimated Patent Expired Year
HQP1351	2035-2041*
APG-2575	2037-2041*
APG-115	2035-2041*
APG-1387	2033-2041*
APG-1252	2034-2041*

*including composition, process, formulation, combination, use, new indication etc; (issued or pending)

Source: Company data Note: All data as of December 31, 2021

Sustainable Competitive Advantage

Ascentage Pharma focuses on developing therapeutics that inhibit protein-protein interactions to restore apoptosis or programmed cell death

Professional and effective clinical groups in China and the US

- ✓ **30+ IND globally**
- ✓ **50+ clinical studies globally**

Multiple strategic alliances provide innovation synergy

Investment Highlights

To discovery and development of innovative first- and best-in-class therapies to address unmet medical needs globally

To become a fully integrated globally-focused biotechnology company.

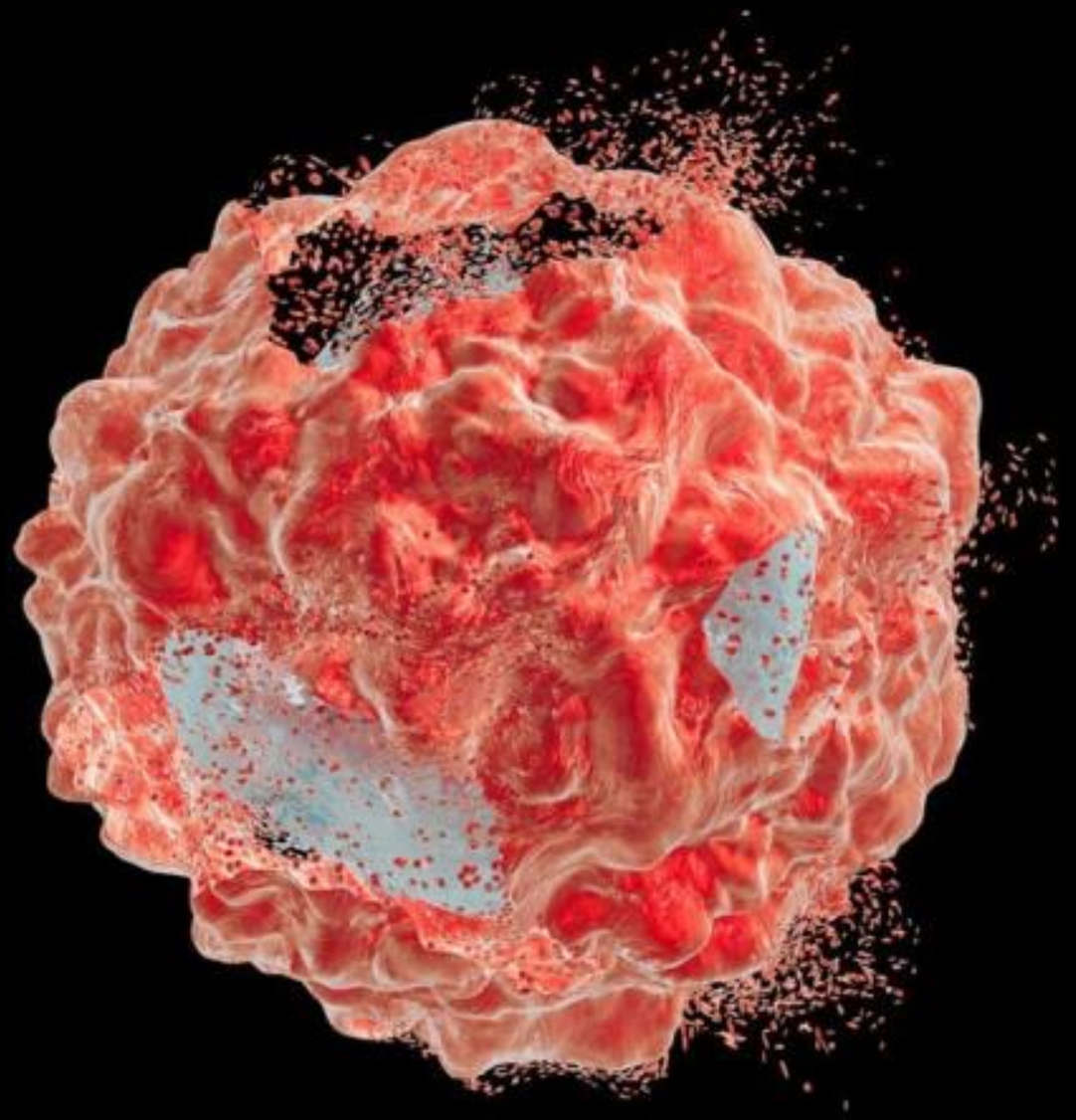
Global leader in apoptosis targeting therapy with commercial stage product

Product pipeline with the first- and/or best-in-class potential

Strong global intellectual property portfolio and compelling combination opportunities

Experienced executive management team and talents

Global collaboration with leading companies and institutions



Ascentage Pharma Group

Advancing Therapies That Restore Apoptosis