Polaris

Leading the Way to New and Better Metabolic Treatments

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Polaris: Best Companion Drug for Hard-to-treat Cancers

Platform	Pipeline	People and Assets
1,600+ Patients Treated with ADI-PEG 20	**1** BLA[1] Rolling Submission Initiated	**~$200M** Cash Position[5] as of Sep 30, 2023
In-house Arginine Degradation Development Platform	**7** Ongoing Clinical Trials[2] - **3** Registrational	**60+** US / International Patents
Proprietary State-of-the-art Manufacturing Facilities	**2** Fast Track Designations[3]	**160+** Employees Globally
	5 Tumor Types in Clinical Trials	
	3 Orphan Drug Designations[4]	

Partners and Collaborators

NIH NATIONAL CANCER INSTITUTE

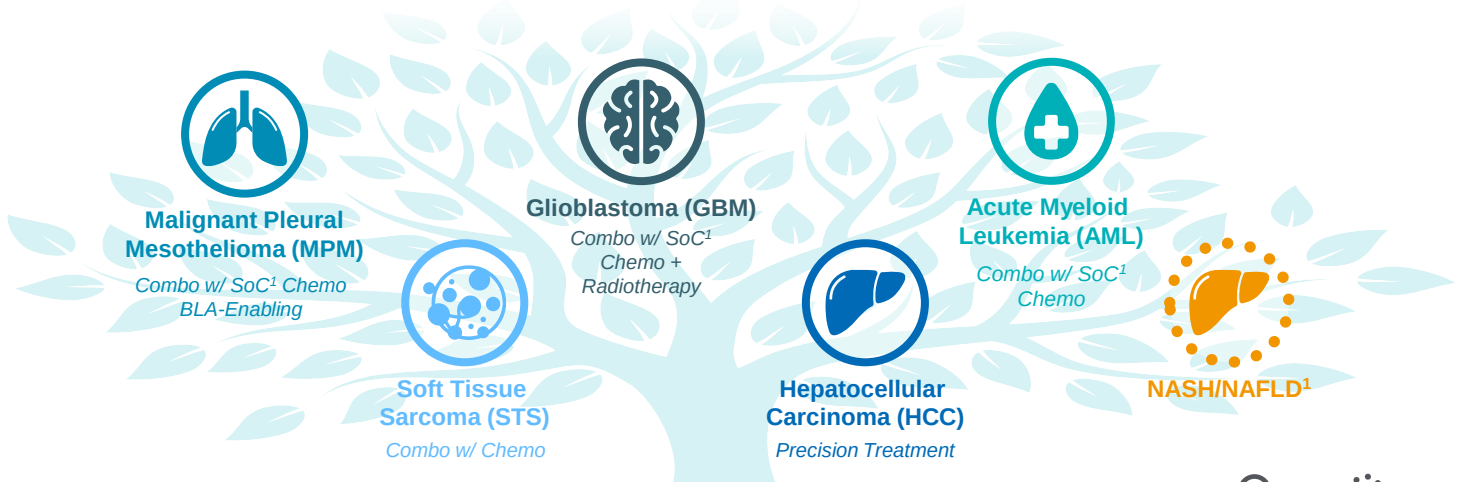
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Memorial Sloan Kettering Cancer Center

Barts Cancer Institute

Source: Company information.
Notes: 1. Biologics License Application. 2. Include trials which have enrolled at least one subject or are initiating and included on ClinicalTrials.gov. 3. Granted by FDA. 4. Granted by FDA & EMA . 5. Unaudited.

Business Overview – Metabolic Therapy Across Multiple Tumor Types



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Discovery and Research | **CMC** | **Clinical Development** | **Commercialization** | **Business Development**

Fully-integrated, end-to-end biological platform encompasses all the key biologic drug development functionalities

Source: Company information.
Notes: 1. Standard of Care (SoC). 2. Nonalcoholic steatohepatitis (NASH) and nonalcoholic fatty liver disease (NAFLD).

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Lead Clinical Program

ADI-PEG20

First in class arginine degradation platform for hard-to-treat cancers

ADI-PEG 20 Background: Potential in Multiple Oncology Indications and NASH

Safety and Efficacy

- Excellent safety profile in over **1,600 patients** based on >30 clinical trials
- Positive phase 3 trial **(improved survival [OS+PFS]) in pleural mesothelioma.** Initiated BLA rolling submission
- Demonstrated safety and efficacy with meaningful clinical benefit to patients across a **wide range of hard-to-treat cancers**
- First-in-class novel pegylated arginine deiminase as a **synergistic backbone for combination therapies**

Blockbuster Potential

- Potential **pan-cancer treatment**
- Potential across liver and metabolic diseases with evidence in **NASH / NAFLD**
  No further testing required by Taiwan FDA for phase 2a trial now enrolling NASH patients and similarly for US FDA trial in obese adolescents
- Monotherapy treatment in obese mice improved insulin sensitivity, dyslipidemia, liver steatosis & **increased FGF21 secretion**[1] thus recapitulating and expanding human findings

Global Rights

- Strong IP position with **12 years exclusivity** upon BLA approval to
- Multiple patents granted for lead asset (**3 ODD granted**); now advancing 2nd generation compound with strong IP position
- 2nd generation attributes include **9-10x higher specific activity**, can be lyophilized so longer shelf life & better storage conditions, higher enzymatic activity after PEGylation process

Fully De-risked Opportunity

Notes: 1. Zhang. Cell Rep Med 2022; 3(1):100498

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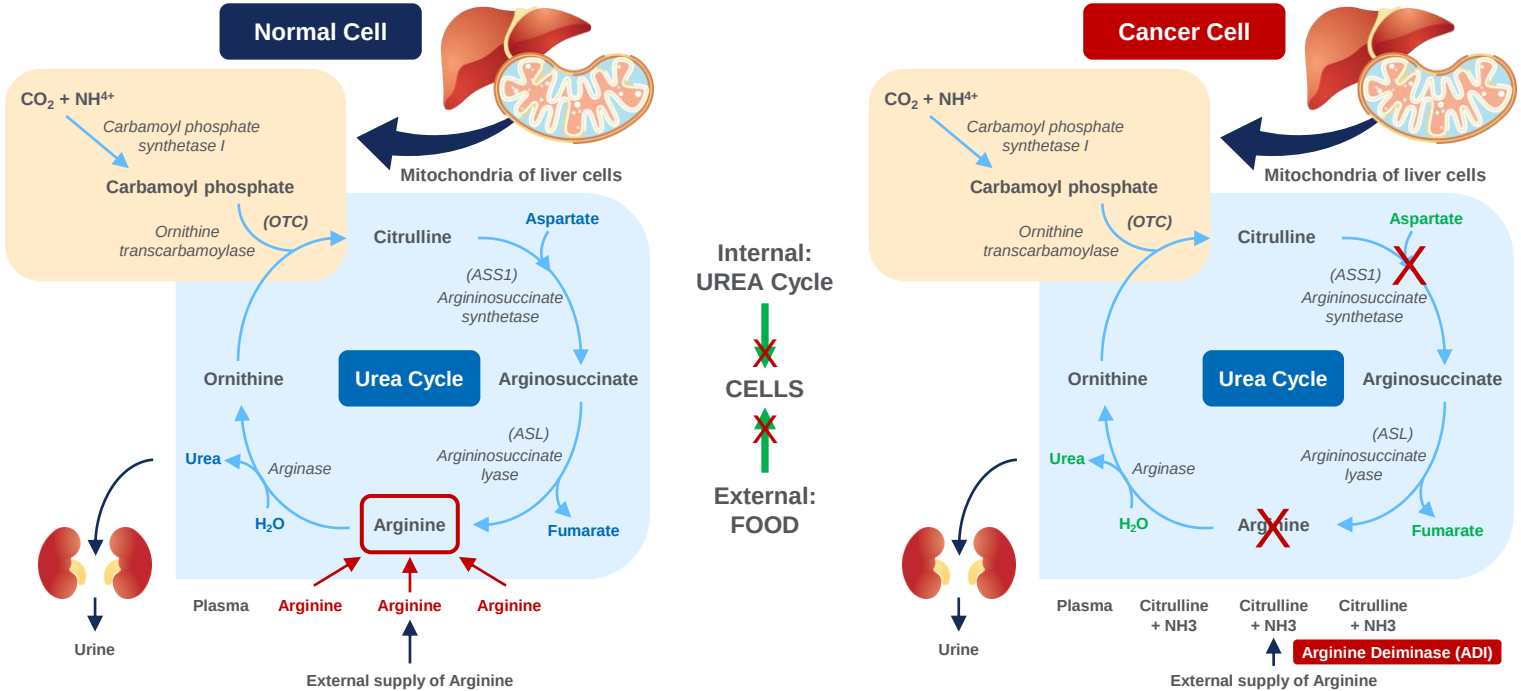
ADI-PEG 20 has a Unique Mechanism of Action

Our core product, PEGylated arginine deiminase ("ADI-PEG 20"), is a microbial enzyme designed to treat cancer by depleting arginine, an amino acid critical to the metabolism, biosynthesis and development of neoplastic growth



Source: Company information, Literature Review.

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Our Pipeline

Indication	Line of Therapy	Therapy	Regulatory Body	Commercial Rights	Pre-Clinical	IND	Ph1	Ph2	Ph3	BLA	Approval / Launch	Next Milestone
Malignant Pleural Mesothelioma (MPM)	1L	Combo w/ SoC Chemo	FDA MRCT	Global	ADI-PEG 20 + Cisplatin + Pemetrexed							BLA Submission to FDA
Soft Tissue Sarcoma (STS)	2L / 2L+	Combo w/ Chemo	FDA	Global	ADI-PEG 20 + Gemcitabine + Docetaxel							Interim data readout
Hepatocellular Carcinoma (HCC)	1L	Mono Precision Treatment	TFDA	Global	ADI-PEG 20							Interim data readout
Glioblastoma (GBM)	1L	Combo w/ SoC Chemo + Radiotherapy	FDA	Global	ADI-PEG 20 + Temozolomide + Radiation ADI-PEG 20 + Temozolomide + Radiation (1)							Interim data readout
Acute Myeloid Leukemia (AML)	1L + Relapsed	Combo w/ SoC Chemo	FDA	Global	ADI-PEG 20 + Venetoclax + Azacitidine							Interim data readout
NASH/NAFLD	1L	Mono	TFDA	Global	ADI-PEG 20							Interim data readout
Multiple Preclincal Pipelines	-	-	-	Global	2nd Gen ADI-PEG 20							IND

Source: Company information, FDA

Note: 1. GBM AGILE Platform in the U.S.

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Potential First-in-class Novel Pegylated Arginine Deiminase as a Synergistic Backbone for Combination Therapies

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Oncology

Solid Tumors

Malignant Pleural Mesothelioma

- *Combo w/ SoC Chemo*
- *BLA enabling - leads in competition in*
- *First to Market potential*

Soft Tissue Sarcoma

- *Combo w/ Chemo*
- *Potentially to reduce dose and improve overall safety profile*

Glioblastoma

- *Combo w/ SoC Chemo + Radiotherapy*
- *Potential complementary to radiotherapy*

Hematology

Hepatocellular Carcinoma

- *Mono therapy Precision Treatment*
- *High efficacy with selective genetic focus on WWOX biomarker*

Acute Myeloid Leukemia

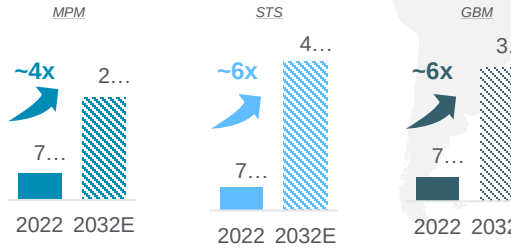
- *Combo w/ SoC Chemo*
- *Explore ADI-PEG 20's potential in hematologic tumor*

Non-oncology

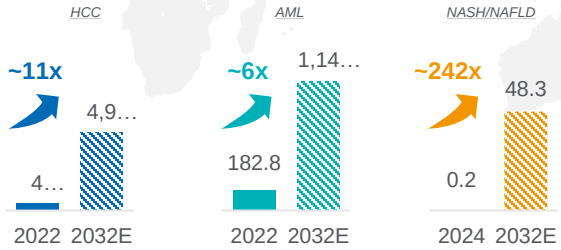
NASH/NAFLD & ••••

- *Mono therapy*
- *Demonstrated effect in mouse model*
- *Tractable pathway to treat obesity and related disorders*

Global cancer metabolic drug market size[1] (US$mm)



Global non-cancer metabolic drug market size (US$bn)



US$56bn

Huge addressable global market in 2032E

Metabolic drugs accounts for

~13.8%[2]

of the global cancer treatment drug market in 2032E

Source: China Insights Consultancy

Notes: 1. Values are not proportionately illustrated against other markets.

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Market Size of Global Metabolic Therapy Market with Key Drivers

Potential to be a **pan-cancer treatment regimen**

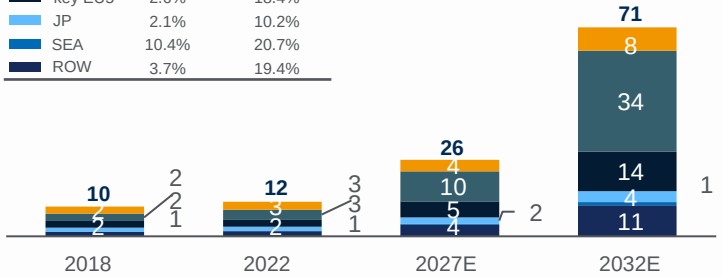
Potential **synergistic effect with other treatment**

Potential to be a **cancer precision treatment regimen**

Targeting cancer metabolic therapy demonstrates **lower side effect**

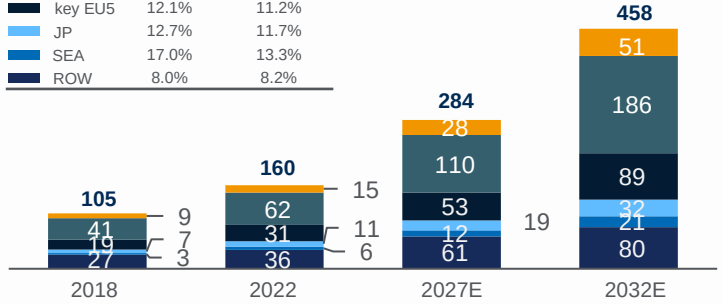
Market size of Global cancer metabolic therapy market (US$bn)

CAGR	2018-2022	2022-2032E
China	2.9%	11.3%
US	6.5%	26.7%
key EU5	2.6%	18.4%
JP	2.1%	10.2%
SEA	10.4%	20.7%
ROW	3.7%	19.4%



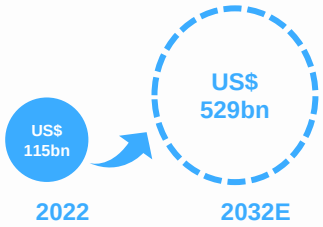
Market size of Global non-cancer metabolic therapy market (US$bn)

CAGR	2018-2022	2022-2032E
China	13.1%	13.4%
US	10.9%	11.7%
key EU5	12.1%	11.2%
JP	12.7%	11.7%
SEA	17.0%	13.3%
ROW	8.0%	8.2%



Global metabolic therapy market size is expected to expand by

5x



Source: China Insights Consultancy.

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Competitive Advantage of ADI-PEG 20

1 Metabolic therapy-based approach with **high safety profile, lower adverse impacts / side effects on normal cells**

ADI-PEG 20 or Placebo Phase 3 Monotherapy Trial in Hepatocellular Carcinoma Treatment Emergent Adverse Events

	ADI-PEG 20 (N = 421)			Placebo (N = 209)		
	CTCAE grade (%)			CTCAE grade (%)		
Grade 3–5 AEs in patients with ≥7.5% Grade 1–2 AEs	3	4	5	3	4	5
Fatigue	1.9	0	0	3.3	0	0
Decreased appetite	1.9	0	0	1.4	0	0
Nausea	0.5	0	0	0.5	0	0
Abdominal pain	4.3	0	0.2	2.4	0	0
Edema peripheral	2.4	0	0	1.4	0	0
Pyrexia	0	0	0	0.5	0	0
Cough	0.2	0	0	0.5	0	0
Abdominal distension	1.2	0	0	0.5	0	0
Diarrhea	1.0	0	0	1.0	0.5	0
Pruritus	0.2	0	0	0.5	0	0
Ascites	2.6	0	0	3.3	0	0
Vomiting	0.7	0	0	0	0	0
Constipation	0.2	0	0	1.0	0	0
Abdominal pain upper	0.2	0	0	1.0	0	0
Dyspnea	1.7	0.5	0.2	2.9	0	0
Back pain	0.5	0	0	2.4	0	0
Insomnia	0.2	0	0	0.5	0	0
Rash	0	0	0	0.5	0	0

Source: Company information, Literature Review.
Note: 1. Adverse Events (AEs).

Abou Alfa. Ann Oncol. 2018; 29:1402)

2 Clinical evidence of **expanded efficacy beyond ASS1 Deficiency Cancers** such as NASH / NAFLD

3 **Synergistic effect** with numerous existing drugs including SoC in combo therapies

- Combo with **Chemotherapy**
- Combo with **Radiotherapy**
- Combo with **Immuno-Oncology Therapy**
- ....

4 Intramuscular injection to **reduce treatment time**

5 Complex Biologics scale up process makes it **difficult for competitors to circumvent patents**

6 Technology is **protected by multiple patents** with 2nd generation advancing into clinic

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MPM Registration Study Endpoints were Highly Statistically Significant

Study design - a MRCT, randomized, double-blind, phase 2/3 clinical study

To evaluate ADI-PEG 20 or Placebo with pemetrexed and cisplatin[1] (ATOMIC) in patients with MPM

MPM Patients (N=249)

ADI-PEG 20 Combo (N=125)	**ADI-PEG 20 Dose:** 36 mg/m^2 given weekly	**Pemetrexed Dose:** 500 mg/m^2 every 3 weeks	**Cisplatin[1] Dose:** 75 mg/m^2 every 3 weeks
Placebo Combo (N=124)	**Placebo Dose:** 36 mg/m^2 given weekly	**Pemetrexed Dose:** 500 mg/m^2 every 3 weeks	**Cisplatin[1] Dose:** 75 mg/m^2 every 3 weeks

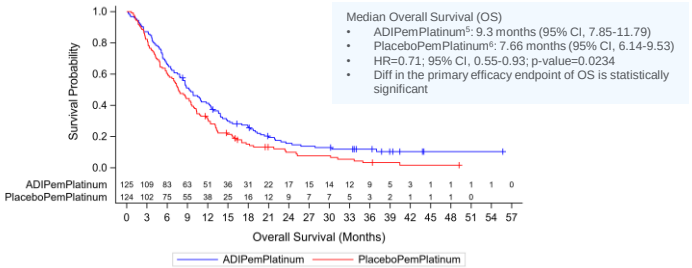
Route of Administration: Intramuscular (IM) + Intravenous (IV)

Primary End-point (EP)
- OS[2]

Secondary End-point (EP)
- PFS[3]

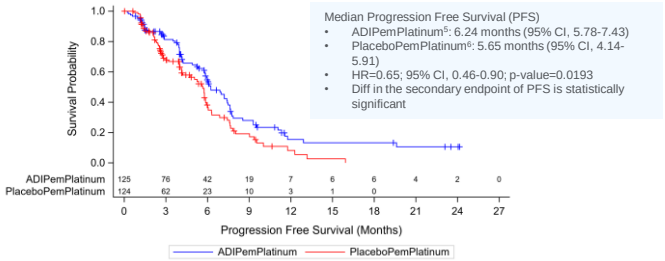
Clinical data summary

Kaplan-Meier Plot of Overall Survival (OS) - ITT Population[4]



Median Overall Survival (OS)
- ADIPemPlatinum[5]: 9.3 months (95% CI, 7.85-11.79)
- PlaceboPemPlatinum[6]: 7.66 months (95% CI, 6.14-9.53)
- HR=0.71; 95% CI, 0.55-0.93; p-value=0.0234
- Diff in the primary efficacy endpoint of OS is statistically significant

Kaplan-Meier Plot of Progression Free Survival (PFS) - ITT Population[4]



Median Progression Free Survival (PFS)
- ADIPemPlatinum[5]: 6.24 months (95% CI, 5.78-7.43)
- PlaceboPemPlatinum[6]: 5.65 months (95% CI, 4.14-5.91)
- HR=0.65; 95% CI, 0.46-0.90; p-value=0.0193
- Diff in the secondary endpoint of PFS is statistically significant

- *Overall Survival is calculated as the time from randomization until death. In the event that no death is documented prior to study termination or analysis cutoff, OS was censored at the last known date the subject is known to be alive (using last contact day or last dose day).*
- *Total number of subjects from the analysis population is 249, including 25 censored subjects (17 from ADIPemPlatinum, 8 from PlaceboPemPlatinum) and 224 subjects with OS events (108 from ADIPemPlatinum, 116 from PlaceboPemPlatinum).*

- *Progression-free survival is calculated as the time from randomization until date of tumor progression or death. In the event that no tumor progression or death is documented prior to end of treatment, analysis cutoff, or the start of confounding anticancer therapy, PFS was censored at the date of the last tumor assessment demonstrating no tumor progression.*
- *Total number of subjects from the analysis population is 249, including 104 censored subjects (54 from ADIPemPlatinum, 50 from PlaceboPemPlatinum) and 145 subjects with PFS events (71 from ADIPemPlatinum, 74 from PlaceboPemPlatinum).*

Source: Company information, Literature Review.
Notes: (1) Subjects who did not tolerate cisplatin were allowed carboplatin area under the plasma concentration–time curve (AUC) 5 mg/mL/m^2. (2) Overall survival. (3) Progression-free survival. (4) ITT = Intent-to-Treat. Analysis population is the ITT Population: Includes all randomized subjects. (5) ADIPemPlatinum refers to the ADI-PEG 20 Group (ADI-PEG 20 + cisplatin + pemetrexed). (6) PlaceboPemPlatinum refers to the Control Group (Placebo + cisplatin + pemetrexed).

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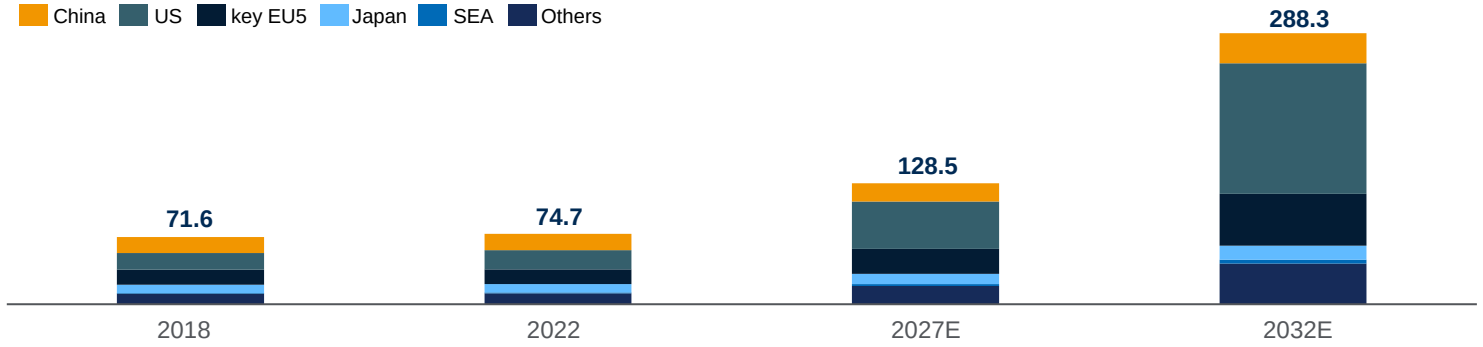
MPM – Market Opportunity and Competitive Landscape

Market size of MPM metabolic drug, 2018-2032E (US$mm)



Competitive landscape of major cell metabolism drugs for MPM

Drug	NCT number	Phase	Status	First posted date	MoA	Sponsor
Cell metabolic pathway: Arginine metabolism						
ADI-PEG 20	NCT02709512	2 and 3	Completed	2016/3/16	Pegylated arginine deiminase	Polaris
INCB001158	NCT02903914	1 and 2	Completed	2016/9/16	Arginase inhibitor	Incyte Corporation

Source: China Insights Consultancy. Notes: Only consider the candidates meeting the following conditions as the competitors: (1) Drug's MoA is targeting one of the major cell metabolic pathway including Glutamine metabolism, Fatty acid synthesis, Nucleotide synthesis, and glucose metabolism. (2) Only including the clinical trial status are Not yet recruiting, Recruiting; Enrolling by invitation; Active but not recruiting, and Completed. (3) Novel drug candidate. The approved drugs are excluded. (4) Clinical trials/drug candidates that have been registered for more than 10 years but have no progression are excluded. (5) At a similar or more advanced stage as compared to Polaris.

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Stakeholder Research Shows a Significant Market Opportunity:

Understand the commercial benefit and demand for ADI-PEG 20 vs. the current and prior standard of care

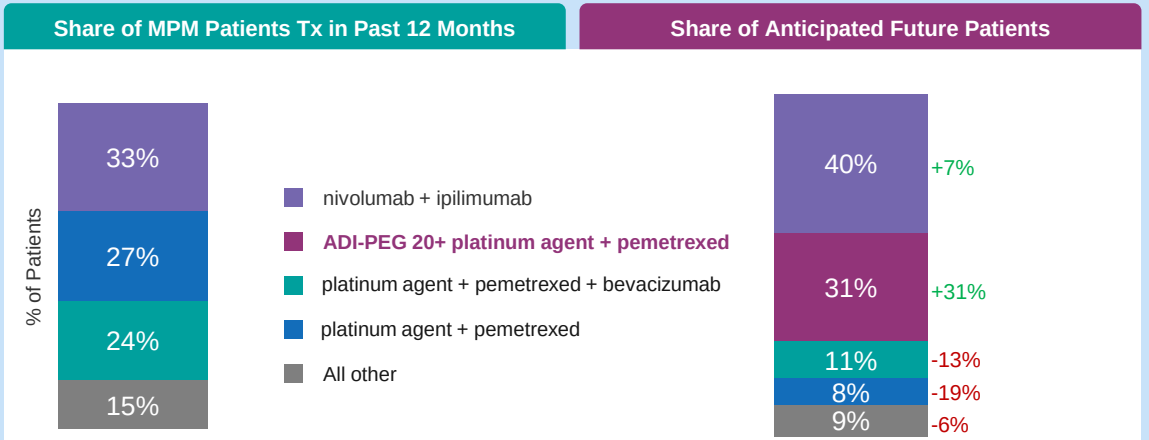
Initial **blinded target product profile impressions for ADI-PEG 20 are positive**

- Almost all oncologists are **interested in seeking more information or trying ADI-PEG 20**

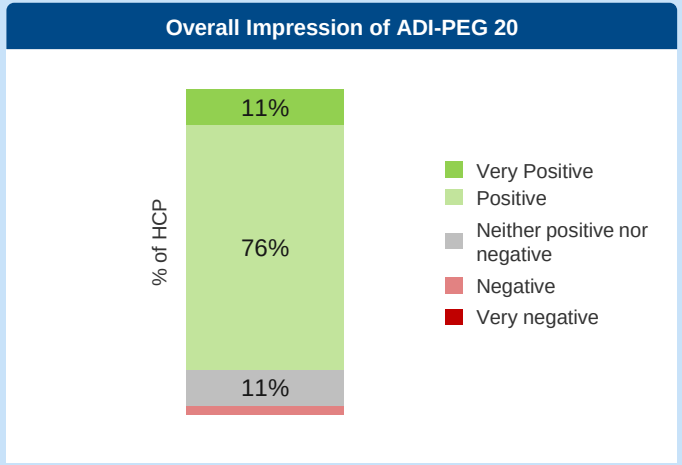
On average, Oncologists will treat their next **3 out of next 10 unresectable non-epithelioid MPM patients with ADI-PEG 20** + platinum agent + pemetrexed

- **ADI-PEG 20 takes share primarily from the prior SOC (platinum agent + pemetrexed) & the bevacizumab combination**

Reported Non-epithelioid MPM Current and Anticipated Use



Positive Impressions of ADI-PEG 20



Base: All Respondents (n = 75)

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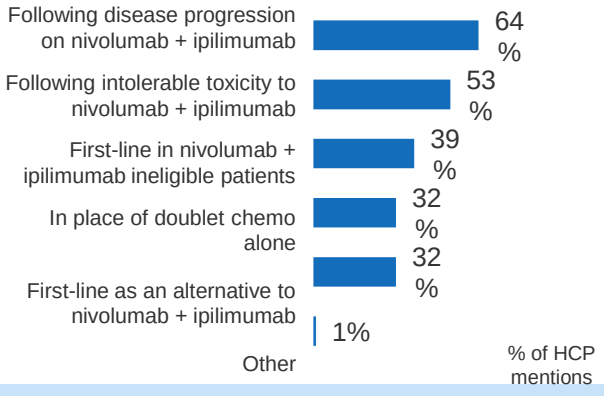
Understand Primary Commercial Patient Type Candidates for ADI-PEG 20

- 1L non-epithelioid unresectable MPM patients are the most frequent patient types that oncologists report as potential for ADI-PEG 20
  - A typical physician with median non-epithelioid unresectable MPM patient volume has **3.6 annual platinum agent + pemetrexed +/- bevacizumab patients** that may be potentially treated with ADI-PEG 20 in 1L instead
- Disease progression or intolerable toxicity to 1L nivolumab + ipilimumab patients are also likely ADI-PEG 20 patient types
  - A typical physician with median non-epithelioid unresectable MPM patient volume has **one annual 2L patient following disease progression on nivo + ipi**

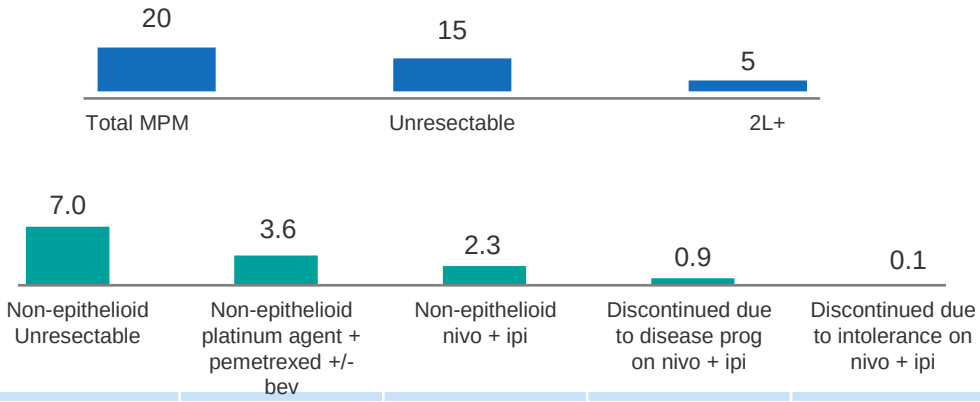
MPM Patient Types for ADI-PEG 20

Potential ADI-PEG 20 Use Scenarios



Median MPM Patients the Past 12 Months

Funnel of Median Patient Types



Base: All Respondents (n = 75)

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ADI-PEG 20 Market Demand Conclusion

ADI- PEG 20 shows potential to reach similar use as the current standard of care, nivolumab + ipilimumab, a third of the present non-epithelioid MPM market share.

Key to achieving this potential for ADI-PEG 20 is **significant efficacy benefit (OS and PFS) over previous SOC, NCCN guidelines and FDA approval**.

ADI-PEG 20 Next Steps to Commercialization

Data and Path to Approval

- ✓ Completion of filing for Biologics License Application (BLA) to U.S. Food and Drug Administration (FDA) in 2024
- ✓ Filings of EU and UK marketing authorization applications planned 2H 2024
- ✓ Program has Fast Track and ODD designations

Manufacturing

- ✓ Full characterization of Vacaville facility
- ✓ State licenses for distribution planned for 1H 2024
- ✓ Facility has initial capacity to produce up to 300,000 doses PA; sufficient for demand in MPM major markets

Commercialization

- ✓ Ongoing evaluation of strategic partnerships and infrastructure required to bring to market
- ✓ Continue focus from 2023 on Medical Affairs, value and HEOR evidence generation
- ✓ Focus in 2024 on launch preparation and execution
- ✓ Anticipated PDUFA date in 2025

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Clinical Program Highlights
ADI-PEG20

STS – Summary of Clinical Design and Clinical Data

Study design - an open label, non-randomized, phase 2 clinical study

To evaluate ADI-PEG 20 with gemcitabine and docetaxel improved clinical outcomes for patients with STS

STS Patients (N=75)

- **Cohort 1**[1]
- **Cohort 2**[2]

Route of Administration: Intramuscular (IM) + Intravenous (IV)

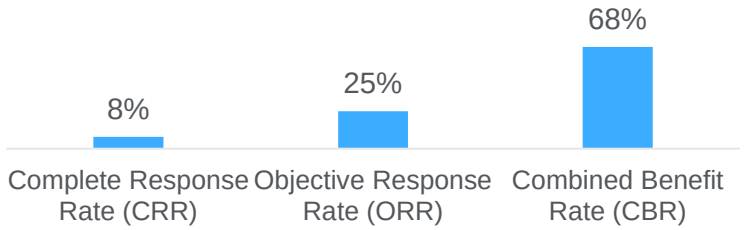
ADI-PEG 20 Dose:	**Gemcitabine Dose:**	**Docetaxel Dose:**
36 mg/m2 Day -7 of Cycle 1 and then on Days 1, 8, and 15 of each subsequent cycle (1 Cycle = 21 days)	600 mg/m2 over 90 minutes on Days 1 and 8 of each cycle (1 Cycle = 21 days)	60 mg/m2 over 60 minutes on Day 8 of each cycle (1 Cycle = 21 days)

Primary End-point
- PFS[3]

Secondary End-point
- OS[4]
- Clinical benefit rate (CBR)
- Safety and tolerability
- Cancer-related mortality

Notes: (1). Cohort 1: Histologically or cytologically confirmed grade 2 or 3 soft tissue sarcoma that is unresectable or metastatic that would be standardly treated with gemcitabine or gemcitabine and docetaxel. For all others, please contact the principal investigator. Prior surgery for primary or metastatic disease after chemotherapy following a response is allowed. Cohort 2: Histologically or cytologically confirmed osteosarcoma, Ewing's sarcoma, or small cell lung cancer that is unresectable or metastatic that have either failed standard of care therapy or would be standardly treated with gemcitabine or gemcitabine and docetaxel. Please refer to NCT03449901 for more details.
(2). Patients started on gemcitabine at a dose of 900 mg/m2 or 750 mg/m2 or docetaxel at a dose of 75 mg/m2 per previous protocol version will be allowed to continue at that dose level. After Cycle 8, patients may continue on ADI-PEG 20 alone (without gemcitabine and docetaxel) upon request.

Clinical data summary



Results showed that sarcoma patients **demonstrated improved response rates** when combining docetaxel and gemcitabine with arginine starvation. The **complete response rate tripled** compared to previous trials, and **the amount of gemcitabine required could be reduced by a third**, **reducing the need for high-dose gemcitabine and mitigating toxicity**.

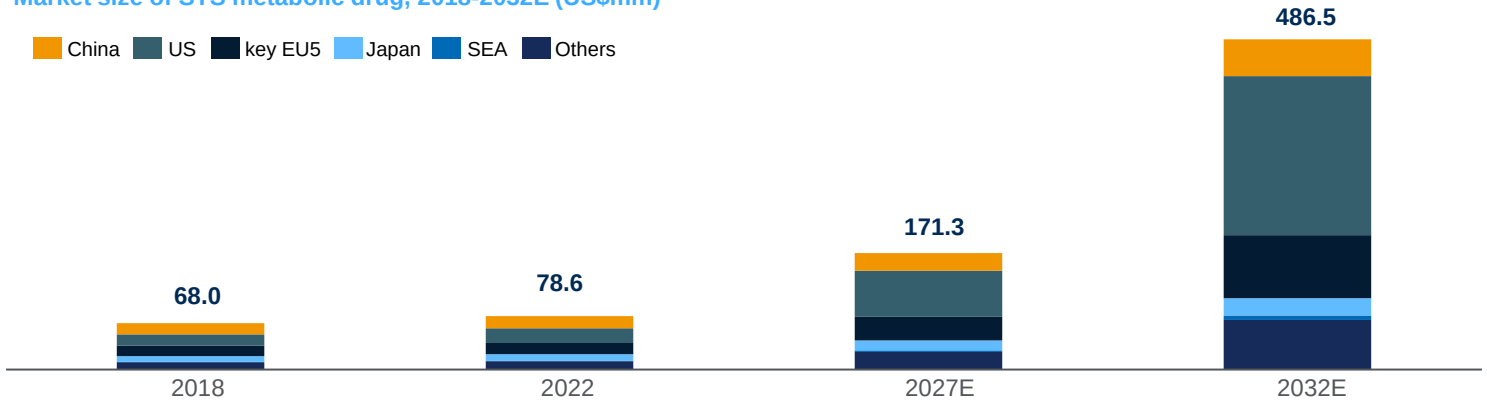
- Interview with Brian A. Van Tine, M.D., Ph.D.[5]

Source: Company information, Literature Review.
Notes: (3). Progression-free survival. (4). Overall survival. (5). Advancing Next-Generation Cancer Metabolic Therapy by Targeting Critical Amino Acid Metabolic Pathways: An Interview with Brian A. Van Tine, MD, PhD

Polaris

STS – Market Opportunity and Competitive Landscape

Market size of STS metabolic drug, 2018-2032E (US$mm)



Competitive landscape of major cell metabolism drugs for STS

Drug	NCT number	Phase	Status	First posted date	MOA	Sponsor
Cell metabolic pathway: Arginine metabolism						
ADI-PEG 20	NCT05813327	1 and 2	Not yet recruiting	2023/4/14	Pegylated arginine deiminase	Polaris
ADI-PEG 20	NCT05712694	3	Not yet recruiting	2023/2/3	Pegylated arginine deiminase	Polaris

Source: China Insights Consultancy. Notes: Only consider the candidates meeting the following conditions as the competitors (1) Drug's MoA is targeting one of the major cell metabolic pathway including Glutamine metabolism, Fatty acid synthesis, Nucleotide synthesis, and glucose metabolism. (2) Only including the clinical trial status are Not yet recruiting, Recruiting; Enrolling by invitation; Active but not recruiting, and Completed. (3) Novel drug candidate. The approved drugs are excluded. (4) Clinical trials/drug candidates that have been registered for more than 10 years but have no progression are excluded. (5) At a similar or more advanced stage as compared to Polaris.

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HCC – Summary of Clinical Design

Study design – a randomized, double-blind, multi-center ph3 study

To evaluate the efficacy of ADI-PEG 20 versus placebo in the systemic treatment of high-arginine-phenotypic subjects with advanced, unresectable HCC

HCC Patients (N=300)

ADI-PEG 20 Mono

Placebo Mono

Route of Administration: Intramuscular (IM)

ADI-PEG 20
Dose: 36 mg/m2
given weekly

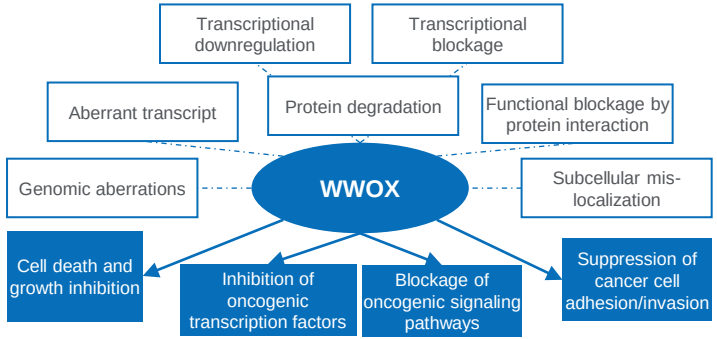
Placebo

Primary End-point
- OS[1]

Secondary End-point
- PFS[2]
- OS[1] in subgroup of WWOX-GG genotype
- Pharmacodynamic
- Immunogenicity

Clinical Design Rationale / MoA

- HCC patients with the WWOX-GG genotype had lower tissue levels of ASS1 and WWOX and higher levels of arginine
- **Higher sensitivity to ADI-PEG 20 treatment** and excellent overall survival in these patients
- HCC patients with high arginine levels may **represent a large group of cancer patients** with an arginine-dependent phenotype, and WWOX-GG patients may represent a subset of this group



Source: Company information, Literature Review.
Notes: 1. Overall survival. 2. Progression-free survival.

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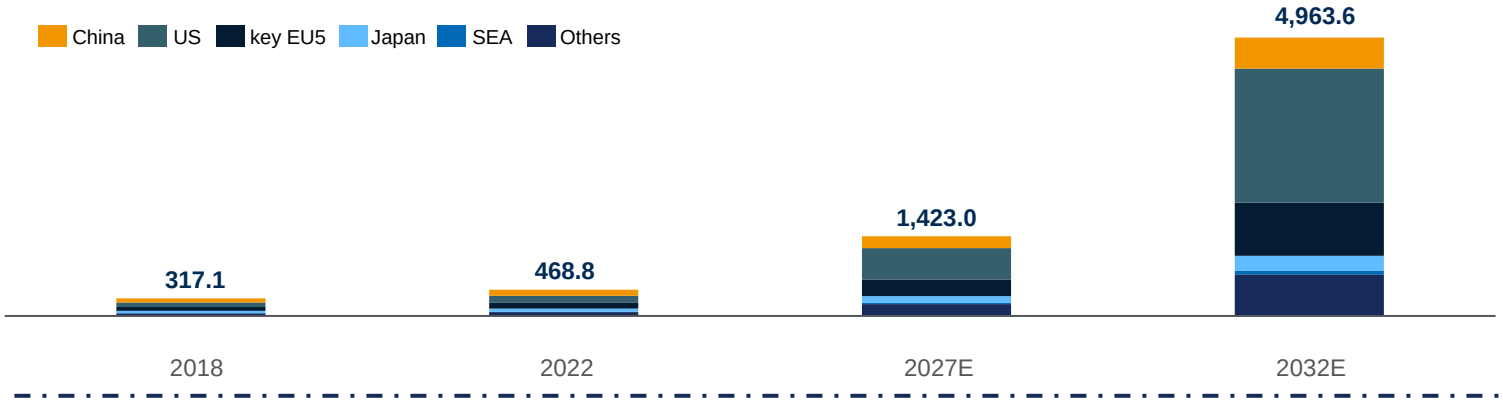
HCC – Market Opportunity and Competitive Landscape

Market size of HCC metabolic drug, 2018-2032E (US$mm)



Competitive landscape of major cell metabolism drugs for HCC

Drug	NCT number	Phase	Status	First posted date	MOA	Sponsor
Cell metabolic pathway: Arginine metabolism						
ADI-PEG 20	NCT05317819	3	Recruiting	2022/4/8	Pegylated arginine deiminase	Polaris
BCT-100	NCT02089763	2	Completed	2014/3/18	Pegylated recombinant human arginase	Bio-Cancer Treatment International
BCT-100	NCT02089633	2	Completed	2014/3/18	Pegylated recombinant human arginase	Bio-Cancer Treatment International
Cell metabolic pathway: Nucleotide synthesis						
mFOLFOX7	NCT05313282	3	Recruiting	2022/4/6	Thymidylate synthase	Jiangsu HengRui Medicine
mFOLFOX8	NCT04191889	2	Recruiting	2019/12/10	Thymidylate synthase	Jiangsu HengRui Medicine

Source: China Insights Consultancy. Notes: Only consider the candidates meeting the following conditions as the competitors (1) Drug's MoA is targeting one of the major cell metabolic pathway including Glutamine metabolism, Fatty acid synthesis, Nucleotide synthesis, and glucose metabolism. (2) Only including the clinical trial status are Not yet recruiting, Recruiting; Enrolling by invitation; Active but not recruiting, and Completed. (3) Novel drug candidate. The approved drugs are excluded. (4) Clinical trials/drug candidates that have been registered for more than 10 years but have no progression are excluded. (5) At a similar or more advanced stage as compared to Polaris.

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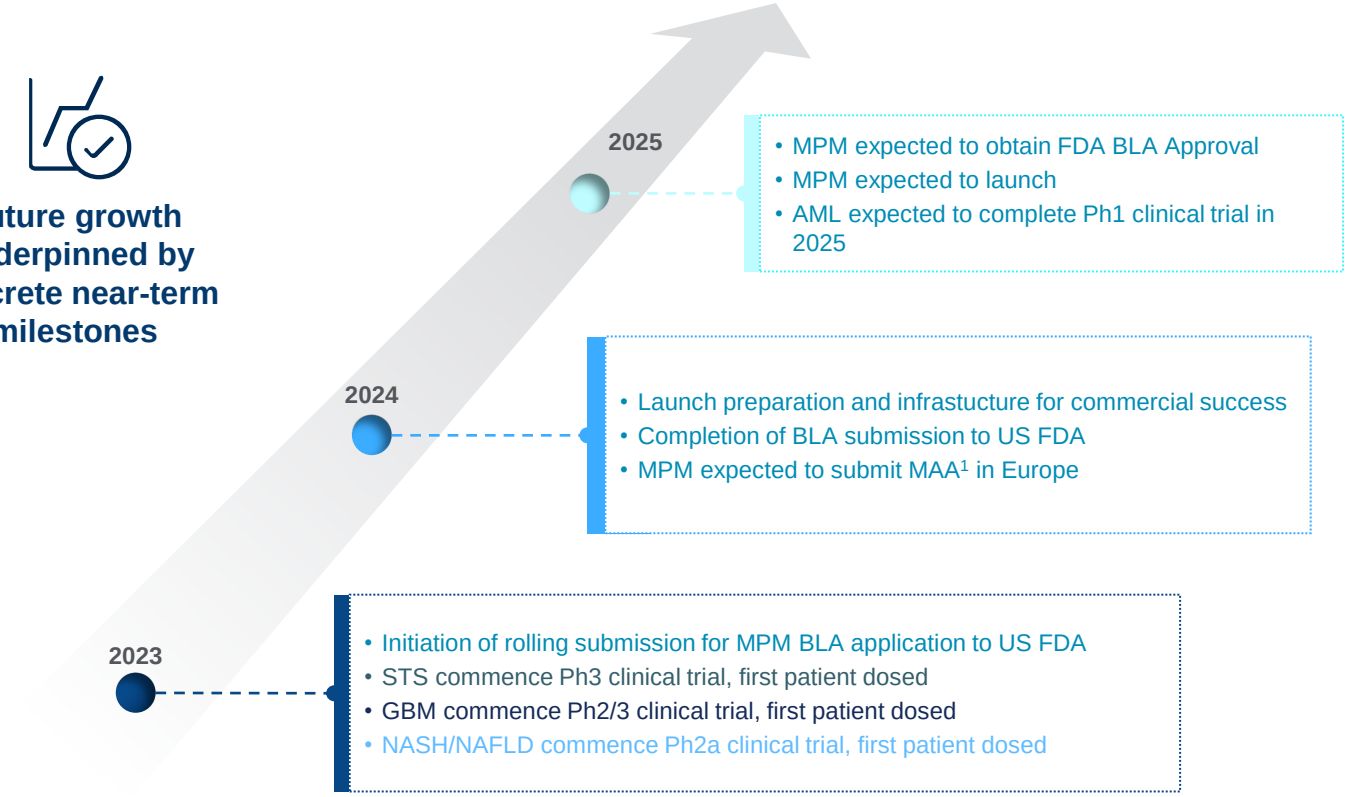
Milestones and Key Catalysts

Future growth underpinned by concrete near-term milestones



Source: Company information.
Note: 1. Marketing Authorization Applications.

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