Jazz Pharmaceuticals Pipeline

Our patient-centric approach to R&D begins with difficult-to-treat, unmet patient needs. We are dedicated to developing life-changing medicines for people with rare disease — often with limited or no therapeutic options. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics.

This document includes information about investigational products, or investigational indications for products that may have marketing authorizations for other indications in the European Union (EU) or other countries throughout the world. Safety and efficacy may not have been established, and there is no guarantee that pipeline products or investigational uses will receive approval from health authorities. Likewise, any forward-looking statements such as our ability to identify scientific breakthroughs with the potential to result in life-changing medicines are subject to risks and uncertainties, which include, without limitation, risks and uncertainties associated with pharmaceutical product development, and other risks and uncertainties affecting Jazz Pharmaceuticals and its development programs, described in Jazz's periodic reports on file with the Securities and Exchange Commission.

Oncology

PROGRAM	POTENTIAL INDICATION(S)	PRE-CLINICAL / PHASE 1 / PHASE 2 / PHASE 3 / PHASE 4/ REGULATORY
Zanidatamab + SOC chemo ± tislelizumab (1L)	GEA	
Zanidatamab + SOC chemo ± PD-1/L-1 (1L)	BTC	
Zanidatamab + chemo	Previously T-DXd treated mBC	
Zanidatamab + chemo + pembrolizumab (1L)	HER2+ and PD-L1+ advanced GEA	
I-SPY 2 Zanidatamab + SOC	Breast cancer	
Zanidatamab + paclitaxel and ramucirumab	Advanced GEA	
Zanidatamab	Previously treated solid tumors (pan-tumor)	
	Neoadjuvant and adjuvant breast cancer	
	Early-stage breast cancer	
PRE-I-SPY Zanidatamab + tucatinib	Breast cancer	

Oncology

PROGRAM	POTENTIAL INDICATION(S)	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	PHASE 4/ REGULATORY

Overview: Zanidatamab, or Ziihera® (zanidatamab-hrii) in the United States and the EU, is a bispecific HER2-directed antibody that binds to two extracellular sites on HER2. Zanidatamab has been granted two Fast Track designations by the U.S. Food and Drug Administration (FDA): one as a single agent for refractory biliary tract cancers (BTC) and one in combination with standard-of-care (SOC) chemotherapy for first-line gastroesophageal adenocarcinoma (1L GEA). Additionally, zanidatamab has received Orphan Drug designations from the FDA for the treatment of BTC, and gastric (including gastroesophageal junction) cancer, and esophageal cancer, as well as Orphan Drug designations from the European Medicines Agency for the treatment of BTC, gastric/gastroesophageal junction cancer and oesophageal cancer.

Clinical Trials:

Phase 3:

1. The Phase 3 HERIZON-GEA-01 trial (NCT05152147) evaluates zanidatamab in combination with chemotherapy and with or without the checkpoint inhibitor tislelizumab as a first-line treatment for metastatic HER2-positive (HER2+) GEA.
2. The Phase 3 HERIZON-BTC-302 trial (NCT06282575) evaluates zanidatamab and CisGem (cisplatin plus gemcitabine) with or without the addition of a programmed death protein 1/ligand 1 (PD-1/L-1) inhibitor versus CisGem with or without a PD-1/L1 inhibitor in adult participants.
3. The Phase 3 EmpowHER trial (NCT06435429) evaluates zanidatamab compared to trastuzumab, each in combination with physician's choice of chemotherapy, for the treatment of participants with metastatic HER2-positive breast cancer who have progressed on, or are intolerant to, previous T-DXd treatment.

Phase 2:

1. The Phase 2 DiscovHER-Pan-206 trial (NCT06695845) evaluating zanidatamab monotherapy in previously-treated patients with HER2+ cancers including breast, gastric, esophageal, gastroesophageal, colorectal, endometrial, non-small cell lung, ovarian, urothelial, salivary and pancreatic.
2. The Phase 2 EmpowHER-BC-208 trial (NCT07102381) evaluating zanidatamab in patients with HER2+ neoadjuvant and adjuvant breast cancer.
3. Phase 2 trial (NCT06043427) evaluating zanidatamab in combination with usual care, paclitaxel and ramucirumab, in HER2+ advanced GEA, in collaboration with the Canadian Cancer Trials Group.
4. The Phase 2 ZANGEA trial (NCT07176312) evaluating zanidatamab in combination with pembrolizumab and chemotherapy in patients with HER2+ and PD-L1 positive metastatic GEA, conducted in collaboration with Institut für Klinische Krebsforschung IKF GmbH.
5. Phase 2 investigation of serial studies to predict the therapeutic response with imaging and molecular analysis 2 (I-SPY 2) trial (NCT01042379) assessing the efficacy of novel drugs in sequence with standard chemotherapy to advance approaches to personalized medicine. This trial is conducted in collaboration with QuantumLeap Healthcare Collaborative.
6. Phase 2 single-arm open-label pilot trial (NCT05035836) evaluating zanidatamab in patients with early-stage, low-risk, HER2-positive breast cancer, conducted in collaboration with MD Anderson Cancer Center.

Zanidatamab is also being investigated in Phase 1 studies, including the I-SPY Phase 1/1b platform trial (NCT05868226) with multiple ongoing drug regiment arms, evaluating single agents or combinations for breast cancer patients. Promising treatment regiments are to be transferred into the I-SPY 2 SMART Design Trial (NCT01042379).

Lurbinectedin

- 2L SCLC
- R/R Ewing sarcoma

Overview: Lurbinectedin, or Zepzelca® in the United States and Canada, is an alkylating drug that binds guanine residues within DNA, which triggers a cascade of events that can affect the activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in disruption of the cell cycle and eventual cell death.

Clinical Trials: In addition to being approved for extensive-stage small cell lung cancer (SCLC), the effectiveness of lurbinectedin is being in pediatric and young adults with relapsed/refractory ewing sarcoma.

1. The Phase 3 LAGOON (NCT05153239) trial evaluating and comparing the activity and safety of lurbinectedin as a single agent and in combination with irinotecan in SCLC patients. This trial is being conducted by PharmaMar as part of Jazz Pharmaceuticals' partnership with the company.
2. The ongoing Phase 1/2 (NCT05734066) trial evaluating the effectiveness and safety of lurbinectedin monotherapy in pediatric and young adult participants with recurrent/refractory Ewing sarcoma.

Dordaviprone (ONC201)

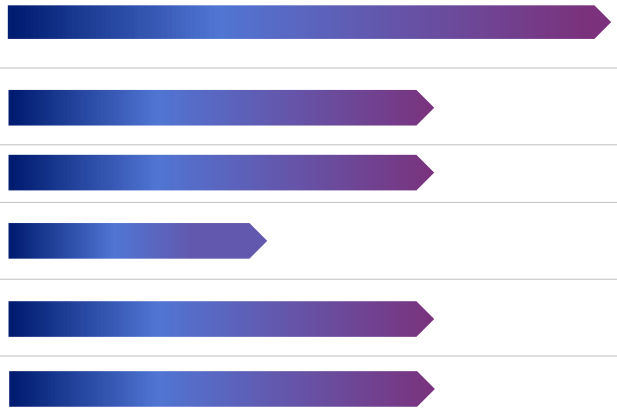
- Newly diagnosed H3 K27M-mutant diffuse glioma

Overview: Dordaviprone, or Modeyso™ in the United States, (formerly known as ONC201) is a protease activator of the mitochondrial caseinolytic protease P (ClpP) and also inhibits dopamine D2 receptor (DRD2). In vitro, dordaviprone activates the integrated stress response, induces apoptosis, and alters mitochondrial metabolism, leading to restored histone H3 K27 trimethylation in H3 K27M-mutant diffuse glioma.

Clinical trials: The Phase 3 ACTION confirmatory trial (NCT05580562) evaluating the safety and clinical benefit of Modeyso in newly diagnosed patients with H3 K27M-mutant diffuse glioma following radiotherapy.

Oncology

PROGRAM	POTENTIAL INDICATION(S)	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	PHASE 4/ REGULATORY
JZP351	Newly diagnosed adults with standard- and HR-AML (AMLSG 30-18)					
	Newly diagnosed older adults with HR-AML					
	HR- MDS (EMSCO)					
	Low-intensity dosing for higher risk MDS					
JZP351 + other approved therapies	R/R AML or HMA Failure MDS					
	de novo or R/R AML					



Overview: JZP351, or Vyxeos®/Vyxeos Liposomal in approved markets, is a liposomal combination of daunorubicin, an anthracycline topoisomerase inhibitor, and cytarabine, a nucleoside metabolic inhibitor.

Clinical Trials:

Phase 2:

1. Phase 2 trial (NCT05564390) evaluating JZP351 as monotherapy or in combination for first-line treatment of adults with high-risk AML (MyeloMATCH), conducted in collaboration with University of Texas MD Anderson Cancer Center.
2. Phase 2 trial (NCT04493164) evaluating JZP351 in combination with ivosidenib in adults with IDH1 AML or higher-risk myelodysplastic syndromes (MDS), conducted in collaboration with University of Texas MD Anderson Cancer Center.

Additional Phase 2 and Phase 3 trials of JZP351 are evaluating the agent in various age populations and are being conducted with cooperative groups such as the AML Study Group (AMLSG).

JZP815	Solid tumors and hematologic malignancies					

Overview: An investigational pan-RAF inhibitor for the treatment of solid tumors and hematologic malignancies that contain mutations in the mitogen-activated protein kinase (MAPK) pathway. JZP815 targets specific components of the MAPK pathway that, when activated by oncogenic mutations, can be a frequent driver of human cancer. JZP815 potentially inhibits both monomer- and dimer-driven RAF signaling (e.g., RAS-induced), prevents paradoxical pathway activation induced by BRAF selective inhabitation and is active against class 1, class 2 and class 3 BRAF mutants as well as BRAF fusions and CRAF mutants.

Clinical Trials: A Phase 1, open-label, first-in-human study (NCT05557045).

JZP898	Solid tumors					

Overview: Investigational JZP898, previously WTX-613, is a conditionally activated IFNα2b cytokine pro-drug.

Clinical Trials: The safety, tolerability, pharmacokinetics, immunogenicity and preliminary antitumor activity of JZP898 both as a monotherapy and in combination with pembrolizumab is being investigated in Phase 1, first-in-human study (NCT06108050).

JZP3507 (ONC206)	PCPG					
	Recurrent meningioma					
	CNS tumors					

Overview: JZP3507 (formerly ONC206) is a dual targeted investigational therapy that is an agonist of the mitochondrial protease ClpP and an antagonist of the G protein-coupled receptor DRD2.

Clinical Trials:

Phase 2:

1. Phase 2 trial (NCT07282587) is evaluating the efficacy and safety of JZP3507 in participants with Pheochromocytoma and Paraganglioma (PCPG).
2. Phase 2 trial (NCT07533942) is evaluating the efficacy, safety, tolerability, and pharmacokinetics of JZP3507 in adults with recurrent meningioma.

Additional trials include a Phase 1 trial (NCT04732065) evaluating JZP3507 in participants with newly diagnosed or recurrent diffuse midline gliomas and other recurrent malignant CNS tumors.

Oncology

PROGRAM	POTENTIAL INDICATION(S)	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	PHASE 4/ REGULATORY
KRAS Inhibitor	Solid tumors					
Overview: KRAS (Kirsten rat sarcoma virus) inhibitor program acquired from Redx Pharma.						
JZP3508 (ONC212)	IND-enabling studies					
Overview: JZP3508 (formerly ONC212) is a dual agonist of the mitochondrial protease ClpP and the G protein-coupled receptor GPR132.						
CombiPlex	N/A					
Overview: Evaluating patented CombiPlex® platform in a wide range of tumor types. Evaluating improvement in cancer therapy by using extremely small (nano-scale) carriers to deliver optimal ratios of multiple anticancer agents directly to cancer cells over a prolonged period of time.						
Undisclosed Targets	N/A					

Neuroscience

PROGRAM	POTENTIAL INDICATION(S)	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	PHASE 4/ REGULATORY
Cannabidiol	Seizures associated with LGS, DS, TSC in Japan					
	Focal-onset seizures					
Overview: Epidiolex® (cannabidiol), known as Epidyolex® in the EU, United Kingdom (U.K.), Australia and Israel, is a prescription, plant-derived cannabis-based medicine administered as an oral solution. In the United States, Epidiolex is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) in patients 1 year of age and older. In the EU and U.K., Epidyolex is indicated for use as adjunctive therapy of seizures associated with LGS or DS, in conjunction with clobazam, for patients 2 years of age and older. Epidyolex is also indicated for use as adjunctive therapy of seizures associated with TSC for patients 2 years of age and older.						
Clinical Trials: 1. An ongoing Phase 3 trial in Japan evaluating the efficacy and safety of Epidyolex in patients with LGS, DS and TSC. 2. A Phase 1b trial (NCT07233239) evaluating Epidiolex as an adjunctive treatment in participants with focal-onset seizures (FOS).						
JZP047	Absence epilepsy					
JZP053 (SAN2355)	Epilepsy					
Undisclosed Targets	Sleep					
	Epilepsy					
	Other neuroscience					

SOC = standard-of-care, **1L** = first line, **GEA** = gastroesophageal adenocarcinoma, **2L** = second line, **BTC** = biliary tract cancer, **3L** = third line, **mBC** = metastatic breast cancer, **SCLC** = small cell lung cancer, **AML** = acute myeloid leukemia, **HR** = high-risk, **MDS** = myelodysplastic syndromes, **AMLSG** = acute myeloid leukemia study group, **R/R** = relapsing/refractory, **HMA** = hypomethylating agents, **CNS** = central nervous system, **LGS** = Lennox-Gastaut syndrome, **DS** = Dravet syndrome, **TSC** = Tuberous sclerosis complex, **FOS** = Focal-onset seizures.