A Phase 1 First-in-Human, Open-Label, Nonrandomized, Multicenter Study of JZP815 in Patients with Advanced or Metastatic Solid Tumors Harboring Alterations in the MAPK Pathway (NCT05557045)

Study Overview

Purpose	To investigate the safety, dosing, and antitumor activity of JZP815 in patients with advanced or metastatic solid tumors harboring alterations in the MAPK pathway
Condition(s)	Advanced or metastatic solid tumors harboring alterations in the MAPK pathway
Drug(s)	JZP815
Study Phase	Phase 1, first-in-human
Participating Countries	US

Selected Outcome Measures

Primary Outcome Measures:

- Incidence of dose-limiting toxicities (dose exploration phase)
- Incidence and severity of TEAEs and SAEs
- Change from baseline in hemoglobin, absolute neutrophil count, platelets, and hematocrit
- Change from baseline in AST and ALT, creatinine, and total bilirubin
- Change from baseline in heart rate and blood pressure
- Incidence of dose interruptions and reductions
- ORR as defined by RECIST v1.1 (dose expansion phase)
- DOR (dose expansion phase)

Secondary Outcome Measures:

- Pharmacokinetic parameters (dose exploration phase)
- Dose proportionality of JZP815 and its metabolites (dose exploration phase)
- ORR as defined by RECIST v1.1 (dose exploration phase)
- PFS (dose expansion phase)
- OS (dose expansion phase)

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http://www.clinicaltrials.gov
(Identifier: NCT05557045)

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Key Eligibility Criteria

Key Inclusion Criteria:

- Patients must be ⩾18 years of age
- Patients must have a histological or cytological diagnosis of an advanced or metastatic solid tumor carrying a documented, clinically significant MAPK pathway alteration
- Patients must have exhausted all available standard-of-care therapies
- Patients must have an ECOG performance status of 0 or 1
- Patients must have measurable disease per RECIST v1.1
- Patients must have adequate organ function
- Patients must have anticipated life expectancy of ⩾12 weeks
- For dose exploration phase: Tumor must be safely amendable to core needle or excisional biopsy
- For dose expansion phase: Patient must be diagnosed with the tumor type(s) carrying the mutation(s) specified and meet protocol specified requirements for prior therapy

Key Exclusion Criteria:

- Patient has known uncontrolled brain metastases
- Patient has active fungal, bacterial, and/or known viral infection, including HIV or hepatitis A, B, or C
- Patient has concomitant malignancies or previous malignancies with a disease-free interval <2 years at the time of enrollment
- Patient has clinically significant cardiovascular disease
- Patient has uncontrolled or severe intercurrent medical condition
- Patient has a gastrointestinal condition that could impair absorption of study intervention or cause inability to ingest study intervention
- Patient has received any cancer-directed therapy within 28 days or 5 half-lives of starting study intervention
- Patient uses any known strong or moderate inducers or inhibitors of CYP3A4 that cannot be discontinued ⩾28 days or 5 half-lives before starting study intervention
- Patient uses proton pump inhibitors or histamine-2 receptor antagonists that cannot be discontinued ⩾2 weeks before first dose, or has planned use at any time during the study
- Patient has concurrent therapy with any other investigational agent

Treatment Regimen

- **Dose exploration phase:** JZP815 will be administered as oral capsules at a starting dose of 20 mg BID approximately 12 hours apart, in the morning and in the evening
- **Dose expansion phase:** JZP815 will be administered at the RP2D established in Part A

ALT = alanine aminotransferase, AST = aspartate aminotransferase, BID = twice daily, CYP3A4 = cytochrome P450 3A4, DOR = duration of response, ECOG = Eastern Cooperative Oncology Group, HIV = human immunodeficiency virus, MAPK = mitogen activated protein kinase, ORR = objective response rate, OS = overall survival, PFS = progression-free survival, RECIST v1.1 = Response Evaluation Criteria in Solid Tumors version 1.1, RP2D = recommended phase 2 dose, SAE = serious adverse event, TEAE = treatment-emergent adverse event.

Jazz Pharmaceuticals