Joenja®
leniolisib

APPROVED FOR PATIENTS AGED 4+ WHO WEIGH 27 KG OR GREATER

The first and only precision therapy that targets the underlying immune defect in patients with APDS[1-3]



APDS, activated PI3Kδ syndrome.

Indications and Usage

JOENJA® (leniolisib) is a kinase inhibitor indicated for the treatment of activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) in adult and pediatric patients 4 years of age and older who weigh 27 kg or greater.

Select Safety Information

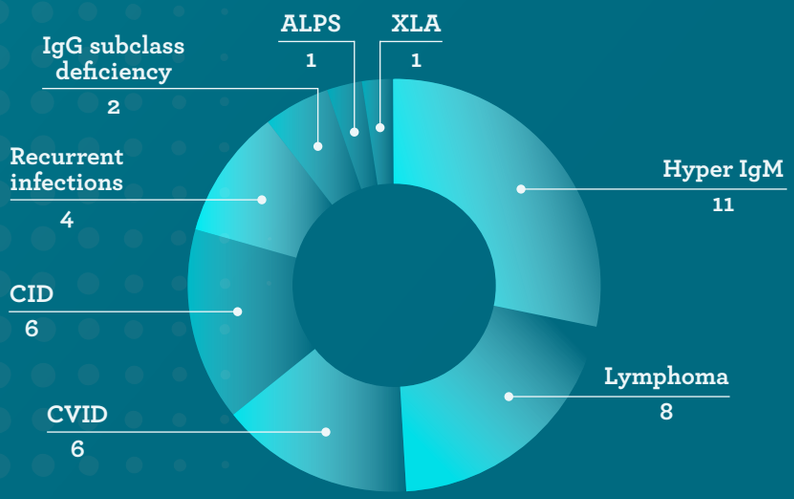
Verify pregnancy status in females of reproductive potential prior to initiating treatment with JOENJA.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

APDS is a progressive, underdiagnosed primary immunodeficiency (PI)[3-6]

APDS has been diagnosed as another PI or condition, causing delays in diagnosis[6]

Of 39 patients who had an initial clinical diagnosis other than APDS[7]:



Adapted from Jamee M, Moniri S, Zaki Dizaji M, et al. Clinical, immunological, and genetic features in patients with activated PI3Kδ syndrome (APDS): a systematic review. *Clin Rev Allergy Immunol*. 2020;59(3):323-333.

ALPS, autoimmune lymphoproliferative syndrome; CID, combined immunodeficiency; CVID, common variable immunodeficiency; IgG, immunoglobulin G; IgM, immunoglobulin M; XLA, X-linked agammaglobulinemia.

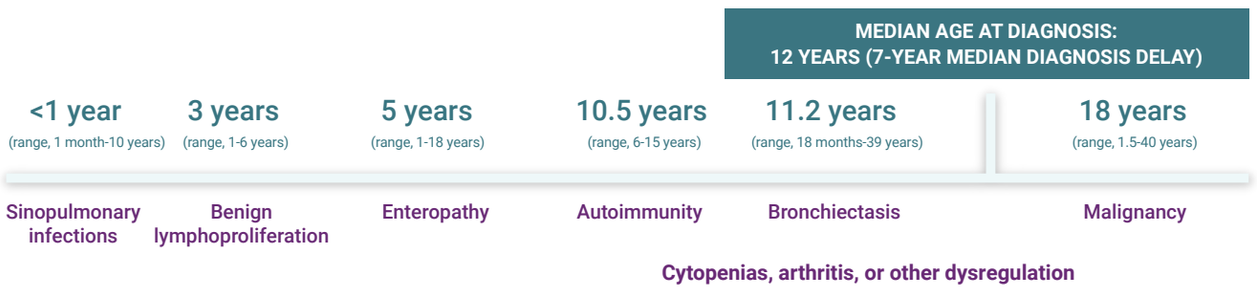
A genetic test can help inform a diagnosis of APDS

Recognizing the symptoms and conducting appropriate genetic testing are crucial for diagnosing and managing APDS.[6,8]

Visit navigateAPDS.com to learn more about a sponsored genetic testing option

Seemingly common symptoms may signal underlying immune deficiency and dysregulation[5,7]

Timeline of the most common pathologies seen in APDS[7-10]



There is a 50% chance of APDS being passed down from parent to child[11-13]

- Consider testing for APDS if presented with **any of these clinical features[7]:**
  - Previously treated with mTOR inhibition or other immunosuppressants
  - Elevated IgM levels
  - Bronchiectasis
  - Non-Hodgkin lymphoma
  - Herpes virus infections

Missing these common pathologies **may result in delayed diagnosis[6]**

mTOR, mammalian target of rapamycin.

Genetic testing can help inform a diagnosis of APDS for patients and their families[6,8,9,13]

- Because APDS is an autosomal-dominant, inherited condition, family members of individuals with APDS should consider genetic testing, including parents, siblings, grandparents, aunts, uncles, and cousins
  - Approximately 20% of patients diagnosed with APDS had no familial connection and have de novo mutations

Recognize atypical immune symptoms that may indicate APDS[5,7,13-15]

If you suspect PI, genetic testing can help inform an accurate diagnosis. Even a limited number of visible symptoms may indicate APDS

People with APDS usually experience 1 or more of the following symptoms:



Autoimmune and autoinflammatory disease
17%-42%

Neurodevelopmental delay
10%-31%

Recurrent sinopulmonary infections
96%-100%

Autoimmune cytopenias
19%-30%

Lymphoma
12%-25%

Bronchiectasis
18%-60%

Enteropathy
25%-51%

Lymphoproliferation, including splenomegaly, hepatomegaly, and lymphadenopathy
71%-89%

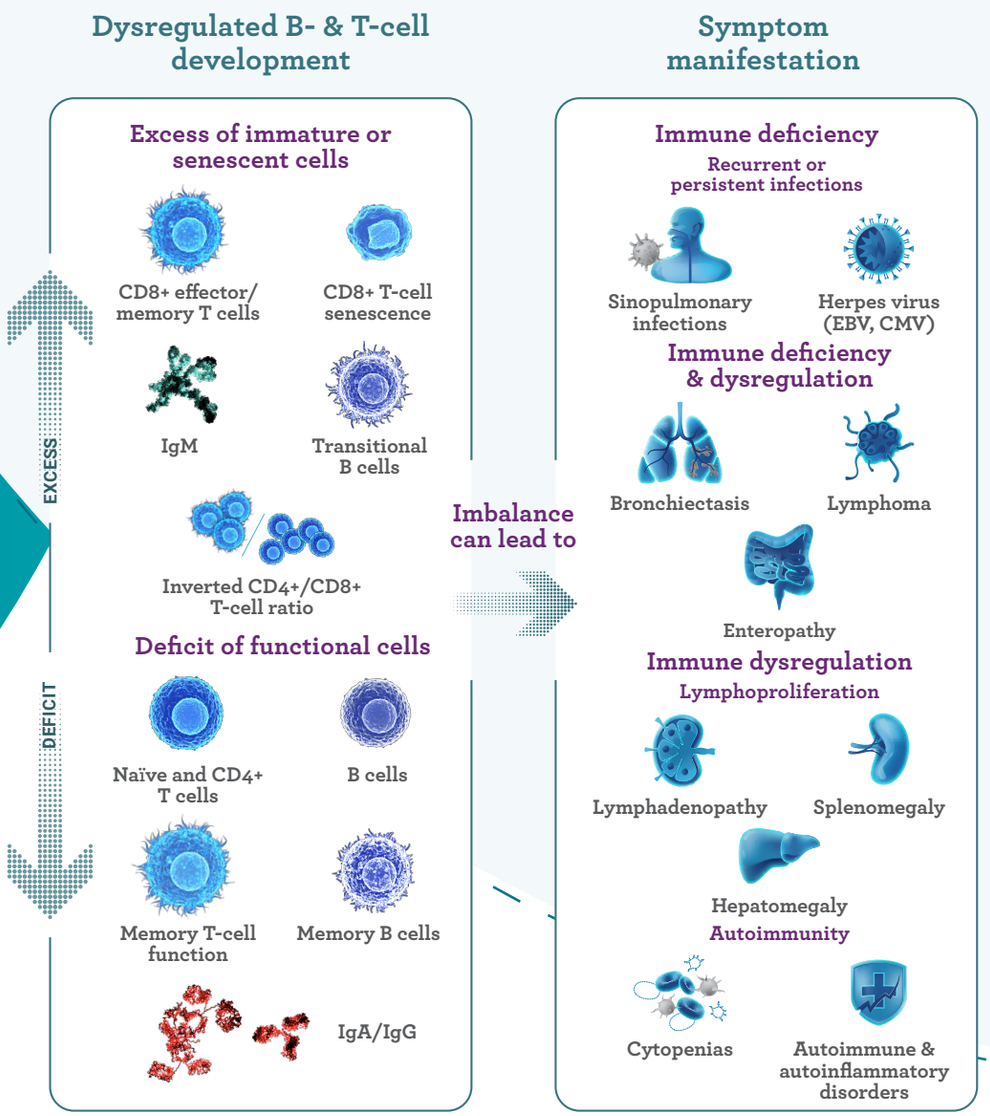
Persistent or recurrent herpes virus infections
36%-49%

Failure to thrive
45%-62%

If you suspect your patient may have a PI, genetic testing that includes the genes that cause APDS can help inform a timely diagnosis

- **A sponsored genetic testing option and genetic counseling are available** for eligible patients and their families, regardless of insurance coverage or financial need.[6,8] Visit navigateAPDS.com to learn more about a sponsored genetic testing option.

A hyperactive PI3Kδ pathway drives immune deficiency and dysregulation responsible for APDS symptom manifestation[5]



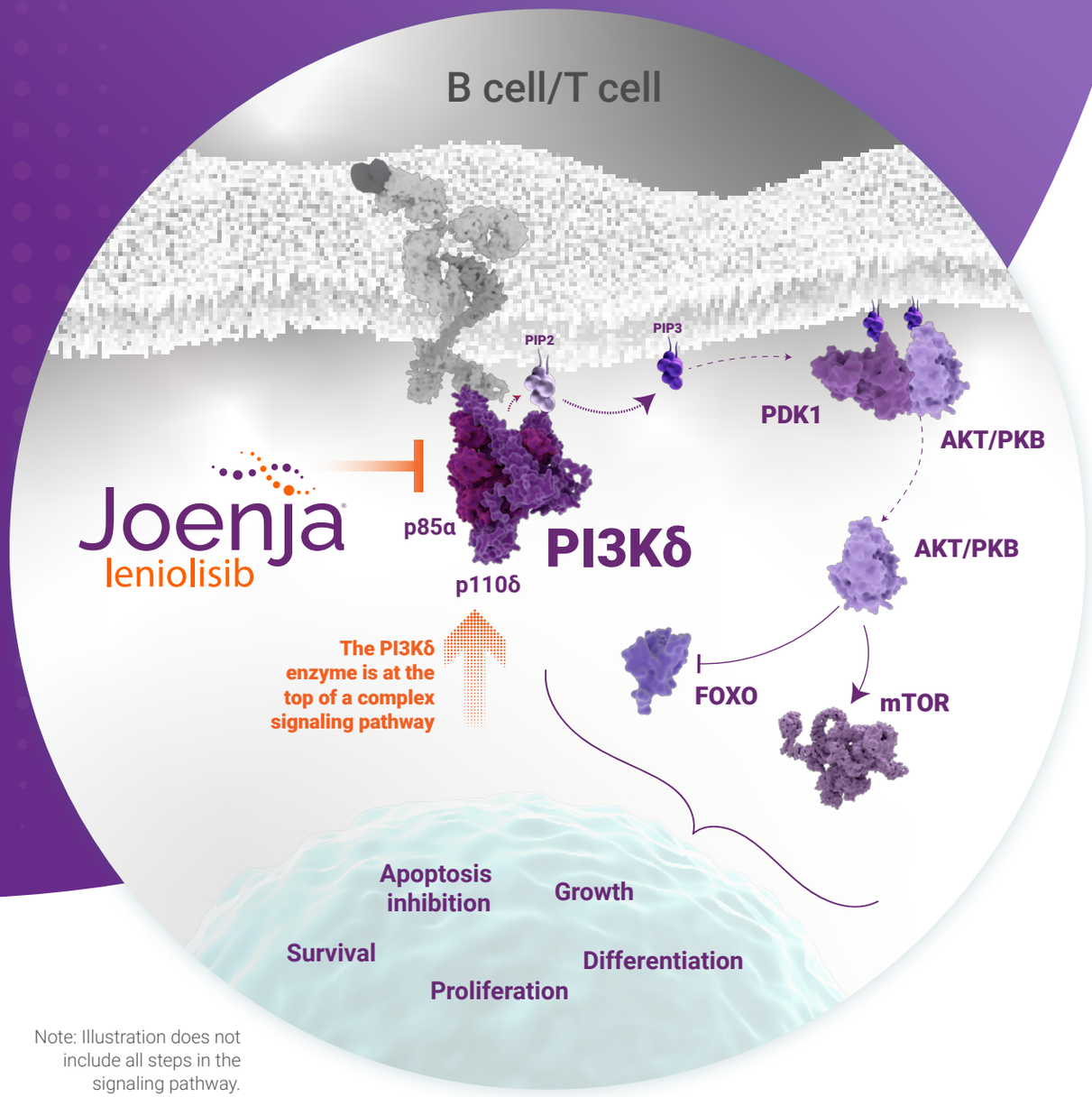
- Uncontrolled immune dysregulation and deficiency may result in severe lymphoproliferation, recurrent infections, autoimmune disorders, and lymphoma[5]
- Lymphoproliferation is a common feature of immune dysregulation in patients with APDS and can be associated with an increased risk of lymphoma[7]

CD, cluster of differentiation; CMV, cytomegalovirus; EBV, Epstein-Barr virus; IgA, immunoglobulin A.

Newer genetic panels now include APDS variants. If genetic testing was done prior to 2018 and your patient has symptoms of APDS, consider retesting.

Joenja is designed to correct the underlying immune defect caused by APDS to help normalize the hyperactive PI3Kδ pathway[1,3,5]

PI3Kδ signaling in B and T cells



Note: Illustration does not include all steps in the signaling pathway.

AKT/PKB, protein kinase B; FOXO, forkhead box O; p85α, the regulatory subunit of the PI3Kδ enzyme; p110δ, the catalytic subunit of the PI3Kδ enzyme; PDK1, phosphoinositide-dependent kinase 1; PIP2, phosphatidylinositol (4,5)-bisphosphate; PIP3, phosphatidylinositol (3,4,5)-trisphosphate.

Select Safety Information

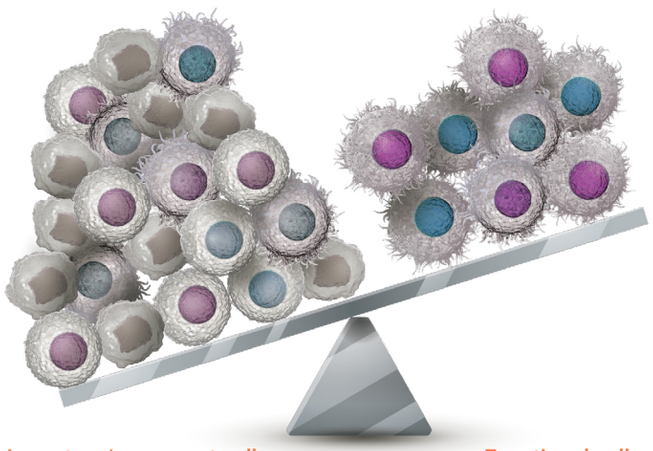
JOENJA may cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus and to use highly effective methods of contraception during treatment with JOENJA and for 1 week after the last dose. Additionally, advise women not to breastfeed during treatment with JOENJA and for 1 week after the last dose.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

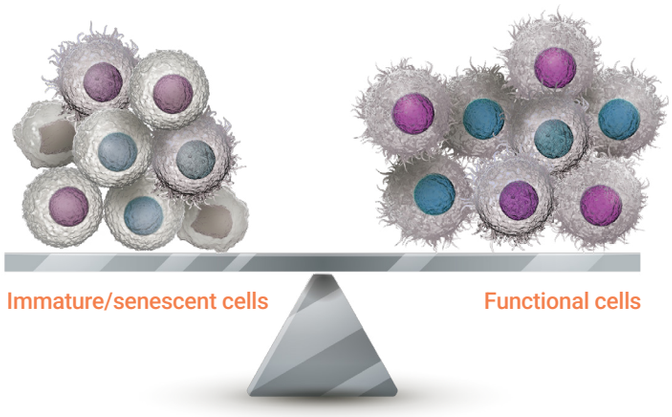
Joenja targets the underlying immune defect of APDS and helps normalize the hyperactive PI3Kδ pathway[1,3,5]

As a precision therapy, Joenja addresses both immune deficiency and immune dysregulation in patients with APDS

Before Joenja treatment



Joenja facilitates a balanced PI3Kδ pathway to support proper immune function



This is a graphical representation of a complex biological process.

Joenja is an **immune modulator that targets the overactive PI3Kδ pathway** to correct the underlying immune defect and help normalize the PI3Kδ pathway

Select Safety Information

Live, attenuated vaccinations may be less effective if administered during JOENJA treatment.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja® leniolisib

Joenja is supported by robust clinical trial data

Adolescent & Adult Trial: 12+ Years Old[1,3,16,17]

Part 1: Dose-Finding Study, 12 weeks | N=6

- Nonrandomized, open-label, dose-finding study in 6 patients with APDS; dose range was 10 mg, 30 mg, and 70 mg BID for 4 weeks at each dose
  - Oral dose of 70 mg BID selected for Part 2

Part 2: Efficacy and Safety Evaluation, randomized period | 12 weeks | N=31

- Randomized, triple-blinded (patient, caregiver, investigator), placebo-controlled, fixed-dose study of 70 mg BID
- Co-primary efficacy end points (improvement in lymphoproliferation and normalization of immunophenotype)
  - Change from baseline in the $\log_{10}$-transformed SPD of index lesions
  - Change from baseline in percentage of naïve B cells out of total B cells
- Secondary and exploratory end point assessments
- Safety assessment

Long-Term Safety: Adolescents & Adults 12+[1,17]

- A nonrandomized open-label extension (OLE) study to evaluate the long-term safety, tolerability, efficacy, and pharmacokinetics of Joenja in patients with APDS (N=37)
  - Thirty-five patients from Parts 1 and 2
  - Two patients previously treated with an investigational PI3Kδ inhibitor
- Primary outcome measure: long-term safety and tolerability

BID, twice a day; SPD, sum of product diameters.

Select Safety Information

JOENJA may cause hypersensitivity reaction(s), including anaphylaxis. Advise patients to discontinue JOENJA and to seek immediate medical attention if they develop any signs and symptoms of serious allergic reactions.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja was studied in patients with confirmed *PIK3CD* or *PIK3R1* variants[1]

Baseline demographics and disease characteristics in patients with APDS[1]

Demographics	Joenja (n=21)	Placebo (n=10)
Age,* y (mean SD)	**22.2** (10)	**26.7** (13.43)
Age categories		
<18 y, n (%)	**8** (38)	**4** (40)
(min, max)	(12, 17)	(15, 17)
≥18 y, n (%)	**13** (62)	**6** (60)
(min, max)	(18, 54)	(18, 48)
Sex, n (%)		
Male	**11** (52)	**4** (40)
Female	**10** (48)	**6** (60)
Race, n (%)		
Asian	**1** (5)	**1** (10)
Black	**1** (5)	**1** (10)
White	**18** (86)	**7** (70)
Other	**1** (5)	**1** (10)
Ethnicity, n (%)		
Hispanic or Latino	**0**	**1** (10)
Not Hispanic or Latino	**14** (67)	**7** (70)
Not reported	**7** (33)	**2** (20)
Disease Characteristics		
APDS 1 (*PIK3CD* variant), n (%)	16 (76)	9 (90)
APDS 2 (*PIK3R1* variant), n (%)	5 (24)	1 (10)
Concomitant glucocorticoids, n (%)	12 (57)	6 (60)
Concomitant immunoglobulin G (IgG), n (%)	14 (67)	7 (70)
Previous rapamycin/sirolimus use, n (%)	4 (19)	3 (30)

- More than half of patients in each treatment arm were receiving glucocorticoids, IRT, or both[1,3]

Patients had nodal and/or extranodal lymphoproliferation, as measured by index nodal lesion selected by the Cheson methodology on CT or MRI and clinical findings and manifestations compatible with APDS (eg, history of repeated oto-sino-pulmonary infections, organ dysfunction). Immunosuppressive medications or PI3Kδ inhibitors (selective or nonselective) were prohibited within 6 weeks of baseline (day -1 and the visit prior to first study drug administration) and throughout the study. In addition, patients who had previous or concurrent B-cell depleters (eg, rituximab) within 6 months of baseline were excluded from the study unless absolute B lymphocytes in the blood were normal. B-cell depleters were prohibited throughout the study.[1]

*Patient age from study Day -4 up to initial JOENJA dosing.[1]
CT, computed tomography; IRT, immunoglobulin replacement therapy; MRI, magnetic resonance imaging; SD, standard deviation.

Select Safety Information

Use of JOENJA in patients with moderate to severe hepatic impairment is not recommended.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja® leniolisib

CO-PRIMARY END POINTS DEMONSTRATED

Joenja significantly reduced lymphadenopathy, helping to restore immune balance[1]

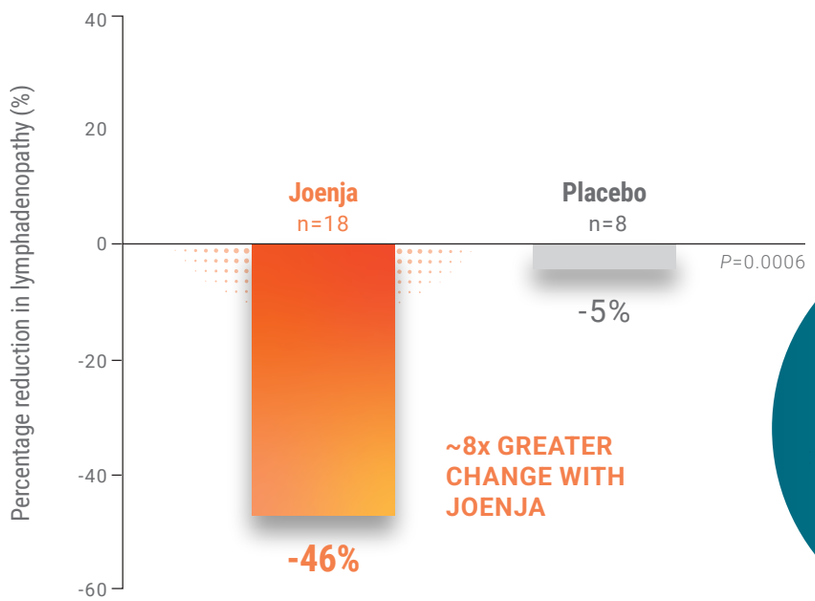
Log_{10}-transformed SPD of index lesions (excluding patients with 0 lesions at baseline) at week 12[1]*

	Joenja (n/N=18/21)†	Placebo (n/N=8/10)†
Baseline mean (SD)	**3.03** (0.42)	**3.05** (0.39)
Change from baseline, LS mean (SE)	**-0.27** (0.04)	**-0.02** (0.05)
Difference vs placebo (95% CI)		**-0.25** (-0.38, -0.12)

***P*=0.0006**

- Improvement in lymphoproliferation as measured by a change from baseline in lymphadenopathy measured by the log_{10}-transformed SPD of index lymph nodes[1,3]

At week 12, patients saw a significant reduction in lymphadenopathy*† with Joenja vs placebo[1,6]



- Reduction computed based on estimates for the adjusted mean changes[6]

46%
REDUCTION WITH JOENJA VS 5% WITH PLACEBO[6]

Note: The LS mean change from baseline, difference in LS mean change from baseline between Joenja and placebo and its *P* value were obtained from an ANCOVA model with treatment, glucocorticoids use and IRT at baseline, and baseline measurement as covariates.[1]
*Change in index lesion size was measured using the log_{10}-transformed SPD of the largest lymph nodes (maximum of 6) identified as per the Cheson criteria on CT/MRI.[1]
†The analysis excluded 2 patients from each treatment group due to protocol deviations and 1 Joenja patient having complete resolution of the index lesion identified at baseline.[1]
ANCOVA, analysis of covariance; CI, confidence interval; LS, least squares; SE, standard error.

Select Safety Information

Avoid co-administration of JOENJA with other medications known to be strong CYP3A4 inhibitors, strong or moderate CYP3A4 inducers, or BCRP, OATP1B1, and OATP1B3 substrates.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

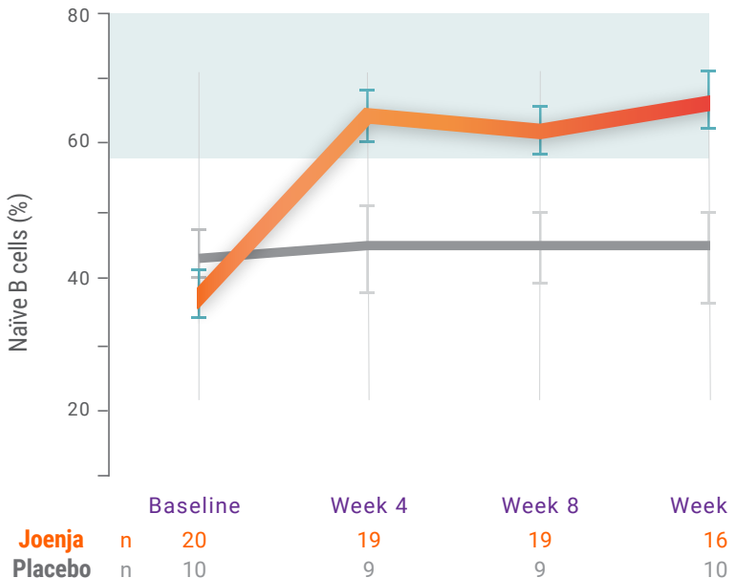
CO-PRIMARY END POINTS DEMONSTRATED (CONT'D)

Joenja significantly increased naïve B cells[3]

Significantly improved immunophenotype vs placebo at week 12[1,3]

- In patients with <48% of naïve B cells at baseline,* the adjusted mean difference between Joenja (n=8) and placebo (n=5) in the percentage of naïve B cells out of total B cells was 37.30 (95% CI: 24.06, 50.54), *P*=0.0002†
- The adjusted mean change from baseline (SE) for Joenja was 37.39 (5.34) and 0.09 (6.66) for placebo†

Absolute percentage of naïve B cells over time[3]



		Baseline	Week 4	Week 8	Week 12
Joenja	n	20	19	19	16
Placebo	n	10	9	9	10

MEAN NAÏVE B-CELL LEVELS WITHIN NORMAL RANGE BY WEEK 4 AND MAINTAINED THROUGH WEEK 12 WITH JOENJA

*Cell surface markers used to distinguish naïve B cells on flow cytometry were CD19+, CD27-, and CD10-. Baseline is defined as the arithmetic mean of the baseline and day 1 values when both were available, and if either value was missing, the existing value was used.[1]
†The analysis excluded 2 patients from each treatment group due to protocol deviations, 5 Joenja patients and 3 placebo patients with ≥48% naïve B cells at baseline, 5 Joenja patients with no day 85 measurement, and 1 Joenja patient with no baseline measurement.[1]

Select Safety Information

Most common adverse reaction (incidence >10%):

- Adult and pediatric patients 12 years of age and older: headache, sinusitis, atopic dermatitis, and weight gain.
- Pediatric patients 4 to <12 years of age who weigh 27 kg or greater: abdominal pain, cough, and respiratory tract infection.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja® leniolisib

SECONDARY AND EXPLORATORY END POINTS

Joenja significantly reduced splenomegaly[3]

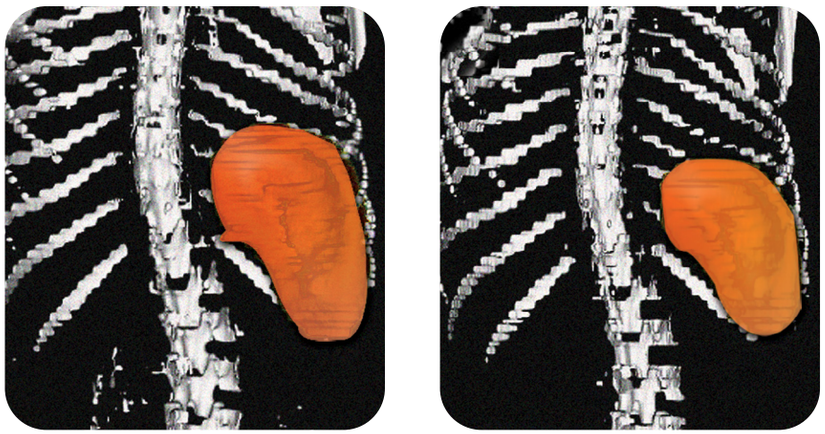
Significant reductions in spleen size by 2D and 3D analysis compared to placebo

- The adjusted mean difference in bidimensional spleen size between Joenja (n=19) and placebo (n=9) was -13.5 cm^2 (95% CI: -24.1, -2.91), *P*=0.0148
- The adjusted mean difference in 3D spleen volume between Joenja (n=19) and placebo (n=9) was -186 cm^3 (95% CI: -297, -76.2), *P*=0.0020

Secondary measure: Spleen volume scan results of actual patient illustrate average improvement documented for patients taking Joenja[3, 5]

Prior to treatment:
491 mL

At week 12:
314 mL



Actual images of a 29-year-old female's response of spleen size reduction, representing the median response in the study. As individual results vary, images may not be representative of all patients.

AT WEEK 12

27%

REDUCTION IN MEAN 3D SPLEEN VOLUME*

Other secondary end points included patient-reported benefits with Joenja that were assessed using the SF-36 (Short Form 36) Survey and WPAI-CIQ (Work Productivity Activity Impairment plus Classroom Impairment Questionnaire), visual analogue scales for Physician's Global Assessment (PGA), and Patient's Global Assessment (PtGA), and patient narratives by investigator. Clinical relevance from these assessments was not established.[18]

*In the PD analysis set, the mean (SD) percentage change from baseline to week 12 in 3D spleen volume (mm^3) was -26.68% (12.137) with Joenja (n=19) and -1.37% (24.238) with placebo (n=9). The ANCOVA model was used with treatment as a fixed effect and log_{10}-transformed baseline as a covariate for index and non-index lesions. The use of both glucocorticoids and intravenous Ig at baseline was included as categorical (yes/no) covariates.[5]

This analysis excluded 2 patients in each treatment group. In the Joenja group, 1 patient with a complete index lesion response was excluded, and 3 patients were excluded for no non-index lesion at baseline.[3]

Ig, immunoglobulin; PD, pharmacodynamics.

Select Safety Information

Seven (33%) patients 12 years and older (n=21) and 5 (63%) patients 4 to 12 years of age and weighing more than 27 kg or greater (n=8) developed an absolute neutrophil count (ANC) between 500 and 1500 cells/microL after receiving JOENJA. No patients developed an ANC <500 cells/microL and there were no reports of infection associated with neutropenia.

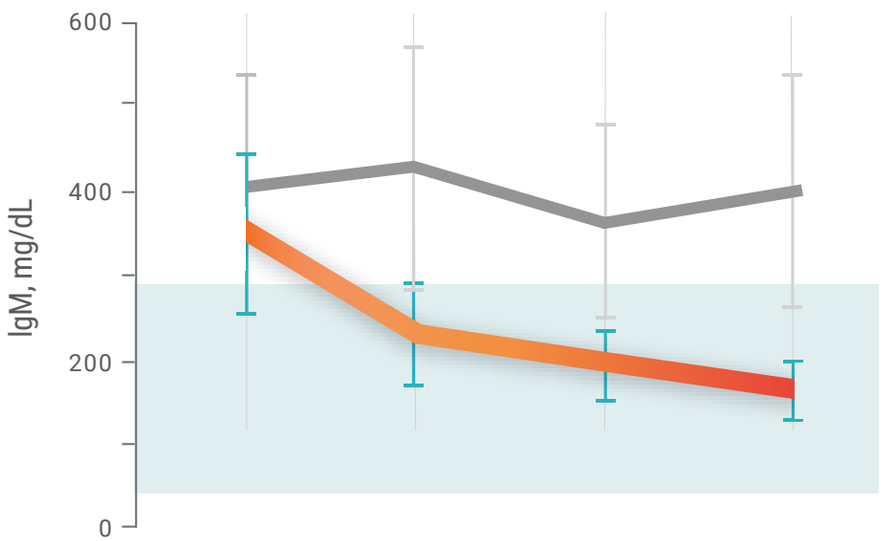
Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

SECONDARY AND EXPLORATORY END POINTS (CONT'D)

An exploratory end point showed Joenja reduced IgM levels[5]

- In the Joenja arm, IgM was elevated above normal limits in 6 patients at baseline, and by week 12 was reduced in all, with 50% returning to within normal limits
- In contrast, IgM was elevated above normal limits at baseline in 4 patients in the placebo arm, and by day 85, levels remained stable or elevated, with 0% returning to within normal limits

Mean serum IgM reduced to within normal limits[3]



		Baseline	Week 4	Week 8	Week 12
Joenja	n	21	20	21	21
Placebo	n	10	10	10	10

Soluble biomarkers, including IgM, were prespecified exploratory end points in the protocol. Although an observational decrease in IgM was noted in some patients, no statistical significance can be made from this analysis, and no conclusions should be drawn.

Select Safety Information

Joenja is available in 40 mg, 50 mg, and 70 mg tablets.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja® leniolisib

Joenja safety results in the randomized, placebo-controlled pivotal study

Adverse reactions reported by ≥2 Joenja-treated patients and more frequently than placebo[1]

	Joenja (n=21) n (%)	**Placebo** (n=10) n (%)
Headache	**5** (24)	**2** (20)
Sinusitis	**4** (19)	**0**
Dermatitis atopic*	**3** (14)	**0**
Tachycardia†	**2** (10)	**0**
Diarrhea	**2** (10)	**0**
Fatigue	**2** (10)	**1** (10)
Pyrexia	**2** (10)	**0**
Back pain	**2** (10)	**0**
Neck pain	**2** (10)	**0**
Alopecia	**2** (10)	**0**

- No serious drug-related adverse reactions were reported[3]
- No patients withdrew due to an adverse drug reaction[3]
- The most common adverse reactions (>10%) were headache, sinusitis, and dermatitis atopic[1]

*Dermatitis atopic: including dermatitis atopic and eczema.[1]
†Tachycardia: including tachycardia and sinus tachycardia.[1]

Select Safety Information

Verify pregnancy status in females of reproductive potential prior to initiating treatment with JOENJA.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

IN THE OLE STUDY

Additional safety results from an interim analysis

At the data cutoff*

- Thirty-seven of 38 patients received Joenja 70 mg orally twice daily for at least 25 weeks; 66% were exposed for 96 weeks or longer[1]
- Median duration of Joenja treatment was approximately 2 years[1]
- Four patients had more than 5 years of Joenja exposure[1]
- In the open-label clinical trial, 5 patients (14%) experienced weight gain[1]

Most common AEs[17,19]	n
Upper respiratory tract infection	9
Headache	6
Pyrexia	6
Otitis externa	5
Weight increase	5
COVID-19 positive	5
COVID-19 negative	14

Distribution and grades† of AEs

- Thirty-two of 37 patients had ≥1 AE (333 AEs reported)[17]
- 78.4% were grade 1, 48.6% were grade 2, and 27% were grade 3[17]
- No grade 4 AEs were reported[17]
- One patient who had a grade 5 AE with significant baseline comorbidities suffered cardiac arrest resulting in death on day 879; investigator determined that the death was not related to study drug[17]
- No serious AEs were related to Joenja treatment[17]

AEs associated with Joenja

- The AEs reported as related to study drug were weight increase (3 patients), arthralgia (1 patient), hyperglycemia (1 patient), and decreased neutrophil count (1 patient)[17]

*Data cutoff was December 13, 2021.[17]

†CTCAE were used to determine AE grade. If CTCAE grading did not exist for an AE, the following definitions were used: 1, mild; 2, moderate; 3, severe; 4, life-threatening; 5, death.[19]

AE, adverse event; CTCAE, common terminology criteria for adverse events.

Select Safety Information

JOENJA may cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus and to use highly effective methods of contraception during treatment with JOENJA and for 1 week after the last dose. Additionally, advise women not to breastfeed during treatment with JOENJA and for 1 week after the last dose.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

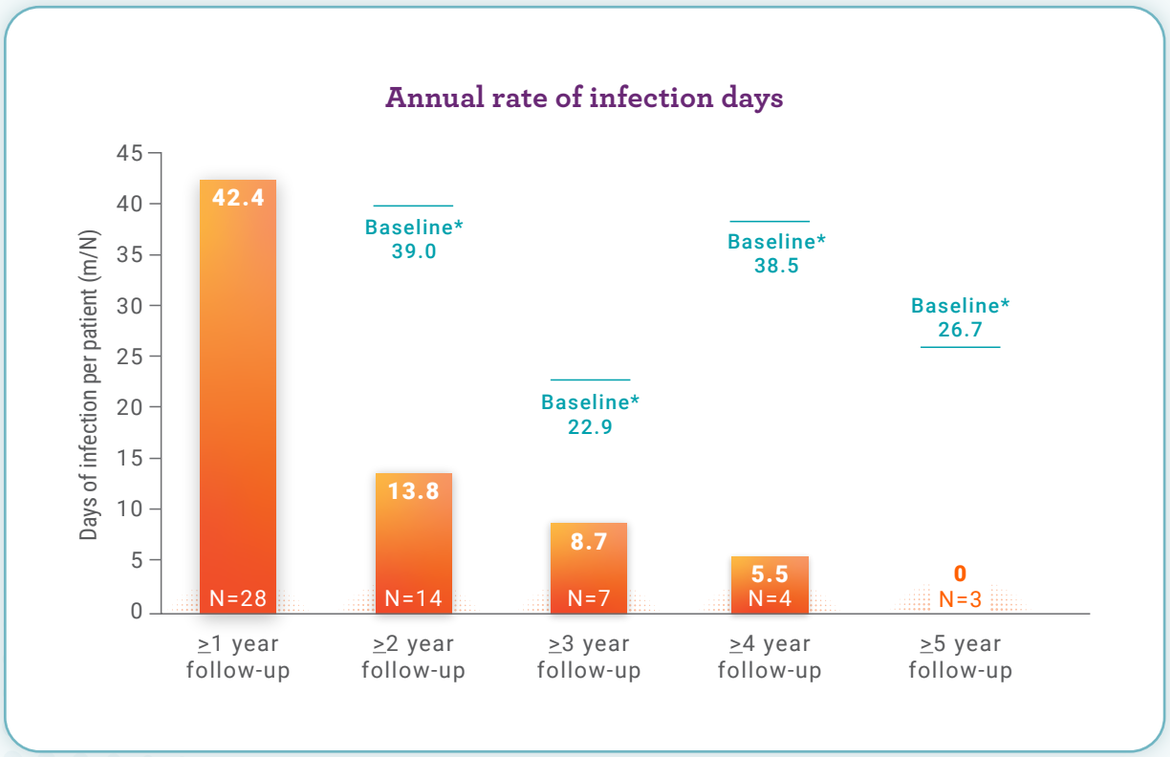
Joenja® leniolisib

ADDITIONAL FINDINGS FROM THE OLE STUDY

Annual infection rates[19]

Infection rates reported per each additional year of treatment with Joenja

Infections that developed during the study were reported as AEs. Investigators were requested to inquire about signs and symptoms of infections at each visit, in particular bacterial enterocolitis. Patients were not provided an infection diary to document infections occurring between visits.



- No change in antibiotic use despite the reduction in IRT utilization

Although safety was the primary objective of the open-label study, this post hoc analysis from the OLE study was not powered to provide any statistical significance of efficacy and therefore no conclusions should be drawn.

*Baseline infections are each group's year 1 annualized rate of infections. N values changed because patients were in the study for different lengths of time.[19] Data analyzed using a log-linear negative binomial model including an offset for time spent in study, an effect for time of the start of infection (in years), and presence of baseline infection as a covariate. One patient was excluded from the analysis due to a wrong year recorded for an infection.[19]
m/N, number of infection days/number of patients in follow-up category.

Select Safety Information

Live, attenuated vaccinations may be less effective if administered during JOENJA treatment.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

ADDITIONAL FINDINGS FROM THE OLE STUDY (CONT'D)

Physician-reported IRT reductions and discontinuations[19]

- Data on concomitant medication usage were recorded at each patient visit

Twenty-seven Joenja patients were receiving IRT at the start of the OLE study

AT THE DATA CUTOFF



17 PATIENTS REMAINED ON IRT



4 PATIENTS REDUCED THEIR IRT UTILIZATION



6 PATIENTS DISCONTINUED IRT USE*

- Four patients had been IRT-free for 1 to 2.5 years
- The median time to IRT reduction was 12.1 months, and the median time to IRT discontinuation was 11.9 months

IRT use was captured by the investigator as concomitant medication at each study visit per protocol in this open-label study. IRT was not prespecified as an end point or analysis. This is an observation from a post hoc analysis, so no determination of statistical significance can be made and no conclusions should be drawn.

The OLE study is ongoing and has 4 patients who have had more than 5 years of Joenja exposure[1]

*One of these patients had a subsequent one-time dose of IRT.[19]

Select Safety Information

JOENJA may cause hypersensitivity reaction(s), including anaphylaxis. Advise patients to discontinue JOENJA and to seek immediate medical attention if they develop any signs and symptoms of serious allergic reactions.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja® leniolisib

Joenja offers convenient, twice-daily oral dosing for patients aged 4+ who weigh 27 kg or greater [1]

Joenja is taken every 12 hours and can be taken anywhere, with or without food

Dosing for Joenja is based on weight* and ranges from 40 mg to 70 mg twice daily

Body weight	1 tablet twice a day
27 kg to <38 kg (60 lb to <84 lb)	40 mg
38 kg to <45 kg (84 lb to <99 lb)	50 mg
≥45 kg (≥99 lb)	70 mg

*There is no recommended dosage for patients younger than 4 years of age or who weigh less than 27 kg.

Advise patients that if a dose is missed by more than 6 hours, they should wait and take the next dose at the usual time.





Image represents the 70 mg strength only.

Adherence counseling may be beneficial for patients who remain on treatment

Select Safety Information

Use of JOENJA in patients with moderate to severe hepatic impairment is not recommended.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

APDS Assist—opening doors to help your patients with APDS move forward

APDS Assist provides comprehensive support for you and your patients every step of the way



APDS Care Coordinators

Here to help you navigate coverage, access, and other support options when you prescribe Joenja



ACEs*

Provide one-on-one support and educational resources for you and your patients



APDS Assist Specialty Pharmacists

Available to answer questions you and your patients may have about their Joenja medication

Ways APDS Assist can help your patients with APDS

Our commitment is to **get your patients started on Joenja as quickly as possible** while we work with your office to provide insurance support.

ACEs can help your patients connect with local and nationwide support groups and educational resources along their Joenja journey.

Access to Joenja is our priority. **Depending on the patient's insurance and other eligibility criteria, an APDS Care Coordinator can help identify support resources as needed.**

*Please note that ACEs do not offer medical or treatment advice or replace discussions with a physician.

Learn more about how APDS Assist can support your patients

ACE, APDS Clinical Educator.

Select Safety Information

Avoid co-administration of JOENJA with other medications known to be strong CYP3A4 inhibitors, strong or moderate CYP3A4 inducers, or BCRP, OATP1B1, and OATP1B3 substrates.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja® leniolisib

Important Safety Information

Indications and Usage

JOENJA® (leniolisib) is a kinase inhibitor indicated for the treatment of activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) in adult and pediatric patients 4 years of age and older who weigh 27 kg or greater.

Important Safety Information

Verify pregnancy status in females of reproductive potential prior to initiating treatment with JOENJA.

JOENJA may cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus and to use highly effective methods of contraception during treatment with JOENJA and for 1 week after the last dose. Additionally, advise women not to breastfeed during treatment with JOENJA and for 1 week after the last dose.

Live, attenuated vaccinations may be less effective if administered during JOENJA treatment.

JOENJA may cause hypersensitivity reaction(s), including anaphylaxis. Advise patients to discontinue JOENJA and to seek immediate medical attention if they develop any signs and symptoms of serious allergic reactions.

Use of JOENJA in patients with moderate to severe hepatic impairment is not recommended.

Avoid co-administration of JOENJA with other medications known to be strong CYP3A4 inhibitors, strong or moderate CYP3A4 inducers, or BCRP, OATP1B1, and OATP1B3 substrates.

Most common adverse reaction (incidence >10%):

- Adult and pediatric patients 12 years of age and older: headache, sinusitis, atopic dermatitis, and weight gain.
- Pediatric patients 4 to <12 years of age who weigh 27 kg or greater: abdominal pain, cough, and respiratory tract infection.

Seven (33%) patients 12 years and older (n=21) and 5 (63%) patients 4 to 12 years of age and weighing more than 27 kg or greater (n=8) developed an absolute neutrophil count (ANC) between 500 and 1500 cells/microL after receiving JOENJA. No patients developed an ANC <500 cells/microL and there were no reports of infection associated with neutropenia.

Before prescribing JOENJA, please read the full Prescribing Information.

Joenja is available in 40 mg, 50 mg, and 70 mg tablets.

References

References: 1. Joenja (leniolisib). Prescribing information. Pharming Healthcare, Inc; 2026. **2.** Pharming Group. Pharming announces US FDA approval of Joenja® (leniolisib) as the first and only treatment indicated for APDS. Press release. March 24, 2023. Accessed January 9, 2026. https://www.pharming.com/news/pharming-announces-us-fda-approval-joenja-leniolisib-first-and-only-treatment-indicated-apds **3.** Rao VK, Webster S, Šedivá A, et al. A randomized, placebo-controlled phase 3 trial of the PI3Kδ inhibitor leniolisib for activated PI3Kδ syndrome. *Blood*. 2023;141(9):971-983. doi:10.1182/blood.2022018546 **4.** Angulo I, Vadas O, Garçon F, et al. Phosphoinositide 3-kinase δ gene mutation predisposes to respiratory infection and airway damage. *Science*. 2013;342(6160):866-871. doi:10.1126/science.1243292 **5.** Rao VK, Webster S, Šedivá A, et al. A randomized, placebo-controlled phase 3 trial of the PI3Kδ inhibitor leniolisib for activated PI3Kδ syndrome [supplementary appendix]. *Blood*. 2023;141(9):971-983. doi:10.1182/blood.2022018546 **6.** Data on file. Pharming Healthcare, Inc. **7.** Jamee M, Moniri S, Zaki-Dizaji M, et al. Clinical, immunological, and genetic features in patients with activated PI3Kδ syndrome (APDS): a systematic review. *Clin Rev Allergy Immunol*. 2020;59(3):323-333. doi:10.1007/s12016-019-08738-9 **8.** Coulter TI, Chandra A, Bacon CM, et al. Clinical spectrum and features of activated phosphoinositide 3-kinase δ syndrome: a large patient cohort study. *J Allergy Clin Immunol*. 2017;139(2):597-606.e4. doi:10.1016/j.jaci.2016.06.021 **9.** Elkaim E, Neven B, Bruneau J, et al. Clinical and immunologic phenotype associated with activated phosphoinositide 3-kinase δ syndrome 2: a cohort study. *J Allergy Clin Immunol*. 2016;138(1):210-218.e9. doi:10.1016/j.jaci.2016.03.022 **10.** Maccari ME, Abolhassani H, Aghamohammadi A, et al. Disease evolution and response to rapamycin in activated phosphoinositide 3-kinase δ syndrome: The European Society for Immunodeficiencies-Activated Phosphoinositide 3-Kinase δ Syndrome Registry. *Front Immunol*. 2018;9:543. doi:10.3389/fimmu.2018.00543 **11.** Michalovich D, Nejentsev S. Activated PI3 kinase delta syndrome: from genetics to therapy. *Front Immunol*. 2018;9:369. doi:10.3389/fimmu.2018.00369 **12.** Lucas CL, Kuehn HS, Zhao F, et al. Dominant-activating germline mutations in the gene encoding the PI(3)K catalytic subunit p110δ result in T cell senescence and human immunodeficiency. *Nat Immunol*. 2014;15(1):88-97. doi:10.1038/ni.2771 **13.** Sacco K, Uzel G. Activated PI3K delta syndrome. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews® [Internet]. University of Washington, Seattle; 1993-2025. **14.** Anderson JT, Cowan J, Condino-Neto A, Levy D, Prusty S. Health-related quality of life in primary immunodeficiencies: impact of delayed diagnosis and treatment burden. *Clin Immunol*. 2022;236:108931. doi:10.1016/j.clim.2022.108931 **15.** Shawaludin MQA, Zainudeen ZT, Taib F, Husin A, Ali A, Hamid IJA. A rare case report of activated PI3K delta syndrome (APDS): diagnostic pitfalls. *BMC Pediatr*. 2025;25(1):898. doi:10.1186/s12887-025-06286-0 **16.** Rao VK, Webster S, Dalm VASH, et al. Effective "activated PI3Kδ syndrome"–targeted therapy with the PI3Kδ inhibitor leniolisib. *Blood*. 2017;130(21):2307-2316. doi:10.1182/blood-2017-08-80119 **17.** Rao VK, Kulm E, Šedivá A, et al. Interim analysis: open-label extension study of leniolisib for patients with APDS. *J Allergy Clin Immunol*. 2024;153(1):265-274.e9. doi:10.1016/j.jaci.2023.09.032 **18.** Extension to the study of efficacy of CDZ173 in patients with APDS/PASLI. ClinicalTrials.gov Identifier: NCT02859727. Accessed January 2026. ClinicalTrials.gov **19.** Rao VK. Interim analysis of safety and hematological parameters of an ongoing long-term open-label extension study of investigational PI3Kδ inhibitor leniolisib for patients with activated PI3K delta syndrome (APDS). Deck presented at: The 64th American Society of Hematology (ASH) Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja® leniolisib

Joenja is the only FDA-approved precision therapy for patients 4+ who weigh 27 kg or greater that targets the underlying immune defect in APDS[1-3]

Joenja helped normalize the immune system. [1,3,6]

Significant improvements were observed in both lymphadenopathy and B-cell function in the adolescent and adult trial (ages 12+)[1,3,6]

- Significant improvements across both end points, including normalization of naïve B-cell levels by week 4, maintained through week 12
- Significant mean reduction in lymphadenopathy by 46% from baseline

The OLE study is ongoing[1]

- 97% of patients in the OLE study received Joenja for at least 25 weeks
  - 66% were exposed for 96 weeks or longer
- Four patients had more than 5 years of Joenja exposure
  - Median duration of Joenja exposure was ~2 years

Joenja safety results

- Treatment was well tolerated, with no serious adverse events or patient withdrawals reported[1]
- Adverse reactions reported in pediatric patients 4 to <12 years of age who weigh 27 kg or greater were consistent with adverse reactions reported in adults and pediatric patients 12 years of age and older[1]
- Adult and adolescent patients 12 years of age and older: The most common adverse reactions (incidence >10%) were headache, sinusitis, atopic dermatitis, and weight gain[1,17]
- Pediatric patients 4 to <12 years of age who weigh 27 kg or greater: The most common adverse reactions (incidence >10%) were abdominal pain, cough, and respiratory tract infection[1]

If you suspect your patients may have APDS, genetic testing can help inform a timely diagnosis for them and their families[6,8]

Stay informed on all things Joenja
Sign up for updates

FDA, Food and Drug Administration.

Select Safety Information

Most common adverse reaction (incidence >10%):

- Adult and pediatric patients 12 years of age and older: headache, sinusitis, atopic dermatitis, and weight gain.
- Pediatric patients 4 to <12 years of age who weigh 27 kg or greater: abdominal pain, cough, and respiratory tract infection.

Please see Important Safety Information on page 20. Before prescribing JOENJA, please read the full Prescribing Information.

Pharming

Joenja and logo are registered trademarks of Pharming Intellectual Property, B.V.
© 2026 Pharming Healthcare, Inc. All rights reserved.
JOE-US-2023-0077v6 09/26

Joenja leniolisib