

Variant: *NM_001204.7(BMPR2):c.1016T>A (p.Val339Asp)*

Version: 2.0

CA350341378 [↗](#)

425863 (ClinVar) [↗](#)

Gene: BMPR2 ([HGNC:659](#))

Condition: pulmonary arterial hypertension ([MONDO:0015924](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 0efa5eda-89d2-4f02-bd03-05d9e86ebba1

Approved on: 2026/4/9

Published on: 2026/4/9

HGVS expressions

NM_001204.7(BMPR2):c.1016T>A (p.Val339Asp)

NM_001204.7:c.1016T>A

NC_000002.12:g.202530842T>A

CM000664.2:g.202530842T>A

NC_000002.11:g.203395565T>A

CM000664.1:g.203395565T>A

NC_000002.10:g.203103810T>A

NG_009363.1:g.159516T>A

ENST00000374580.10:c.1016T>A

ENST00000638587.1:c.947T>A

ENST00000374574.2:c.1016T>A

ENST00000374580.8:c.1016T>A

NM_001204.6:c.1016T>A

Likely Pathogenic

Met criteria codes **5**

PP2 PP3 PM1 PM2_Supporting

PS4_Supporting

Not Met criteria codes **1**

BP4

Evidence Links **0**

Expert Panel

Pulmonary Hypertension VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Pulmonary Hypertension

Expert Panel Specifications to the ACMG/AMP Variant

Interpretation Guidelines for BMPR2 Version 2.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Pulmonary Hypertension VCEP

The NM_001204.7(BMPR2) c.1016T>A (p.Val339Asp) variant is harboured in exon 8 of the gene, encoding the functionally relevant catalytic kinase domain (PM1_met). The variant has been twice reported in the Japanese population in one IPAH and one HPAH subject (PMID: 23579436 and PMID: 23675998), (PS4_supporting). This variant is absent from gnomAD v2.1.1 (controls) and v4.1.0 (PM2_supporting).

BMPR2 has a low rate of benign missense variation (misZ = 3.28, gnomAD v4.1) and missense variants are a common mechanism of disease (PP2). The REVEL prediction algorithm score is 0.967, AlphaMissense is 0.9992 indicating pathogenicity (PP3_met). PP1 and PS2

were not assessed due to absence of co-segregation data and parental data respectively. No other amino acid change at the same position has been reported for PAH (PS1 and PM5 not assessed). Functional studies have not been conducted for this variant (PS3 not assessed). In summary, this variant meets the criteria to be classified as likely pathogenic for pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PM1, PM2_supporting, PP2, PP3, PS4_supporting (VCEP specification version 2.0, 1/30/2026).

Met criteria codes

PP2			In gnomAD v4.1, BMPR2 has a z-score of 3.28 for missense variants which is above the threshold of 3.09 (PMID: 404967) for constraint.
PP3			Variant has a REVEL score of 0.967, which meets the criteria for indicated pathogenicity (≥ 0.75).
PM1			Variant is located in the functionally relevant catalytic kinase domain.
PM2_Supporting			Variant is absent from gnomAD v2.1.1 and 4.1.0
PS4_Supporting			The p.Val339Asp variant has been reported in one IPAH and one HPAH patient from the Japanese population (PMIDs: 23579436, 23675998).

Not Met criteria codes

BP4			Variant has a REVEL score of 0.967, which exceeds the threshold for indicated benignity (≤ 0.25).
-----	---	---	--

Curation History



 ▾

 ▾

Showing 1 to 2 of 2 rows

--

