

## Supplementary Methods

### **KDR gene expression analysis**

Human PAECs were cultured as previously described<sup>1</sup> from lung tissue samples of heritable PAH patients (n=4, BMPR2 mutation carriers), sporadic BMPR2 mutation non-carrier PAH patients (n=5), and controls (n=4, obtained from pneumonectomy for tumors) and were used for the study between passages 3 and 5. Patients studied were part of a program approved by our institutional Ethics Committee and had given written informed consent (ID RCB: 2018-A01252-53, approved on June 18, 2006).

Total RNA was extracted using TRIzol reagent according to standard procedures. RNA quantity and quality was assessed using the Nanodrop-ND-1000 (Nanodrop Technologies,). One microgram of total RNA was reverse-transcribed using a QuantiTect Reverse Transcription Kit (Qiagen,).

The obtained cDNA was used for real-time PCR experiments using 2 ng of cDNA, 0.3  $\mu$ M of each primer and 10  $\mu$ l of Sybr Green PCR master mix (Applied Biosystems) in a total volume of 20  $\mu$ l. Primers used were designed to target exonic regions of KDR and RPL32 as reference gene. Each sample was run in triplicate in independent reactions on an ABI PRISM 7700 Detection system (Applied Biosystems). The results were analyzed according to the  $2^{-\Delta\Delta Ct}$  method.

1. Perros, F. *et al.* Nebivolol for improving endothelial dysfunction, pulmonary vascular remodeling, and right heart function in pulmonary hypertension. *J. Am. Coll. Cardiol.* **65**, 668–680 (2015).

### Supplementary Figure S1

**KDR gene expression was measured in human PAECs from lung tissue samples of controls (n=4), heritable PAH patients (all BMPR2 pathogenic variant carriers) (n=4) and sporadic PAH patients (n=5).**

