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Mark P. Lythgoe, Christopher J. Rhodes, Pavandeep Ghataorhe, Mark Attard, John Wharton, Martin R. Wilkins

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**Why drugs fail in clinical trials in pulmonary arterial hypertension, and strategies to succeed in the future**

Mark P Lythgoe, Christopher J Rhodes, Pavandeep Ghataorhe, Mark Attard, John Wharton and Martin R Wilkins

Department of Medicine, Imperial College London, W12 0NN

Correspondence to:  
Professor M R Wilkins  
m.wilkins@imperial.ac.uk

**Abstract**

The past three decades have witnessed a welcome expansion of the therapeutic armamentarium for the management of pulmonary arterial hypertension (PAH). But against this backdrop there have been some notable disappointments in drug development. Here we use these as case studies to emphasise the importance of informed drug target selection, the early evaluation of dose-response relationships in human studies and the value of deep-phenotyping of patients in clinical studies to better understand inter-individual variation in patient response. The integration of 'omics' technologies and advanced clinical imaging offer the potential to reduce the risk, and so cost, of drug development in PAH and bring much needed new medicines to those patients most likely to benefit with greater efficiency.

**Key Words:** Pulmonary Arterial Hypertension, Serotonin, Statins, Vasointestinal Polypeptide, Imatinib, Drug Development

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