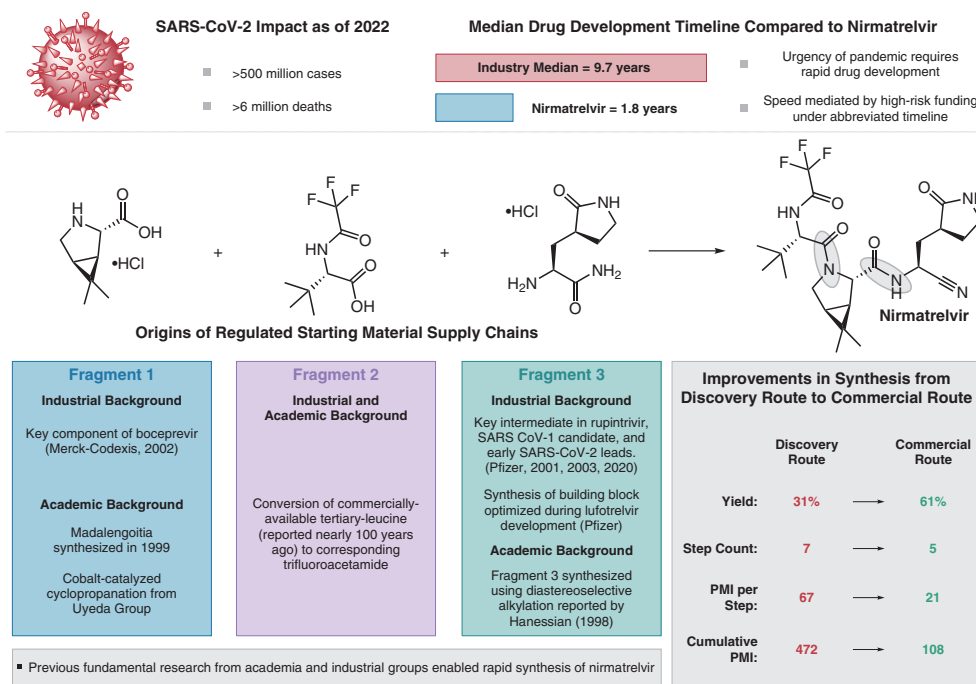


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Development of the Commercial Manufacturing Process for Nirmatrelvir in 17 Months
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Development of the Commercial Manufacturing Process for Nirmatrelvir in 17 Months



Significance: The team at Pfizer has accomplished a remarkable feat by condensing the drug development timeline to just 1.8 years for nirmatrelvir. This stands in stark contrast to the industry median of ten years for drug development. During this time, they were able to develop a robust and sustainable synthesis of nirmatrelvir while also traversing obstacles such as building robust supply chains on an aggressive timeline. The team leveraged previous studies from internal and external drug development and academic groups to rapidly establish supply lines to the three key starting materials. This manuscript demonstrates the importance of fundamental research and work completed for compounds that are not commercialized that can enable dramatic future breakthroughs. Additionally, there are lessons we can learn from this achievement about accelerating drug discovery and how drug development decision-making can change under strict time constraints.

Comment: Ragan and co-workers provide insight into the rapid development of nirmatrelvir, a bioavailable inhibitor of SARS-CoV-2 M^{Pro}. Due to the urgency and need for a treatment to SARS-CoV-2, Pfizer conducted an expedited drug discovery and commercial development campaign of nirmatrelvir. The first synthesis of the compound was achieved, a commercial route was developed, testing for efficacy and safety was performed, and emergency use authorization was granted all in just 17 months. The authors detail the extra challenges the team faced on an aggressive timeline such as high-risk funding during parallel development of nirmatrelvir, crucial planning of supply chains, and holding a high standard for sustainability for the process. The commercial route to nirmatrelvir improved on the discovery route by doubling the overall yield, reducing the total step count from seven to five steps, and decreasing the overall cumulative PMI from 472 to 108.

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