What a Diff'rence a Dalton Makes. From the University Lab to PIQUR

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PQR309 emerged from a program on PI3K/mTOR inhibitors at the University of Basel carried out by the group of Vladimir Cmiljanovic, supervised on the chemistry side by Bernd Giese and on the bio medicinal side by Matthias Wymann who also are the founders of the company Piqur Therapeutics. Piqur's Bimiralisib (PQR309) is currently in clinical development in indications such as solid tumors of head and neck and B cell lymphoma as an orally administered agent. Dual PI3K/mTOR inhibitors PQR309 and BKM120 (Novartis' Buparlisib) are structurally similar and differ by only one Dalton in molecular weight. This change however, has profound consequences in terms of biological profile, but also in terms of synthesis. The differences result from specific molecular interactions, on one hand, with the target proteins (PI3K and mTOR) and on the other hand, off target proteins such as micro tubules. Furthermore, the two individual scaffolds lead to distinct chemical reactivities calling for different synthetic approaches especially on scales necessary for clinical supply.