

Development and Scale-Up of an Optimized Route to the ALK Inhibitor CEP-28122

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Evolution of the process strategies to prepare CEP-28122, an anaplastic lymphoma kinase (ALK) inhibitor, will be presented. The initial medicinal chemistry route, used for the preparation of key supplies for biological screening, is also reviewed. In addition, the process research and development of the final optimized process for manufacture of preclinical and clinical supplies will be exemplified with new synthetic strategies and methodology. Details regarding a blocking group strategy for selective nitration; discovery of a one-pot transfer hydrogenation to effect a reductive amination, nitro group reduction, and dehalogenation; an enzymatic resolution of a critical intermediate; and the discovery of a novel, stable, in situ generated mixed mesylate hydrochloride salt of the API will be disclosed. CEP-28122 is a complex small molecule comprised of three core subunits, two of which contain one or more chiral centers.

