CDKL5 disorder has emerged as an important clinical entity in which patients are affected by severe cognitive and motor disabilities, epilepsy and autistic traits. No therapy is yet available. Studies with Cdkl5-null mice suggest that some symptoms can be reversed, but the limited knowledge of CDKL5 function hinders the development of drug-based therapeutic strategies. The repositioning of existing drugs for CDKL5 disorder represents an attractive possibility for rapid initiation of clinical studies, since a number of the time- and cost-consuming steps of discovery can be bypassed. With this proposal we will use specific computer-based bioinformatic and chemoinformatic approaches to identify some approved drugs with potential for CDKL5 disorder. The therapeutic utility of these therapeutic candidates will be tested on a platform of Cdkl5 deficient neurons that are characterized by several morphological and molecular defects. Compounds that appear capable of reversing some defects linked to the absence of Cdkl5 will be considered relevant for future evaluation in pre-clinical studies in a mouse model of Cdkl5 thus advancing the drug(s) for translation to the clinic.