Challenges in the development of an orphan drug

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A list of rare diseases is comprised of approximately 7,000-8000 different disorders affecting more than 300 million people worldwide. A disease or disorder is defined as rare in Europe when it affects less than 5 citizens in 10.000.
A rare disease could be also considered as an orphan disease when there is not a treatment or the actual therapy is not considered a valuable treatment.
Research in this field has been performed almost completely by Pharmaceutical companies (more than 90%), even if the small percentage of the population affected, sometime the patients geographical distribution , the lack of available clinical parameters discouraged to implement the research.
The Orphan Drug Act of 1983 is a law passed in USA, designed to facilitate the development and commercialization of drugs to treat rare diseases, offering benefits as reduced taxes for the sponsor or market exclusivity. A similar approach has been implemented in Japan and Australia. In Europe regs 141 and 847 of 2000 had as objective the implementation of research for orphan drugs. These laws for sure helped the investments in this field, because in USA before Congress enacted the ODA in 1983 only 38 drugs were approved in the USA specifically to treat orphan diseases, and now more than 400 drugs have received marketing authorization, and 2000 different orphan drug designations have been granted by the Office of Orphan Products. Among them, cancer was the main group of diseases targeted, followed by cardiovascular diseases and then metabolic diseases; 50% of all of these products were used in pediatric age.
R&D in Orphan Drugsgenerally follows the same regulatory development path as any other pharmaceutical product, including pharmacokinetics, pharmacodynamics, stability, safety and efficacy. The difference could be in some statistical burdens, that could be lessened for the epidemiological distribution.
In any case, developing and selling an orphan drugs remains an high risk activity, from a business point of view. It remains difficult to evaluate a financial return, but it is relatively easy to evaluate the (great!) financial effort to be invested in developing a drug, orphan or not. Moreover, the percentage of success in clinical trials for orphan drugs in Europe is not particularly encouraging: only 87 molecules out of 1000 have the changes to be marketed.
We'd like introduce some case history in orphan drugs: some born in a different indications, some were the final result of the disease's study. And in this review we evaluate problems and opportunities in this interesting research area.