Developing a product for the Global market place: Strategies for Success

This article will consider the rationale and benefits of identifying global development and commercialization needs early in the product life-cycle and then discuss some strategies for framing the global development.

Careful planning and assessment will permit the needs of the major countries and regions to be incorporated into a single global development program which will meet the needs of the major pharmaceutical markets.

Although a company may potentially only wish to commercialise their products initially in a single market, inclusion of the needs of the other regions within the development plan will generate a roadmap for future registration opportunities that can be used for partnering or out-licensing strategies.

In addition, even if a global dossier is not prepared, consulting the agencies in other regions will establish a documented path forward which similarly can be of value and shared with potential partners. Ultimately, it will be more efficient in terms of resources and time to accommodate the needs of as many regions as possible in the initial dossier. The global submission dossier can be built in a sufficiently granular format that the bulk of the dossier will be common with only certain sections, including Module 1 being tailored to individual regions.

The key success criteria for a global development program are to start planning early and to really assess the desired end goal in terms of a product with competitive labelling, which will also meet market access needs. Good planning and review of strategic scenarios relative to the competitive and regulatory landscape are critical to map out a development plan with key go/no go criteria. This will help frame the path for development yet offer data driven milestones to guide further investments. This approach should be applied during strategic assessment and is required at the latest in early clinical development and the key strategy documents revisited and refined throughout development. Some potential considerations are outlined below:

Target product profile (TPP)

The TPP needs to be well-defined with key elements considered for all regions. For example, are the proposed indications acceptable in all regions? Is the epidemiology of the disease the same? Are there differences in medical practice for treatment of the disease? What are the precedents and existing competitor products? How will the company's product be differentiated?

The TPP should be pressure tested, ideally via a Global Expert Panel, who can advise on the viability of the maximum and minimum claims targeted in the TPP. They could also comment on other indications that would be appropriate for the mechanism of action of the product.

Global Expert Panel

In addition to reviewing the target product profile, a panel of global Regulatory and Health Technology Assessment (HTA) experts, together with Key Opinion Leaders, will be able to provide advice on the proposed global development program and how it would meet the needs of their particular region or market. This panel would also be able to provide advice on potential differences in terms of clinical efficacy or safety in patient populations in different regions, which could be anticipated based on preliminary clinical data and the mechanism of action of the product. This would inform a decision on whether data generated in one region could be extrapolated to the population in another region, as described in the ICH E5 guidance.

Health Authority Interaction Strategy

This strategy should address such questions as: Which agencies should be consulted and in which order? The Company should consider how differences in Agency feedback will be addressed in the global development programme. The timeframes for consulting global agencies is ideally aligned so that all feedback can be incorporated into the clinical programme. Or, if major issues or feedback is obtained, a particular region may be excluded from the global program.

Key issues such as choice of comparator, primary and secondary endpoints to be used in the pivotal clinical studies should be confirmed with Regulatory Agencies. In some cases it may be possible to agree that different primary endpoints are used in the same trial for different regions. It also increasingly apparent the technical approval is not the only hurdle which should be addressed during product development. The data required by various national Health Technology Assessments (HTA) bodies and other payers need to be addressed. The Health Authority strategy should also therefore consider whether HTA bodies should be consulted either individually or via voluntary parallel advice. Finally, the optimal route for obtaining advice needs to be identified e.g. in the EU is this national, regional or national followed by regional? Parallel scientific advice procedures across regions can facilitate global development: e.g. EMA/FDA or EMA/PMDA advice procedures. The final dynamic is the consideration of parallel regulatory and HTA advice e.g. MHRA / NICE advice. Given the number of options available for obtaining insight into the global development programme requirements, the strategy for Health Authority interactions needs to be well-defined, robust and reviewed as studies are completed and data becomes available during the development programme.

Filing route and fast to market considerations

Fast to market strategies could also be reviewed for example demonstration of efficacy in a niche patient population with an unmet clinical need. Depending on the proposed therapeutic indication, an orphan drug application may be possible in the EU, US, Japan which may provide a faster route to market. However, the benefits of a fast to market strategy would need to be reviewed against the earlier triggering of market or data exclusivity for the product as a whole, potentially reducing the period of protection for a wider population.

There are a number of global opportunities for either early access or accelerated review for example the US Breakthrough Therapy Designation, the recently introduced PRIME initiative in the EU, accelerated review in the US and conditional approval in the EU and US, or exceptional approval in the EU.
An early assessment of the potential for a product to qualify for consideration of these routes will inform subsequent discussions with Regulatory Agencies. These opportunities must also be balanced relative to reimbursement planning. Expedited programs frequently suffer from inadequate information to support both labelling and reimbursement success and the trade offs must be strategically considered.

Risk minimisation assessment

Examination of identified or potential safety issues for the product should also be initiated at an early stage, so that the specific areas of interest can be examined as far as possible in the nonclinical or clinical program. The risk minimisation strategy should be reviewed regularly as further data are available or if the external environment changes, due to issues with similar products or changes in regulatory guidance. It is also beneficial to draft a developmental Risk Management Plan early in the process and ensure that is updated whenever significant new non-clinical or clinical data become available from either the internal development programme or published literature.

In a similar vein, for biopharmaceutical products, an early assessment of the potential for immunogenicity would be helpful in informing the product development and would be relevant for all regions. This risk assessment would integrate information on the intrinsic molecular features (B- & T-cell epitopes), extrinsic factors (product and process-related, formulation etc.), patient genotype / phenotype / co-morbidities and conditions of use.

How we can help

NDA Group can provide the above strategic assessments which, particularly when employed early in development (CTA/IND planning and Phase 1), will help inform an efficient global development program which enables the needs of regulators and payers in multiple regions to be addressed in the most expeditious fashion and delivers a product which is targeted for successful commercialisation.