The Benefits of a Robust Target Product Profile

The following was written with a multi-disciplinary development team sharing their perspectives regarding the benefits of developing a robust TPP:

1. Early Stage development considerations for a robust TPP, including Aspirational and Directional content -

As a drug candidate enters the clinical development stage, it is essential that all stakeholders understand and share the same aspirational targets for the prioritized asset. This "strategic alignment," as it has been called, ideally focuses each of the functional areas on a common trajectory. Equally important are the other options that stakeholders decide to exclude. The tool that enables this critical stepping off point into the clinic stage of development is the Target Product Profile, or TPP.

Case Study:

During early development, a therapeutic team faced a market with an established competitor's drug about to go generic. Leveraging how to best structure the TPP before their clinical trial design stage, the team incorporated 3 patient profile scenarios based on advancement of technologies that identified patients for whom the established therapy was non-ideal. The team updated their TPP throughout clinical development, aligning the team and their diagnostic partners to keep development focused on the 3 scenarios until a best option was identified.

At this stage of initial clinical development, there are more aspirational targets established by the TPP than those supported by data. However, this strategic alignment brings to bear all the expertise and resources necessary to determine how best to achieve the aspirational goals for a drug candidate. Therefore, having translational science, medical development, regulatory, finance, supply chain, commercial and legal functions all participate in designing and setting initial TPP targets is essential to guiding the team through the inevitable ups and downs of early drug development.

Case Study:

Early in the clinical development of a targeted drug, a series of workshops with broad participation were held: the participants included the global product director, project director, senior scientific staff, clinical development director, regulatory and legal leads, medical affairs director, and global strategic brand directors. A centerpiece of this multi-functional workshop was the development of the drug TPP, aligning all the functions and developing the long-term plan to update and modify the TPP as needed. The drug maintained its original timeline to successful launch despite some necessary modifications of goals after clinical trial data analysis.

2. Mid Stage development of the TPP, requiring filling in content, updates, and modifications as data replaces aspirations -

It has been said that the goal of early drug development is to 'fail early, fail fast," meaning that early development is the least costly stage to discontinue those drug candidates that have not, and will not, deliver the data to support further investment; at least not under the established terms and targets defined by the TPP. For those drug candidates that survive to mid-stage proof-of-concept (PoC) studies, they have begun to reveal important aspects of their medicinal character; safety and therapeutic dose for sure, but also the specific patient population and course of disease progression compared to historical controls and background standards of care. All of these critical insights begin to replace aspirational targets in the TPP with more sound facts and data.

Case Study:

During early development of a novel MOA drug, the TPP generated reflected a large inclusive targeted market based on pre-clinical models of how MOA would be effective in a number of indications; a high aspirational target. As the drug moved through clinical trials in one indication, the TPP aspirational target hardened into the "expected" target and other options were not advanced leading to difficulty in translating success from initial 3rd line indication to 1st line. Despite an early lead on competitors in the general MOA space, the first mover did not capture the highest market share after a few years.

The multi-disciplinary team can now assess, with a sharp eye on facts, whether the drug development trajectory is on-track or needs adjusting. At this stage, the TPP will, in addition to strategic direction and team alignment, begin to define ranges of expected performance. In other words, a picture of the upside and downside potential of the drug candidate begins to take shape against a well-defined and unmet medical need. Critical questions can start to be asked and answered such as whether or not a companion diagnostic is needed to select those patients most likely to benefit from treatment. All this goes into the design and costing for the next round of clinical development trials. In addition, better calibrated revenue forecasts can be developed providing a clearer view of the potential return on investment to the business and serve as justification for multi-million-dollar investment decisions.

Case Study:

A therapy team was faced with uncertainty regarding how certain genomic information would be used in conjunction with their Phase II therapeutic candidate:

- Patient pharmacogenomic (PGx) data would be "information only" for the prescriber
- PGx data would be recommended in labeling
- PGx data is required for the prescription

The TPP was managed consistently to align clinical, regulatory, marketing, and diagnostic teams with the ongoing clinical trial design and execution. After clinical data determined that PGx testing would be required, the path forward that had been considered and designed through the TPP allowed for receiving FDA approval with little to no time lost.

3. Late Stage development assessing critical points of development and alignment to investment considerations versus true opportunity; what happens when results do not match, even miss, aspirations.

At the later stages of development, the landscape canvas that was once blank, has now become richly colored with contours and a horizon based on clinical study end points. The senior executive team can prioritize the drug candidate in the overall portfolio, now having an understanding of its' risk ranking. It is likely investors and analysts will have reviewed the data and determined the potential value of the asset and issued reports now available to the public. The TPP will now have more facts and data than aspirational targets. The remaining gray area is whether the benefits

observed so far will translate in larger Phase III regulatory trials. The TPP now serves in a regulatory capacity to help stakeholders develop a regulatory risk assessment and assemble a data package for an anticipated submission. Organizationally, the TPP is used for internal preparation of launch activities. Commercial teams who will be responsible for the execution of a go-to-market plan will want to know everything they can about the drug candidate's characteristics and its performance in the clinic.

Case Study:

An initially successful marketed therapy had a rapid decline in prescriptions after publications describing a dangerous, although very rare, adverse event for some patients on the therapy. The company convened a broad-based team to confront the problem, with all options in the updated TPP: pull the drug from the market, advise physicians on adverse event and how to identify early symptoms, and find a practical solution to identify the small subset of patient susceptible to the adverse event. Medical affairs, marketing, regulatory, and pharmacogenomics teams worked together to rapidly put in place a medical communications program for physicians and patients, a pharmacogenomics program to identify at-risk patients, and a regulatory process with the FDA and EMA to speed these solutions to market. In a few months, at-risk patients were effectively identified and the drug regained the trust of physicians. Market share returned to the previous trajectory.

In addition, the TPP provides the target patient population, the underlying unmet need and whether a companion diagnostic will be used. A fierce focus aligning all stakeholders on the TPP targets is critical as this round of activity requires an incredible amount of investment and resources to prepare for launch and the appropriate pre-launch scientific exchange crucial for meeting senior executive, investors, and financial market expectations. The TPP along with more granular market data will be used to develop revenue forecasts by geography and determine the extent of resources needed for customer facing activities. Local P+L holders will use TPP information for budget needs and marketing mix in their short-and long-term plans.

Patients in need are depending on the organization to get it right and the organization also needs the return on investment as a reward for innovation and to fund future attractive drug candidate opportunities. A lot is at stake and the TPP, when done right, serves as a foundational element of any drug development program.

Case Study:

A regular updating of the TPP for a targeted therapy during Phase II trials highlighted for the team a clear market opportunity. Previous TPPs had decided the use of a lab-based companion diagnostic was optimal for US and EU markets. The discussions around this update determined that a parallel development of a Point-of-Care companion diagnostic during Phase III for RoW markets was appropriate for patient-pay environments, and to allow for the controlled development of messaging around therapeutic choices in these markets.

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