Giles & Associates Consultancy Inc. (GAC)

Common Pitfalls for Target Product Profiles — and How to Avoid Them

Clients often ask us to assess the value of products in their pipeline. That includes gathering customer (prescriber, payer, patient) input on the target product profile (TPP) and product attributes. Our work on these projects has revealed a surprisingly common mistake: **Products in mid-to-late stage clinical development often lack effective profiles for making informed clinical development and commercial decisions.**

Too often, the TPP focuses heavily on clinical requirements of the pivotal trials to meet regulatory hurdles for approval. It may define core claims required for the label, but can overlook crucial factors for success — such as generating market demand, addressing unmet needs, and achieving clear competitive differentiation. Here are some underlying dynamics that create a narrow focus and an ineffective TPP:

- **A typical TPP to support a product's development** will establish the statistically relevant data needed for product approval by regulatory authorities. But it will usually lack the clinically meaningful product characteristics or outcome data that can establish the product's value.
- **A clinically-driven TPP** focuses on the outline of the label and identifies the target indication, patient populations to be served, formulations, route of administration, dosing frequency, pharmacology, warnings/AE/contraindications, clinical trials and packaging. It characterizes the product — but it does not address what is required to achieve product trial and ongoing use, target sales, market share, market access and pricing goals.
- **An R&D-driven TPP** can be motivated by the internal priorities to minimize clinical budgets and timelines. When there's immense pressure to fund the least expensive and shortest clinical path for rapid regulatory approval, important marketing requirements are often overlooked.

Regardless of the driving motivations behind TPPs, we have observed several pitfalls that can create significant challenges. To help companies avoid TPP shortcomings, we explain these common problems below, and ways to avoid them — including vital questions and considerations designed to strengthen TPP.

The wrong lead indication

We see products fail because the lead indication was selected based on the largest "most attractive" market — which is not necessarily the best fit for the product's performance. Large competitive markets require a higher burden of differentiation and come with greater price scrutiny.

To strengthen TPP: A smaller indication that allows unique access to a discrete segment of the population is often more attractive. Life cycle management can be used to expand later into the larger segment.

We helped a client focus a lead indication on a unique orphan category, steering them away from an initial indication into a large but highly saturated market that is expected to decline by one-third over the next few years due to competitive price pressure. The orphan segment was poorly served, and the product could demonstrate superior performance and command a premium price.

Target Product Profiles: How to Avoid Common Pitfalls

Pfizer determined to enter the competitive PDL-1 market with the ultra orphan Merkel cell carcinoma to gain rapid approval and access.

Target claims lack specificity

A regulatory-driven profile may require statistical improvement vs. placebo or equivalence to standard of care – but the market will require specific and clinically meaningful claims. It is important to test a range of scenarios with stakeholders, to solicit expected responses. These will be part of your minimal, base and optimal product profiles and link to the minimal to optimal forecasts.

If attributes do not have clear points of customer-identified value against important attributes, do they even meet a minimal standard?

To strengthen TPP: We conduct primary research to capture clinicians' prescribing intentions aligned with each attribute variable. This clinician research is then shared and tested with payers to assess market access requirements and ranges.

Keep in mind that the attributes tested are not in isolation. In some markets, efficacy improvement may be unacceptable if that is the only competitive differentiation. But if that comes with some combination of improved tolerability, safety, dosing frequency or reduced treatment duration – the combination may lead to a strong competitive advantage.

Don't assume you know the answers. In one class of drugs where compliance was critically important, we tested 1X daily, 2X weekly and 1X weekly dosing. The less frequent dosing was not a highly important variable, due to concerns about risk for dosing confusion and the clinical impact of missing a weekly dose, resulting in greater risk for sub-therapeutic blood levels.

In NSCLC, Merck focused Keytruda on PD-1 high expressers compared with all comers for Opdivo. Focusing on the targeted profile allowed a higher clinical response (45 percent vs 19 percent) and competitive differentiation.

Relying on a base case profile

A frequent commercial complaint we hear is, "I am stuck with the forecast, even though the product results delivered a lesser product profile than forecasted and under-performed." Too often, when a client asks us to test a profile, we discover they only have one: Namely, the base case profile that the clinical trial is being developed against.

To strengthen TPP: We always test a range of three profile cases – Minimal (below which you would not launch), Base (most likely to achieve) and Optimal (stretch attributes that may include higher adoption, market access and/or pricing). Without that range of possibilities, it's not possible to test variable response to attributes and model their impact on adoption and forecasts.

Insufficient differentiation

It is highly unlikely that you are developing a head-to-head trial. Still, conduct a side-by-side comparison of your target product attributes against those of the current and future landscape. If they do not have clear points of customer-identified value against important attributes, do they even meet a minimal standard?

In the cholesterol-lowering market, Pfizer discontinued development of its PSCK9 inhibitor, due to inability to show the long-term durable response required to differentiate compared with the statins and currently marketed PSCK9 inhibitors.

To strengthen TPP: Find points of differentiation. Compared to the competition, will it shorten the duration of treatment? Will it have a higher cure rate? Can it improve safety or tolerability and associated treatment costs? What are the long-term real world outcomes that are needed to compete against existing and emerging products?

DIFFERENTIATION QUESTIONS

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With the expansion of Accountable Care Organizations (ACO's) clinicians treating chronic conditions (such as diabetes, allergy and now Crohn's disease) are being held accountable for the overall cost of care. What is this calculation, and what advantage can you provide?

Emphasizes MOA and forgets unmet needs

One of the big fallacies is that a unique mechanism of action (MOA) means that a product will be seen as different or improved due to its novelty. Yet the MOA is actually the rationale to support an improved clinical response.

To strengthen TPP: If there is no clinical differentiation vs. current products, can a new MOA be clinically differentiated as a second-line agent when first-line fails? Is this line of treatment reflected in the patient profile and the forecast?

Overlooks patient selection variability

Hitting an endpoint for approval is not enough to gain market access or adoption. Plan for sub-analysis of responder data. While the product may be approved for a broader population, payer and government authorities may only grant access to a sub-population. Increasingly, companies are utilizing companion diagnostics to help pre-identify likely responders.

To strengthen TPP: At minimum, try to characterize post-hoc the characteristics (age, gender, race, disease severity, etc.) where you have the data to show superiority or an improved response. As payers look at more shared risk contracting – the ability to carve out and own a sub-population may make clinical and economic sense.

PDL1 checkpoint inhibitors were a novel MOA for use in treating various cancers, yet payers in Europe have frequently declined to cover them consistent with their regulatory approval, citing lack of long-term benefits and lack of strong clinical differentiation. Instead, they are being targeted for second line treatment, or restricted to sub-populations populations with identified higher response rates, until longer-term outcomes data is available. In the past, a new oncology treatment was given blanket access – but the bar is being raised.

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Forecasting lacks flexibility

Without distinct attribute analysis that assesses a range of values for the attribute, it is difficult to adjust the price assumptions or forecast up or down, as the pivotal study results are made available. A "one size fits all" TPP doesn't provide the planning and forecasting flexibility needed for launch success.

To strengthen TPP: The best-in-class practices occur when the commercial (New Product Planning) and clinical teams work together to ask: "'What can the product do? What is needed to succeed?"

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GAC helps commercial teams come to the table with the clinical teams better prepared to defend product claims. By fostering partnership, we help companies increase asset values. We are dedicated to guide companies toward informed decisions.

Giles & Associates Consultancy Inc. (GAC) *is a healthcare-dedicated strategic consulting company working with large and small innovators to help guide innovation and sustainable growth strategies. GAC is located at 51 Sherwood Terrace, Suite P, Lake Bluff, IL 60044.* Common Pitfalls for Target Product Profiles *was written by* ***Aimee Berner,*** *a principal at GAC with a long history of pharmaceutical strategic development and commercialization. She can be reached at aberner@gilesaa.com or 847-682-4202.*