

DIABETES THREATS AND OPPORTUNITIES



The diabetes marketplace is becoming increasingly complex, fragmented and competitive

GLP-1 Analogues set to replace DPP-IVs as First Line Properly positioning a GLP-1 analogue is key

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Work conducted by Pharmaceutical Business Research Associates ([PBRA](#)) confirms that all the GLP-1 analog products, including those recently approved and others in late-stage pipeline, intend to position themselves as first-line agents to be preferred over DPP-IV inhibitors. A number of assessment and strategic planning projects to properly position the GLP-1s are underway.

Positioning GLP-1s

1. Properly segmenting and targeting both endos and PCPs

The two specialties represent vastly different market segments in terms of their treatment approaches and needs. Endos seek to treat diabetes while PCPs treat a complex of symptoms. The GLP-1 competitors

understand that targeting and effectively communicating with the two specialties requires messaging that can address the respective needs of each. Toward this end, all of them are seeking to develop an optimal message platform.

2. Effectively segmenting, positioning and targeting endos and cards

For approximately five years, endos and cards have been in a protracted war over who owns diabetes. The FDA's refusal to approve Pargluva® and all the other dual-PPAR compounds represented a win for cardiology in the war's opening battle. The two specialties and their major organizations (ADA and AHA) differ on fundamental issues, for example: the very reality and

utility of cardio-metabolic syndrome, the value of HbA1c vs. fasting blood glucose, and whether diabetes is actually a cardiovascular disease. The GLP-1 analogs recognize that Pargluva® (muraglitazar/BMS) failed miserably in trying to unite these 2 camps and *the competitors are exploring a marketing course that both specialties can find acceptable.*

3. Weight loss as the not-so-subtle key to commercial success

Lilly-Amylin and, more recently, Novo have spoken about the weight loss benefit of their respective products.

Clearly, the SGLT-2 inhibitors are waiting in the wings with their modest hypoglycemic benefits, hoping that the GLP-1s run aground from safety issues thereby allowing the SGLT-2s

to enjoy commercial success as the anti-diabetic class with weight loss benefits.

Cautionary lessons in this direction exist in the case of rimonabant and the other CB-1 receptor antagonists. The centrally acting weight loss products, now in late stage development, pose a challenge on one side, while the traditional reluctance of physicians regarding weight therapies pose difficulties on the other side. The GLP-1 competitors all recognize glycemic control and weight loss as the key differentiators for establishing themselves as first line therapy and, in the words of one team leader, they are preparing to "ram them through the heart of Januvia® and Onglyza®."

4. Opportunities for new segment development among DOs

Further segmentation challenges exist even within primary care because DOs are emerging as a more potent force in diabetes and obesity, yet these physicians have different treatment approaches than IMs/FPs. Again, the GLP-1 analog competitors well understand that *judicious positioning and segmentation can allow them to develop DOs as an important primary care segment while avoiding antagonizing the traditional MD primaries.* Analyses for exploiting opportunities with DOs are in various stages.

5. How to best position the GLP-1 class against the DPP-IV inhibitors

Januvia® and Onglyza® possess a major advantage over the GLP-1 analogs in terms of a head start. Marketers of the latter believe that while the DPP-IV inhibitor class confers only marginal benefits in terms of glycemic control, Januvia® (sitagliptin, Merck) has achieved blockbuster status on the basis of two basic perceptions. First, whatever glycemic benefits sitagliptin does offer, these persist for extended periods and do not deteriorate in the manner of the sulfonylureas.

Secondly, the DPP-IVs enjoy a consensus perception of safety as they neither burn out beta cells in the manner of sulfonylureas or cause edema and CHF as the TZDs do. In short, the GLP-1 competitors know that the benefits of safety and modest-but-protracted control by DPP-IV inhibitors hold substantial appeal for PCPs.

Messaging and programs to mitigate nausea management

A major reason that sales of Byetta® have not lived up to expectations relates to the high percentage of patients who experience initial and even persistent nausea. Work we have done indicates the nausea incidence and severity appreciably exceed the transient 10% cited on Byetta's label. In particular, the need to manage patient nausea constitutes a major reason PCPs have steered clear of this product. This phenomenon represents an imprinted perception that all follow-on GLP-1's must skillfully manage. Diabetes educators and PCPs represent important targets for this effort.

Linkages to developing modalities can appreciably accelerate the uptake and penetration of GLP-1's

Several approaches in diabetes care, while still numerically small, have been growing rapidly and marketing managers of the GLP-1 competitors believe these can represent major opportunities for success. One such growth area consists of the number of Type 2 diabetics that use insulin pumps. A few years ago, for example, a project put us in touch with a group at the University of Nebraska that was delivering Victoza® (liraglutide/Novo) with insulin pumps in a Phase II study. Nearly all enrollees achieved a < 7% HbA1c as well as a 12% or greater weight loss in the first year.

In another area, the convergence of smart phones and blood glucose monitors offers a range of opportunities. This represents a convergence opportunity for one GLP-1 competitor, Roche/Genentech, given the corporate tie-in to Roche Diagnostics.

GLP-1 marketing managers hold DPP-IVs and SGLT-2s in low regard

Most marketing managers of the GLP-1 competitors perceive Onglyza® as virtually a "branded knockoff" of Januvia® in that the joint venture will not be able to differentiate the newer product. All of them received the fourth-quarter, 2009 data about Onglyza's® modest sales with a sense of blasé understanding, as if to suggest that even mildly healthy sales would have been a shock.

As far as dapa, few of the GLP-1 marketers take any of the SGLT-2 inhibitors seriously. They regard weight loss from that class as extremely modest, glycemic control as no better than that of existing classes, while the UTI/vaginitis side effects pose a "seriously self-limiting" obstacle.

The disdain among GLP-1 competitors for the product attributes of Onglyza® and dapa extends to their assessment of organizational attitudes at the two companies. They believe Bristol-Myers Squibb, especially in the US, is disengaged from market planning for either product while AstraZeneca maintains a "dog with a bone fixation" and a "tunnel vision" that blinds them to the competitive threat from another class.

This lack of regard for Onglyza® and dapa among the GLP-1 competitors represents an opportunity for the joint venture. By understanding the thinking and planning of these competitors relative to positioning, segmentation and messaging, BMS/AZ can develop tactics and programs to thwart their advances.

GLP-1 competitors believe the BMS-AZ joint venture remains especially vulnerable to the GLP-1 analog ascendancy

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