White Paper

TRINITY

How Five Oncology Treatment Paradigms Determine Strategic Choices for Commercial Success

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EXECUTIVE SUMMARY

New targeted oncology treatment regimens are changing cancer treatment and strategic choices for commercialization.

5 treatment paradigms constitute over 90% of sales in oncology.

New targeted oncology treatment regimens have changed cancer treatment. This white paper charts that development and analyzes five different approaches, providing an overview of how these paradigms determine strategic choices for commercial success. We observe that:

- The oncology treatment landscape has five distinct treatment paradigms.
- Competition, routes of administration, and market dynamics differ dramatically for each paradigm.
- The approach to commercialization needs to differ for each paradigm to increase uptake and ensure successful market penetration.

EVOLUTION OF ONCOLOGY TREATMENT

Oncology treatments have evolved to the point that physicians now have a variety of therapies to treat cancer.

For many decades, cytotoxic chemotherapies have been the standard of pharmaceutical cancer treatment despite exposing patients to severe side effects. Targeted therapies represented the first evolution in oncology treatments. They entered the market with the promise of fewer side effects and better outcomes stemming from rational drug design.

The second evolution came with the advent of immuno-oncology agents, which rely on artificial stimulation of the immune system to treat cancer. Uptake of immuno-oncology agents grew with the introduction of checkpoint inhibitors (CTLA-4 in 2011, PD-1/PD-L1 in 2014). The next generation of oncology therapeutics, including gene and cell therapies, have recently become available to treating physicians. Both cell and gene therapies and immuno-oncology therapies support the trend of personalization, treatments that target a patient's specific need and situation. Cell and gene therapies and immuno-oncology therapies are especially critical for patients who would have poor prognoses with previously available treatments.

FIVE ONCOLOGY TREATMENT PARADIGMS

From nascent to mature, five paradigms constitute 90% of sales in oncology.

TRINITY has undertaken more than 100 commercial oncology projects over the last 12 months. Our engagements have been in support of a variety of products, including therapies for solid tumors and hematologic malignancies, supportive care agents, and biomarkers and diagnostics. Based on this experience, we have identified five major oncology treatment paradigms. Each treatment paradigm is distinguished by its scientific and clinical definition (Table 1). The five treatment paradigms constitute 90% of sales in oncology and may be complemented by other therapies, such as antibody-drug conjugates (ADCs), hormonals, and radiopharmaceuticals, as well as reformulated cytotoxins.

Table 1. Five Oncology Treatment Paradigms

Treatment Paradigm	Legacy Tumor Targeting Antibodies	Biomarker-Based Targeted Therapies	Targeted Hematologic Agents	Checkpoint Inhibitors & Combinations	Cell & Gene Therapy
Description	Tumor cells are specifically targeted by tumor targeting antibodies, engineered by living cells to interact with specific molecules on the tumor cells.	Therapies that require precise stratification of patients by biomarkers allow for more targeted treatments. Despite being in their second generation, new biomarker-based targeted therapies are discovered at a fast pace due to increasing data availability.	Hematological malignancies are amenable to distinct treatment approaches when compared to solid tumors, due to their different physiological environment.	Checkpoint inhibitor therapies target cellular immune checkpoints, which tumors use to evade destruction by the immune system. Interference with this pathway stimulates a patient's immune response against the tumor cells.	Transfer of modified cells into a patient (cell therapy) or the introduction, removal or change in genetic material in the cells of a patient or tumor (gene therapy); only two cell therapies are currently approved in oncology, both chimeric antigen receptor T-cells (CAR-Ts).
Class Life Cycle	Mature	2nd Generation	2nd Generation	1st Generation	Nascent
Common Tumors	• Colorectal • Non-small cell lung cancer	• Lung • Breast • Melanoma • Multiple others	• Multiple myeloma • Diffuse large B-cell lymphoma • Chronic lymphocytic leukemia • Chronic myeloid leukemia	• Lung • Melanoma • Bladder • Gastric	• Diffuse large B-cell lymphoma • Acute lymphoblastic leukemia

STRATEGIC CHOICES FOR COMMERCIAL SUCCESS

Understanding approaches to commercialization is key to identifying the most successful strategic choices in each paradigm.

We have mapped the leading oncology therapy manufacturers and their key products to these five treatment paradigms (Table 2) to better understand their approach to commercialization and to help identify the most successful strategic choices in each paradigm.

Table 2. Leading Companies, Key Products, Market Trends, and Late-Stage Pipeline by Treatment Paradigm

Treatment Paradigm	Legacy Tumor Targeting Antibodies	Biomarker-Based Targeted Therapies	Targeted Hematologic Agents	Checkpoint Inhibitors & Combinations	Cell & Gene Therapy
Leading Companies	Roche, Lilly	Roche, Novartis, Pfizer, AstraZeneca	Celgene, Janssen, AbbVie	Roche, Bristol-Myers Squibb Foundation, Merck, AstraZeneca	Novartis, Celgene, Gilead
Key Products (marketed)	Avastin® Rituxan® Erbitux® Cyramza®	Cotellic® Herceptin®[1] Kadcyla® Lynparza® Rozlytrek™ Tagrisso® Tarceva® Vitrakvi®	Darzalex® Imbruvica® Polivy™ [2] Revlimid® Venclexta®	Imfinzi® Keytruda® Opdivo® Tecentriq® Yervoy®	Kymriah® Yescarta®
Worldwide Sales %[3]	27%	19%	23%	24%	0.3%
Trend Growth '17-'18[4]	4.9%	11.3%	19.7%	53.5%	n/a
Number of Phase 3 Trials[5]	8	34	13	18	18

1. Herceptin can also be categorized as a Legacy Tumor Targeting Antibody
2. Polivy can also be categorized as an antibody-drug conjugate (ADC)
3. Market share 2018 and growth 2017-2018 based on worldwide sales of top 10 highest selling oncology drugs (Source: Cowen & Co.)
4. Total top 10 sales = USD 57.3 B (2018), overall growth 16%
5. Phase 3 trials as of Sep 12, 2019 (source: FDA); Other categories not included in this table: radiopharmaceuticals, hormonals, ADCs, reformulated cytotoxics, supportive care

LEGACY TUMOR TARGETING ANTIBODIES

Legacy tumor targeting antibodies face increasing competition from both biosimilars and the launch of newer novel therapies with similar mechanisms of action. New biosimilar competition affects both the price of the referenced product and also the prices of the set of products in that therapy area. The main strategy to remain relevant in this field is traditional marketing approaches to increase share of voice with physicians who now have a range of options. When articulating their benefits to physicians, biopharmaceutical companies can rely on years of entrenched experience and clinical data with tumor targeting antibodies.

BIOMARKER-BASED TARGETED THERAPIES

For solid tumors, we expect further growth of the biomarker-based targeted therapies, as evidenced by the proportion of oncology trials involving biomarkers, up from 25% in 2010 to 39% in 2018. Generally, the success of biomarker-based therapies is highly dependent on precise upfront diagnostics, but the landscape of diagnostics technologies is continuously in development. Next-generation sequencing (NGS) technologies, for example, which allow for the detection of acquired genetic mutations in tumors, are becoming cheaper and more accurate. The broader use of NGS and steady growth of genomic datasets allow for the detection of new biomarkers and for more precise stratification of patients. To address this challenge, biopharmaceutical companies need to re-evaluate their own capabilities in diagnostics and consider partnerships with diagnostics companies. Roche, for example, is partnering with Foundation Medicine and has acquired Flatiron Health to enhance their biomarker diagnostics capabilities.

In addition, combination therapies of checkpoint inhibitors and biomarker-based therapies should be explored to potentially offer high specificity as well as superior efficacy.

TARGETED HEMATOLOGIC AGENTS

Targeted hematologic agents are well-established treatments in a market that used to be less competitive as available therapies were often combined. The common use of combinations facilitated market access for targeted hematologic agents. However, with the introduction of novel therapies, the hematologic agent market is becoming increasingly competitive. Almost one-third (31%) of approved oncology treatments over the past five years have been for hematologic malignancies. Increased competition has meant that collaboration on, or independent development of, specific biomarker tests is one key to maintaining competitiveness. The most critical drivers of success for targeted hematologic agents are the identification of new biomarker-identifiable patient populations and the development of effective combination therapies.

CHECKPOINT INHIBITORS & COMBINATIONS

Companies can seek to increase uptake of their checkpoint inhibitors by differentiating their therapies, demonstrating effectiveness in patient sub-populations and extending into earlier lines of treatment. There is an opportunity for therapies to identify and clearly articulate their efficacy overall and within sub-groups because physicians are

often not clear which checkpoint inhibitors are best suited to which patient sub-group. Checkpoint inhibitors are not currently well differentiated from each other and the sequence of treatment in many cancer types that benefit from use of checkpoint inhibitors is not consistently defined. Therefore, differentiating each checkpoint inhibitor is key to successful uptake.

There are several ways to achieve differentiation and increase uptake in addition to clearly articulating known points of differentiation between checkpoint inhibitors with Key Opinion Leaders (KOLs). Label extensions to identify and articulate new patient sub-groups is a strategy used by Bristol-Myers Squibb's Opdivo®, which has achieved approval for more than 10 indications within patient sub-groups in the first three years after launch. Identifying an efficacious combination can also increase uptake and usage of a checkpoint inhibitor. Furthermore, ensuring that payers and providers consider the checkpoint inhibitor at an early stage when developing treatment guidelines is important, especially in tightly managed treatment environments.

CELL & GENE THERAPIES

Cell and gene therapies (CGTs) require radically different treatment approaches that necessitate new commercial strategies. Launching CGTs represents a new frontier for biopharmaceutical companies accustomed to traditional biopharmaceuticals. The challenges each specific CGT faces will be specific to each therapy. In addition, CGTs require personalization and tailoring of the therapy, therefore treatment delivery is often complex compared to traditional biopharmaceutical products. Many CGTs with curative intent command high prices and often necessitate innovative pricing models for acceptance. CGTs should therefore mimic the commercial models of ultra-orphan therapies to ensure successful commercialization. Given the high cost of a single treatment, developing pricing models, which clearly and transparently determine the value of the therapy, will be key. Payers need to be included in these discussions as early as possible to ensure access at their respective price levels.

Concerns about safety of CGTs, such as CAR-T therapy, mainly arise from a set of previously uncommon and severe adverse events, most notably cytokine release syndrome. Physicians without easy access to CAR-T therapies show a substantial educational gap, which may prevent them from using CAR-T therapies. Therefore, physician education and ongoing patient tracking are crucial elements of a successful marketing strategy.

Given the complexity of shipping cryogenically frozen cells across borders, companies launching CGTs also need to be confident in their supply chain up until administration to the patient. They need to have fully mapped out a holistic set of stakeholders and influencers involved in the delivery of the therapy to patients.

One observation about biopharmaceuticals in general, and particularly relevant for CGTs, is that the more specialized and advanced a treatment, the more challenges companies face in commercialization.

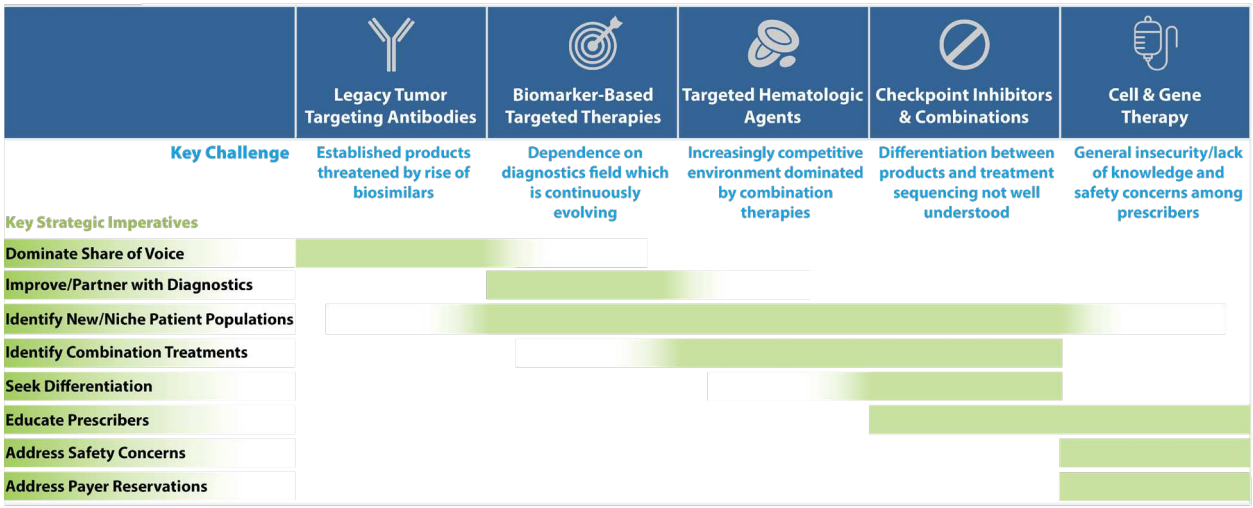
CONCLUSION

Five treatment paradigms for commercial decision-making.

This white paper introduces five treatment paradigms in oncology and suggests appropriate commercial strategies for success. While TRINITY believes each therapy should be treated individually, the five treatment paradigms serve as a powerful foundation for effective strategic decision-making (Figure 1).

Mature therapies, such as legacy tumor targeting antibodies, should aim to increase share of voice relying on entrenched experience and clinical data. Second-generation therapies should consider diagnostics, combinations, and the identification of new biomarker-identifiable patient populations. First-generation therapies, such as checkpoint inhibitors, should seek differentiation by demonstrating effectiveness in patient sub-populations and extending into earlier lines of treatment. Last of all, as a nascent technology, CGTs can benefit from mimicking the commercial models of ultra-orphan therapies to promote successful commercialization and ensure that potential barriers, such as supply chain problems and payer reservations, are cleared.

Figure 1. Strategic Imperatives for Commercialization by Treatment Paradigm



AUTHORS

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Alex has supported biopharmaceutical companies with commercialization challenges for over ten years. A trusted adviser of his clients known for his ability to bring clear, actionable solutions to complex questions, Alex has years of experience bringing the right mix of evidence to advise clients with issues ranging from New Product Planning, pre-launch Commercialization, and Business Development strategy. Now the head of TRINITY's New York City Office and one of the leaders of the firm's oncology practice, Alex started at TRINITY out of college as an associate. Alex holds a BA from Princeton University and an MBA from Columbia University.

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Christian has over five years of consulting experience supported by a strong scientific and medical background. He has consulting experience in several therapeutic areas with a special focus on oncology and has worked with clients in bringing to market CGTs and targeted cancer therapies in Europe and the US. Before joining TRINITY, Christian worked at the Boston Consulting Group and Syneos Health in Munich. Christian holds a PhD in Molecular Biology and a master's degree in Physics from ETH Zurich. He conducted fundamental oncology research as a Research Associate at Harvard Medical School.

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Alexander brings more than 20 years of experience in strategy consulting to TRINITY and over that time he has advised more than 70 clients in over 300 strategic assignments covering all continents and more than 40 countries. He advises life sciences executives and investors on complex issues that require strong content expertise and analytical rigor paired with a deep understanding of what it takes for success in the life sciences industry. Alexander lives in Munich and works globally with his clients, after having spent extended periods of time in New York, Johannesburg and Jakarta. Before joining TRINITY, Alexander worked in Principal and Partner positions with companies such as Monitor Group, Roland Berger and Syneos Health. Alexander has also studied business administration in Germany, the UK, and the US.

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Herman has been working in the life sciences industry for over 20 years in various positions, including designing and running randomized trial research, optimizing of clinical administration of health services, and working as a strategic consultant to the life sciences industry. He joined TRINITY over a decade ago and has worked closely with clients to support strategic decision-making across the product lifecycle. As a leader at TRINITY, he has worked to build TRINITY's European office and helps to run and build the company's centers of excellence in Market Access, Launch, and Health Economics and Outcomes Research (HEOR). Herman earned an MBA from the Tuck School of Business at Dartmouth and an AB from Harvard University.

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About TRINITY

TRINITY is a trusted strategic partner, providing evidence-based solutions for the life sciences. With over 20 years of experience, TRINITY is committed to solving clients' most challenging problems through exceptional levels of service, powerful tools, and data-driven insights. TRINITY's range of products and solutions includes industry-leading benchmarking solutions, powered by TGaS® Advisors. TRINITY, together with its subsidiary TGaS Advisors, has 5 offices throughout the US, including Boston, New York, Princeton, Philadelphia, and San Francisco, as well as Toronto, Canada, Gurgaon, India and Munich, Germany. To learn more about how TRINITY is elevating life sciences and driving from evidence to action, visit trinitylifesciences.com.

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