Ten Trends Transforming the Business of Oncology

By Jeff Stewart and Nader Naeymi-Rad

Today, drug manufacturers are finding themselves in very different waters from those of a decade ago, and many companies are ill prepared to weather the "perfect storm" brewing in oncology. Manufacturers' highly redundant oncology pipelines have created intense competition, and at the very time when oncology developers need most to differentiate their products in the marketplace, traditional commercialization tools, such as access to therapy decision makers, are being swept away.

To gain insight into the commercial changes such as these occurring in the industry, Campbell Alliance initiated the Oncology National Commercial (ONC) study where 75 key industry experts, physicians, payers, and opinion leaders were surveyed. The study revealed an alarming pattern that told us that the oncology space is transforming in such a way that never-before-seen competition is now built into the "DNA" of the business of oncology, and few companies are prepared to operate in the face of this intense competition.

These findings were confirmed by examining manufacturers' oncology pipelines and commercialization efforts and 10 specific transformative trends, of which every oncology product marketer and developer should be made aware, were revealed. These results can be broken down into the following aspects.

Trend 1: Large pharma has dramatically expanded its oncology pipeline.

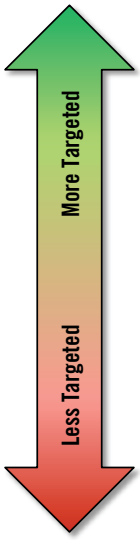
Large pharma has developed and bought its way into oncology to the point where two and a half times as many compounds were in clinical trials in 2010 as were in the large pharma pipeline of 2000. Furthermore, the pipeline includes many more early-stage agents in this time period than before.[1]

All the largest pharmaceutical companies that publish areas of in-licensing interest actively requested additional oncology products for their pipelines in 2010.[2] Hence, the trend toward more robust oncology pipelines is likely to continue.

Bottom-line effect: Competition is sharply greater, based on gross numbers.

Trend 2: The oncology pipeline has become increasingly targeted.

Oncology pipelines are shifting away from therapeutics such as cytotoxic agents and broad



Mechanism of Action	Pipeline Share, 2000	Pipeline Share, 2010	Multiple	Trend
Cell surface receptor (e.g., ADCC)	4.4%	7.5%	1.7X	↑
DNA repair	3.5%	3.1%	0.9X	-
Growth factor/GFR	9.7%	17.3%	1.8X	↑ ↑
Angiogenesis	5.3%	18.4%	3.5X	↑ ↑ ↑
Proliferation (typically kinases)	5.3%	20.8%	2.9X	↑ ↑ ↑
Apoptosis	2.7%	4.7%	1.7X	↑
Other MOA	9.7%	2.0%	0.2X	↓ ↓
Matrix metalloproteinase	1.8%	-	0.0X	↓
Immune modulator	7.1%	5.9%	0.8X	↓
Hormone	10.6%	4.3%	0.4X	↓ ↓
Cell cycle (typically cytotoxics)	39.8%	16.1%	0.4X	↓ ↓ ↓

Figure 1. Oncology therapies are increasingly targeted. Source: Campbell Alliance Analysis

cell-cycle inhibitors that treat cancer with little specificity. The agents filling the 2010 pipeline are much more targeted than the agents filling the 2000 pipeline (Figure 1).[3] This shift is even more dramatic when considering novel agents (as opposed to line extensions). Targeted therapeutics have obvious benefits—increased efficacy and potentially lower side effects. However, an unintended consequence of exquisite targeting is exquisite competition.

Bottom-line effect: There is now great overlap in mechanisms of action and molecular targets among the large-pharma oncology pipeline.

Trend 3: Multiple oncology therapies target the same molecular pathways.

In 2000, oncology agents in clinical trials arose from "fishing expedition" screening efforts that yielded a generally diverse set of targets and mechanisms of action. Large pharmaceutical companies in 2000 could expect some—but far from intense—direct competition. This situation did not outlast the decade.

In 2010, large pharma oncology pipelines were driven by new understanding of molecular pathways. Agents became increasingly engineered to their targets. If we focus on the top 10 targets (Figure 2), outside of the top 5, all of the other targets had only one or two agents targeted to them in the pipeline in 2000. Compare this with 2010, where many more agents targeted the same pathways (and more specifically, particular kinases within these pathways).

Bottom-line effect: The same scientific transparency has led to intense competition.

Trend 4: Multiple agents are now tested against even rare tumors.

In 2000, 63% of new compounds in late-stage clinical trials were tested on one or more of the "big five" solid tumors (breast, colorectal, gastric, lung, and prostate). By 2010, this share had dropped below 50% (Figure 3). The story is one of market competition and a scattering to supposed safe havens of ever smaller patient populations. Unfortunately, these "safe havens" were not as safe as hoped because multiple companies had the same safe havens in mind.

Bottom-line effect: The pipeline for niche indications has become increasingly crowded and may represent even more competition per patient than seen in tumors that affect larger patient populations.

Trend 5: Biomarkers are fragmenting the oncology market.

Biomarkers, on one hand, allow for increased efficacy and smaller clinical trials. On the other hand, biomarkers necessarily narrow the market and funnel compounds with similar mechanisms of action to the same biomarker-defined patients. Key opinion leaders believe that biomarkers are necessarily the wave of the future and will further fragment the market by defining ever smaller patient populations, but may provide fewer payoffs than expected.

Bottom-line effect: By defining even smaller patient populations, biomarkers may limit payoffs.

Top 10, 2000		Top 10, 2010		
Target/Pathway	Compounds in Trials	Compounds in Trials	Target/Pathway	Reason(s) for Interest
Microtubules	11	20	VEGF	▪ Proven target (Avastin) ▪ Multiple tumor types
Topoisomerase	8	18	PI3K/AKT/mTOR	▪ Multiple tumor types
EGFR	8	15	MAP/Erk	▪ Multiple tumor types
VEGF	4	14	EGFR	▪ Proven target (Erbitux, Iressa, and Tarceva) ▪ Multiple tumor types
p53	3	10	Microtubules	▪ Proven target (low risk to develop)
Endothelin	2	10	c-Met/HGFR	▪ Multiple tumor types
MMPI	2	9	Topoisomerase	▪ Proven target (low risk to develop)
Thymidylate Synthetase	2	9	IGF	▪ Overexpressed in wide range of tumors ▪ Overexpression associated with progression
PKC	2	7	PARP	▪ Highly specific target (few side effects) ▪ Widely reported efficacy in early trial (olaparib)
HER2	2	6	Aurora	▪ Overexpressed in a variety of cancers ▪ New mitosis target

Figure 2. Many more agents are targeting the same pathways. Source: Campbell Alliance Analysis

Trend 6: Oncology has become a blockbuster machine.

Oncology is among the fastest-growing therapeutic areas in terms of branded therapeutic revenue. Entering 2010, oncology blockbusters had become much more valuable than they were in 2000. In 2000, only two oncology drugs had more than $1 billion in revenue. In 2010, all of the top 10 oncology drugs exceeded $1 billion in sales (Figure 4).[4,5] This revenue growth has come in the face of decreasing incidence for most cancers in the US.[6] Instead, the revenue growth has come largely through the increasing price of new oncology drugs.[7] Another factor leading to increasing revenue in the oncology space is earlier diagnosis that allows for longer duration of therapy.[8] A third factor is the now-common use of combination therapies in the first line[9] (and each of the constituents of combination therapy costs more in 2010 than in 2000).

Bottom-line effect: There is good news in that an oncology blockbuster is now a blockbuster.

Trend 7: Oncology is saturated with sales representatives.

In the past decade, the growth in oncology sales representatives was 6.9% annually, far outstripping the 3.3% growth in oncologists.[10] This growth has outpaced the growth of oncologists in the US to the point where there are three reps for every 10 oncologists. This increase in sales reps per oncologist limits access by competition. In addition, the survey respondents confirmed that access is increasingly limited, such that about half the time, sales reps are unable to see the oncologist. This limited access suggests that the industry may be over-invested in sales representatives targeting high-prescribing oncologists.

In order to earn a share of ever-limited oncologist access, manufacturers must provide additional perceived value to oncologists. Of the service provided by oncologist-facing resources, "new information" is perceived to be the most valuable. However, because sales reps cannot provide the full range of medical information, the Medical Affairs function is becoming an increasingly important oncologist-facing resource.

Bottom-line effect: Industry leaders expect that oncology sales forces will net increase, and this may imply that access will become even more competitive.

Trend 8: Oncologists are no longer the sole decision makers.

Oncologists began the decade making essentially all the decisions in oncology patient care. Now a host of stakeholders influence oncology therapy choice. The federal government has already begun exerting its new influence over oncology treatments.[11] State governments are increasingly exerting access influence by mandating coverage and mandating IV/oral cost equivalence.[12] Payers are also shifting costs to patients, who are increasingly exposed to high co-pays or coinsurance. When monthly out-of-pocket expenses rise above $500, more than a quarter of patients do not remain adherent to oral oncology therapeutics.[13] A fundamental influence shift has begun.

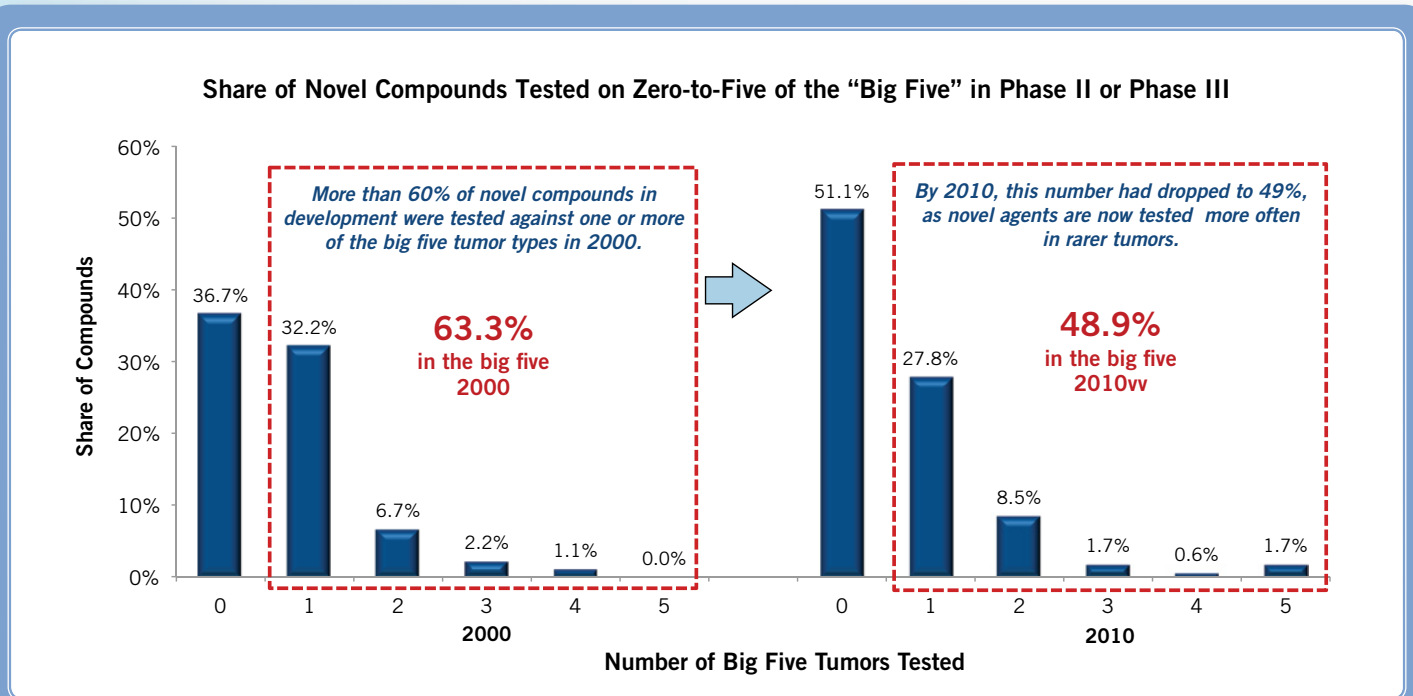


Figure 3. Fewer than half of new agents are currently being tested in the "big five." Source: Campbell Alliance Analysis

Bottom-line effect: As non-oncologists exert ever-greater influence over oncology therapy choice, successful oncology companies will redeploy customer-facing resources to address the needs of these newly important customers.

Trend 9: Payers are beginning to manage oncology.

In 2000, oncology remained an area with few price controls. The typical flow of injectable oncology drugs was via buy-and-bill, where oncologists purchased oncology products from wholesalers and received payment (including substantial markups) from health plans and Medicare Administrative Carriers. By the mid-2000s, oncology practices were able to increase margins by using group purchasing organizations (GPOs) to negotiate more favorable discounts and rebates from manufacturers. Oncologists joined GPOs to have access to decreased product acquisition costs and effectively increase profits. These profits did not pass unnoticed. By 2010, both Medicare and many traditional healthcare plans had responded by changing the reimbursement methodology to average selling price (ASP), which is net of all rebates and discounts. ASP has removed much of the profit potential from buy-and-bill.

According to the industry leaders interviewed, the downstream effects of lower oncologist profitability are just beginning to be felt.

Payers are also controlling access to oncology therapeutics explicitly. Typically, payers seek to control costs by requiring an FDA indication, prior therapy failure, appropriate dosage, appropriate therapy intervals, or compendia listing.[14] Prior authorizations are required for up to 65% of covered lives for the most expensive oncology monoclonal antibodies. Additionally, the least politically sensitive way for payers to control costs for oncology products may be use of clinical pathways to define treatment options available for the oncologist.[15]

Bottom-line effect: According to the industry leaders interviewed, the downstream effects of lower oncologist profitability are just beginning to be felt. Oncologists are shifting unprofitable patients to hospitals. Oncologists themselves are migrating from independent practices to large institutions with financial incentives less aligned with high prescribing. Eroding profit margins are leading to a decreasing direct financial interest of oncologists in therapy choice. Therapy choice may be driven more by "reimbursement confidence" than by access, and decreasing financial incentives may lead to lower prescription rates for expensive therapies.

Entering 2010, oncology blockbusters had become much more valuable than they were in 2000. In 2000, only two oncology drugs had more than $1 billion in revenue. In 2010, all 10 of the top 10 exceeded $1 billion in sales.

2000 (Top 10 Worldwide)		
Blockbuster	Target/Path/MOA	Revenue ($M)
Taxol	Microtubules	1,592
Intron A, Peg-Intron, Rebetol	Immune modulation	1,360
Lupron/Leuplin	GnRH	952
Zoladex	GnRH	734
Paraplatin	DNA disruption	690
Taxotere	Microtubules	687
Nolvadex	Estrogen receptor	576
Gemzar	Nucleoside analog	562
Rituxan/MabThera	CD20	444
Camptosar	Topoisomerase	441
	Total	8,038

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2010 (Top 10 Worldwide)		
Revenue ($M)	Target/Path/MOA	Blockbuster
5,729	VEGF	Avastin
5,605	CD20	Rituxan/MabThera
4,849	HER2	Herceptin
3,944	BCR-ABL	Gleevec
3,034	Microtubules	Taxotere
2,147	GnRH	Lupron/Leuplin
1,921	Aromatase	Arimidex
1,706	Immune modulation	Revlimid
1,706	Folate antimetabolism	Alimta
1,654	EGFR	Erbitux
32,295	Total	

Figure 4. Oncology has become a blockbuster machine. Source: Campbell Alliance Analysis

Trend 10: The combination of commercial and clinical factors may lead to a bursting oncology asset bubble.

Oncology had been a hot area for licensing through the 2000 to 2009 period. In-licensed compounds were evaluated and purchased based on historic trends. Unfortunately for those valuing oncology assets, historic trends have not continued. Many of the key inputs to valuation models appear to be eroding sharply. For example, more intense competition than anticipated should lead to lower market shares than predicted. Trials are more difficult to recruit because of competition for patients, and trials are longer when overall survival, rather than progression-free survival, is the endpoint. Longer trial times lead to less time on the market before loss of exclusivity. Comparator arms now may include extremely expensive biologics.

When we consider the number of phase II and phase III assets in each therapeutic category to the number of deals made in that category, we may estimate the "inventory" of each therapeutic area. Oncology has more than 20 years' inventory to work through.[16]

Bottom-line effect: When a supply glut is combined with eroding valuation fundamentals, a price collapse may be in the works.

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Xalkori®, Pfizer's newly approved NSCLC drug targeted to about 7% of patients harboring a specific gene mutation, will cost $9,600 a month, or about $115K for patients who are on it for a year. *(Forbes, 8/26/11)*

The FDA has granted fast track designation to Bayer's Alpharadin™ (radium-223 chloride), for the treatment of castration-resistant prostate cancer in patients with bone metastases. *(Dow Jones Newswires, 8/23/11)*

Notes and Sources

1. Cowen Therapeutic Categories Outlook 2000 and 2010; Company annual reports; National Cancer Institute; clinicaltrials.gov; Campbell Analysis.
2. Company websites. Accessed January 2010. Note that some large pharma companies (GSK and JNJ, for example) do not publish areas of partnering interest.
3. Note: Includes solid tumors and hematologic tumors; excludes supportive care.
4. Humpreys A and Scussa F. Med Ad News 500: Year of the Megabrand. May 2001. http://www.pharmalive.com/magazines/archive/medadnews/May_2001/Megabrand.cfm.
5. Humpreys A. 20th annual report. Top 200: World's best selling medicines. July 2010. http://www.pharmalive.com/magazines/medad/view.cfm?articleID=9463. www.pharedAdNews. Available at Medadnews.com. Accessed 6 September 2010. Note that supportive care agents are not shown here.
6. SEER. United States Cancer Statistics. http://seer.cancer.gov/. Accessed 27 January 2011.
7. Adapted from Bach PB. Limits on Medicare's ability to control rising spending on cancer Drugs. N Engl J Med. 2009; 306: 626-633.
8. SEER. United States Cancer Statistics. http://seer.cancer.gov/. Accessed 27 January 2011.
9. NCCN Guidelines. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. Accessed 27 January 2011.
10. SDI Health LLC. Used with permission.
11. Bach, 626-33.
12. Note: A number of states include "medical necessity" as an additional standard for coverage beyond the compendia or medical-literature standards, including AL, AZ, AR, CA, FL, IL, LA, ME, MD, MA, MN, NE, NV, NJ, OH, OK, OR, RI, SD, TN, VT, and VA.
13. Patient out-of-pocket cost affects adherence to oral oncology medications. American Health & Drug Benefits. 2010; 3:217.
14. 14ICORE Healthcare. Medical Injectables and Oncology Trend Report. 2009.
15. Licking EF. What new cancer pathway programs means for the drug industry. In Vivo. 2011; 29:34-42.
16. Bonifant B and Fendelman J. Targeted Optimism: Campbell Alliance's 2010 Dealmakers' Intentions Survey. Available at http://www.campbellalliance.com/services/getfile.cfm?id=172.

Key Points

- These 10 trends transforming the oncology marketplace begin with structural changes in the oncology pipeline that lead directly to intense competition. At the same time, changes in underlying oncology economics have prompted an ongoing change in the most effective oncology commercialization strategies.
- Competition is precisely the environment where companies need to be able to differentiate. However, at this same moment, customers and their needs are changing. This means outdated strategies are poorly matched to today's commercial realities.
- We are at an inflection point. Going forward, successful oncology companies will recognize the new reality and organize their portfolios, launch planning, and customer-facing resources to meet this new reality head on. IS NNR

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Jeff Stewart was the first to publish the rNPV methodology that is now the most-used valuation method in the industry. He has been working in pharmaceutical valuation for the past 11 years, the last three with Campbell Alliance.

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