

## Article

# Strategy First, Execution Second: Why Life Science Entrepreneurs Should Adopt a Top-Down Mindset Early

Echoe M. Bouta

is Senior Analyst at Outcome Capital

Oded Ben-Joseph

is Managing Director at Outcome Capital

## ABSTRACT

Despite the dedication of the management team and board to a company's success, an often overlooked component is the dynamics of the segment in which the company operates. In an effort to demonstrate the importance of the external view and how segment dynamics are likely to significantly impact the reality of companies, we analyzed recent data between 2015 and 2017 pertaining to financing events, M&A transactions and initial public offerings (IPOs) in three separate sectors: therapeutic devices, oncology therapeutics and antibiotics. The analysis presented will provide management with a valuable estimation of the required capital to achieve value-inflection milestones as well as the anticipated return on investment upon a liquidity event. These examples demonstrate the fundamentally different dynamics of these sectors, which will impact the path to liquidity as well as the probability to closing an exit transaction. For example, we found that therapeutic device companies have to be at or close to regulatory approval prior to an exit. In contrast, the oncology therapeutics segment supports healthy exits across all stages of clinical development. Despite the high unmet need for novel antibiotics, both financing and exits have been limited in this sector. Return on investment is greater upon an M&A transaction versus an IPO. The presented data demonstrates that exit opportunities and return on capital are largely sector-dependent. Thus, savvy management should adopt an external, market-driven evaluation and analysis rather than inward-looking and uniformed biased judgment. Crafting a mature, market-aligned strategy will increase the probability of success.

Journal of Commercial Biotechnology (2018) 24(2), 46–53. doi: 10.5912/jcb848

Keywords: M&A; IPO; finance; sector

## INTRODUCTION

EVALUATING THE PROSPECTS of a life science company achieving liquidity and shareholder return is a highly complex endeavor hinging on multiple factors such as the strength of the science, the financibility of the value proposition, the size of the market, and the capability of the managing team. A dominant component, often grossly overlooked by management and Board, is the dynamics of the segment in which the company operates. As previously described<sup>1</sup>, it is segment

dynamics that often dictates the reality of a company and its path to success or failure.

Executives seldom adopt an objective and a statistical mindset when considering their specific sector dynamics and instead rely on incomplete and limited information. They focus on the specific circumstances of their company and personal past experiences and draw vague plans resulting in an uneducated financing strategy, predictions about valuations, future acquisition price or various other terms. More often than not, management is oblivious to the odds they face and fail to consider the enormous impact of the dynamics of their segment<sup>2</sup>. Decision-makers are thus likely to commit a planning fallacy, where they will be unrealistically close to best-case scenarios and unlikely to remedy their predictions by simply consulting the statistics of similar cases. However, if appropriate benchmarks are chosen,

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Correspondence:

Oded Ben-Joseph, Outcome Capital, US. Email: oben-joseph@outcomecapital.com

the external view is likely to provide a fairly accurate indication on a realistic approximate value for a transaction and likelihood for success.

The base rate is a prediction based on prior data and probabilities, absent of information specific to a particular situation. With regard to financing or merger and acquisition (M&A) transactions, the base rate is the likelihood that a transaction will close without considering the perceived probability of the specific transaction in mind. Unfortunately, base rate neglect is rampant and statistical facts rarely come into consideration. Instead, management tends to make big decisions based on little or no information and leap from little information to big conclusions. In our experience, management will almost always neglect to take the base rate into account and, consequently, decisions-making is unnecessarily exposed to additional risk to closing. It is this base rate that could provide executives and entrepreneurs with an early indication as to their probability of success and should thus be central to their developing strategy.

In an effort to demonstrate the importance of the external view and how segment dynamics are likely to significantly impact the reality of companies, we analyzed recent data in the three-year period between 2015 and 2017 pertaining to financing events, M&A transactions and initial public offerings (IPOs) in three separate sectors: oncology therapeutics, antibiotics and therapeutic devices.

## METHODS

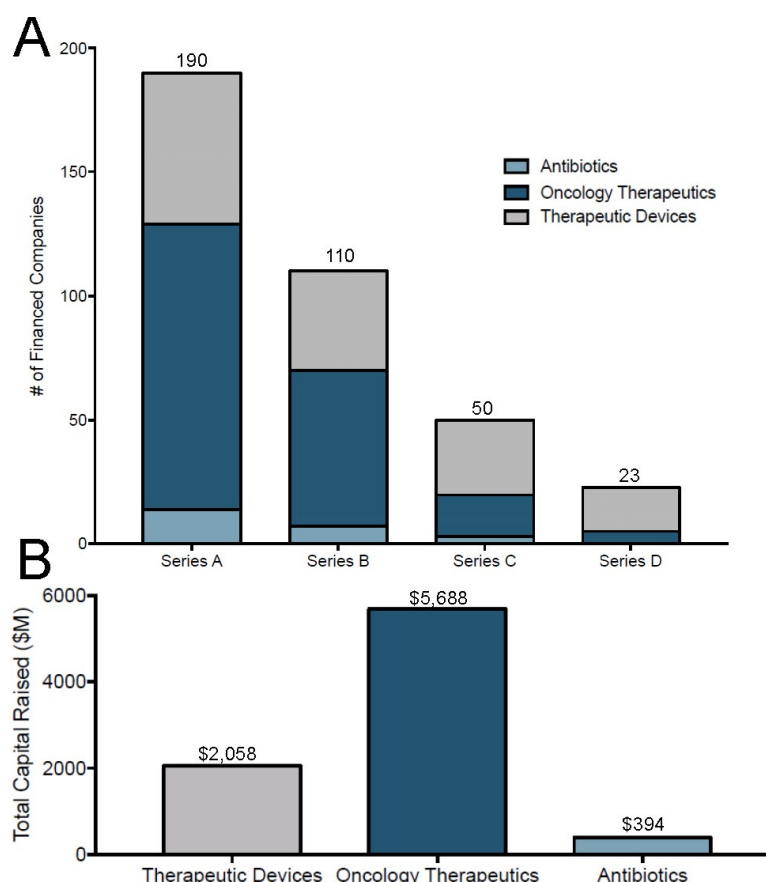
Data was collected from Pitchbook from 01/01/2015-12/20/2017. Oncology therapeutics companies were found by searching for “oncology” and “cancer”. All companies falling within the therapeutic devices sector were screened. Antibiotic companies were found by searching for “antibiotic” and “anti-infective”. In all cases, company descriptions were screened to determine if companies fit the desired sector. Financing encompassed Series A through D. Phase of development was found from ClinicalTrials.gov and company press releases. Outliers were removed via the ROUT method with Q of 1%. Some details on transactions were not always available. Capital to exit and deal size were not always available for all companies, resulting in some exits not included in Figure 5. In particular, smaller M&A deal sizes are not required to be disclosed to shareholders of public companies, resulting in the possible skewing of data to show an average higher deal value. This is particularly a concern in the therapeutic device sector. Exit values are considered the total deal value for M&As. For IPO exit values, market

capitalization at 6 month post-IPO was used as this represents the typical lock-up period for investors holding stock post IPO.

## RESULTS AND DISCUSSION

The amount of capital required to meet value-inflection milestones, investor appetite and likely path to liquidity is largely sector-dependent. The number of funded companies and total capital raise across three sectors is shown in Figure 1. As expected, the number of companies financed decrease based on series; there are far more early-stage Series A financing compared to Series D (Fig. 1A). This is partially due to exits (M&As and IPOs) and failures, given the diminishing probability of success along the product development cycle. The oncology therapeutics segment dominated in terms of number of companies financed and total capital raised, with almost \$6 billion compared to \$2 billion for therapeutics devices and a meager \$400 million for antibiotics (Fig. 1A and B). Two hundred oncology companies received capital versus 149 therapeutic device companies and only 24 antibiotics companies (Table 1). The large market size and recent advancement of immuno-oncology appear to be enticing investors to participate in the long-term promise of the segment. Interestingly, although the antibiotics segment is expected to reach \$57 billion by 2024<sup>3</sup>, relatively little capital is deployed in this space. Difficulty in getting clinical approval and obtaining commercial traction due to the large number of generic options is likely cautioning investors<sup>4</sup>.

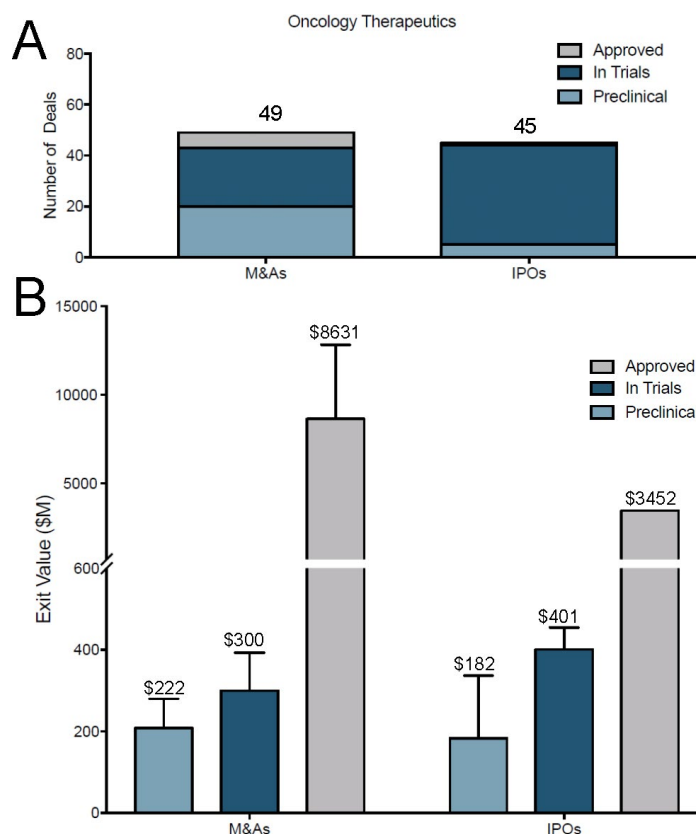
Exit opportunities, comprising of M&As and IPOs, for the three sectors are shown in Figures 2, 3 and 4. It is clear that the oncology segment is highly acquisitive with a high risk tolerance as M&A transactions occurring at all stages, from pre-clinical through FDA approval (Fig. 2A). Acquirers are willing to pay top dollar for oncology assets (Fig. 2B). While there was a significant number of oncology IPOs, most occurred while the most advanced asset was in clinical trials, with very few pre-clinical or FDA-approved assets. Larger exits were observed the further the most advanced asset was in development as acquirers are willing to pay more for de-risked assets (Fig. 2B). It should be noted that there is a large amount of redundancy in the oncology sector as companies contend to develop multiple drugs for similar targets; for example, more than 20 antibodies are currently in development for PD-1 or PD-L1 alone<sup>5</sup> and ClinicalTrials.gov is reporting over 500 combination oncology clinical trials currently active or enrolling. This redundancy will likely result in numerous failures in the coming years as lead products outcompete others. In addition, patient recruitment is becoming a rate limiting factor for these



**Figure 1:** Oncology therapeutics sector dominates in number of financed companies and capital raised compared to the therapeutic devices and antibiotic sectors. Number of funded companies is shown, excluding seed, angel and late series (post-Series D) (A). The total amount of capital raised for each sector is shown (B). Data from 01/15-12/17 collected from Pitchbook.

**Table 1:** Summary of US financing and exit events 2015-2017. Numbers represented as mean  $\pm$  SEM across all phases of development

	Therapeutic Devices	Oncology Therapeutics	Antibiotics
Number of Financed Companies	149	200	24
Total Capital Raised per Sector (\$M)	\$2,058	\$5,688	\$394
Number of M&As	64	49	12
Capital Invested to M&A (\$M)	\$60 $\pm$ 8	\$82 $\pm$ 15	\$182 $\pm$ 89
Time to M&A (years)	13 $\pm$ 1	9 $\pm$ 1	13 $\pm$ 3
M&A Deal Size (\$M)	\$140 $\pm$ 23	\$1443 $\pm$ 743	\$205 $\pm$ 110
M&A Return on Investment Multiple	8 $\pm$ 4	12 $\pm$ 3	2 $\pm$ 1
Number of IPOs	23	45	5
Capital Invested to IPO (\$M)	\$94 $\pm$ 19	\$101 $\pm$ 10	\$93 $\pm$ 12
Time to IPO (years)	13 $\pm$ 2	10 $\pm$ 1	10 $\pm$ 3
Market Cap at 6 months post-IPO (\$M)	\$133 $\pm$ 33	\$473 $\pm$ 106	\$152 $\pm$ 22
IPO Return on Investment Multiple	3 $\pm$ 1	4 $\pm$ 1	2 $\pm$ 1



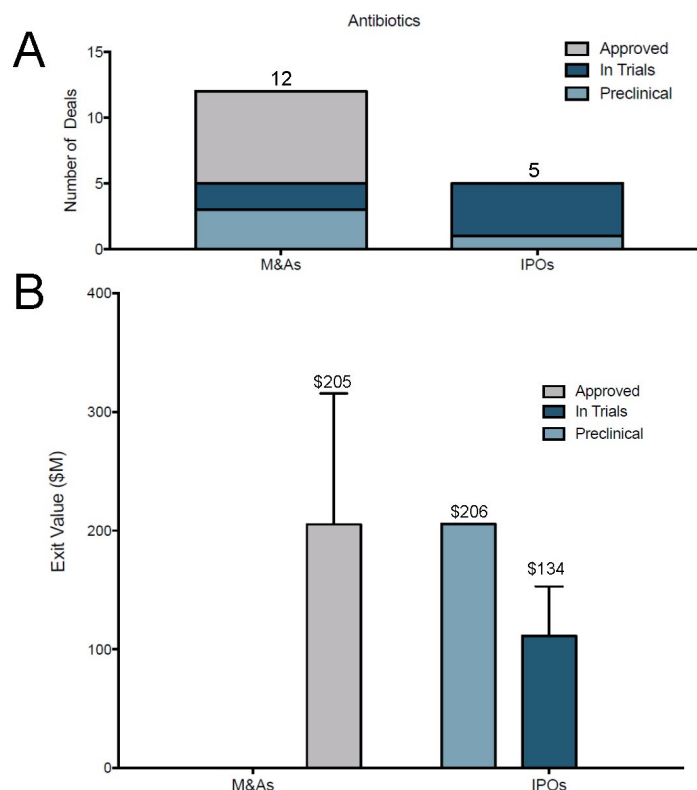
**Figure 2:** Exit opportunities for the oncology therapeutics sector happen early and often. Number of M&As and IPOs for the oncology therapeutics sector is shown (A). Total M&A deal value and market cap at 6 months post-IPO are shown (B). Note the large number of exits and large deal size, even when the assets are early stage. Data from 01/15-12/17 collected from Pitchbook. Error bars represent SEM.

companies. Therefore, while there is a vast amount of opportunity, the segment is heavily crowded suggesting that management teams should focus on clearly differentiated assets.

In sharp contrast, the antibiotics sector shows little exit opportunity with few M&As or IPOs (Fig. 3). This is due, in part, to a lack of appetite resulting from modest revenues from recently approved antibiotics<sup>4</sup> as well as unfavorable returns to private and public investors (Table 1). Of the limited exits, the majority occurred when the lead candidate was in Phase 3 trials or already approved. This indicates that raising both private and public capital for antibiotic assets is likely to be a challenge and that those companies will experienced heightened risk of undercapitalization. It will thus be wise for management teams in the antibiotics sector to focus on large funds with ample “dry powder” to support the company over the long haul, all the way to approval. Also, early partnerships with strategic players is much needed in this segment to curtail development risk. Indeed, there have been several partnership transactions recently,

most notably the \$387 million partnership of Roche with WarpDrive Bio to identify new antibiotic targets.

The therapeutic device sector exhibits distinctly different dynamics. While the sector supported healthy M&A activity and IPO opportunities, exits values are substantially lower than oncology or antibiotics (Fig. 4 and Table 1). Transactions typically took place at a late stage of product development where devices were approved (Fig. 4A). Furthermore, 50% of the companies reported revenues at the time of acquisition. There was no statistical difference between M&A deal value between products in trials or approved (Fig. 4B). In addition, it should be noted that those “in trials” had approval imminent (i.e. finishing clinical trials or approval application filed) and the vast majority were cardiovascular therapeutic devices, indicating that this sub-sector allows for slightly earlier and large deal values. The lower valuations of device companies is understandable given the lower capital requirements to bring a device to market compared to a drug. On average, 510(k) and PMA device approval cost \$31 million and \$94 million<sup>7</sup>, respectively, versus a new drug, where cost is typically in excess of



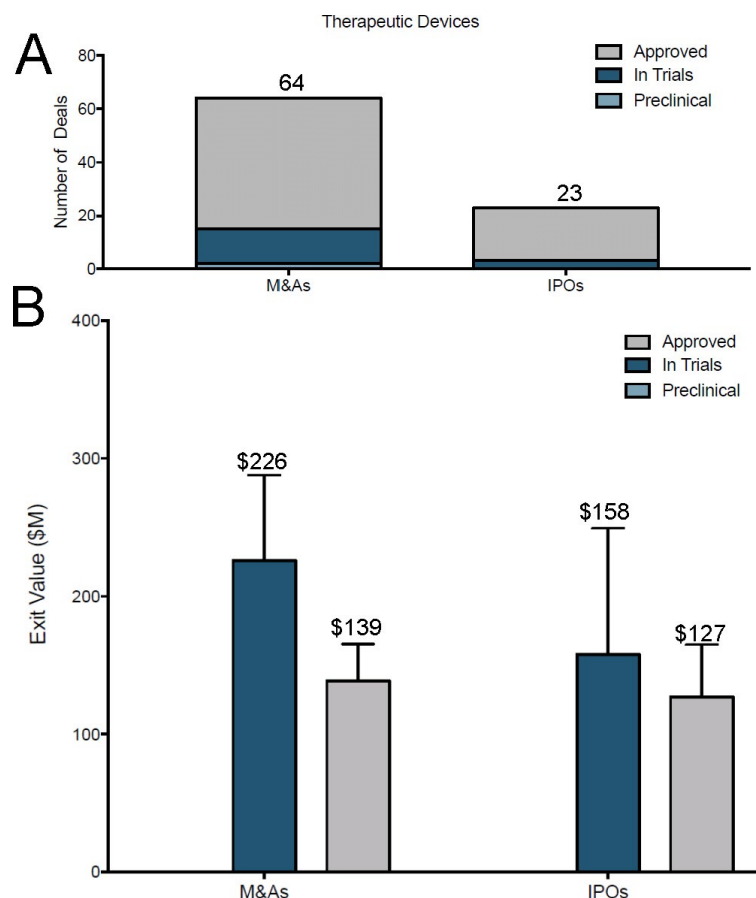
**Figure 3:** Exit opportunities for the antibiotic sector are limited. Number of M&As and IPOs for the antibiotic sector is shown (A). Total M&A deal value and market cap at 6 months post-IPO are shown (B). Note the limited number of exits and when they did occur, it was usually when the company had an asset approved. Data from 01/15-12/17 collected from Pitchbook. Error bars represent SEM.

\$1 billion<sup>6</sup>. Therefore, the reduced capital requirement to achieve return in therapeutic devices, compared to traditional pharmaceutical therapeutics, is reflected in acquisition prices.

Return on investment at various stages of development across the three sectors is illustrated in Figure 5. While oncology therapeutic is a capital-intensive sector requiring large amounts of capital to propel assets through clinical trials, the M&A transaction size supports healthy returns on investment with correlation between invested capital and clinical development and consequently investor appetite (Table 1). Moreover, the oncology sector supports healthy returns at all stage of development as even early pre-clinical assets are attractive to buyers, and represents the best average return on investment. This point is of particular importance to management as it suggests a favorable probability of a successful capital raise (with lower undercapitalization risk) as well as multiple opportunities for a liquidity event across the development path. In contrast, both the antibiotics and therapeutic devices sectors did not support exits of pre-clinical and early clinical assets with most M&A transaction occurring at late clinical development or post-approval (Fig. 3A and 4A). In addition,

the average time to exit is shorter in oncology compared to therapeutic devices and antibiotics, providing further incentives to investors (Table 1). Unlike oncology, the antibiotics sector did not demonstrate that return on investment is proportional the amount of capital raised. However, it should be noted that given the relatively few M&As in antibiotics, it is difficult to draw conclusions on potential for return on investment but it is anticipated that returns in this sector are unlikely to be favorable.

Contrary to common belief by many CEOs and Board members, the public market does not seem to provide attractive return on capital for investors in these sectors. While the public market certainly provides an avenue for raising capital as well as liquidity for investors, the M&A route is more attractive as indicated by valuations at exit (Figs. 2B, 3B, 4B) as well as M&A multiples (Table 1). This observation especially holds true for oncology therapeutics (M&A multiple of  $12 \pm 3$  vs. IPO multiple of  $4 \pm 1$ ) but also for therapeutic devices therapeutics (M&A multiple of  $8 \pm 4$  vs. IPO multiple of  $3 \pm 1$ ).



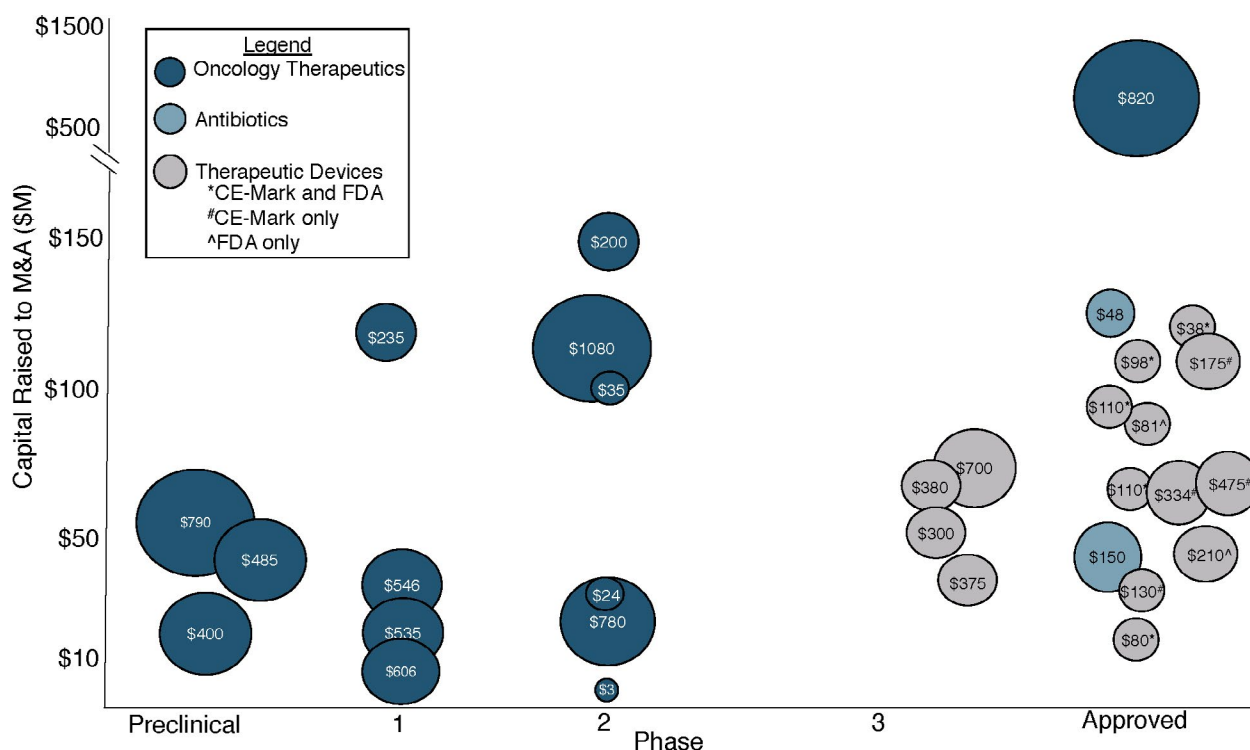
**Figure 4:** Exit opportunities for the therapeutic devices sector is satisfactory. Number of M&As and IPOs for the therapeutic devices sector is shown (A). Total M&A deal value and market cap at 6 months post-IPO are shown (B). M&A is the preferred route of exit for this sector and primarily occurs when the company has an approved asset. Data from 01/15-12/17 collected from Pitchbook. Error bars represent SEM.

## CONCLUSION

So what actionable information can be learned by the adoption of a statistical mindset and a simple reflection on the data? If you are an entrepreneur running a young oncology therapeutics company, provided that the basic science is sound and differentiated, the investment community is likely to support your R&D efforts as substantial amount of capital flows into the segments and M&A returns on capital are lucrative. Moreover, segment dynamics with respect to pharma interest in oncology assets is more likely to allow for multiple exit opportunities along the drug development continuum, which, in turn, would provide a more favorable risk profile for all stakeholders; company, management and investors. The reality of entrepreneurs in the antibiotics segment is markedly different. The risk of undercapitalization is significant and would dictate targeting the limited universe of investors that are not only interested in the segment but also have ample capital to support the company

all the way to phase 3 and beyond. As such, management teams of antibiotics companies should focus on large venture firms while avoiding the numerous small or mid-size firm that are highly unlikely to successfully participate in this sector. From a statistical point of view, these dynamics indicate that early discussion with corporate partners to propel product development is key. The required capital to exit in the therapeutic device sector seems favorable compared to antibiotics or oncology therapeutics suggesting appetite by the investment community to participate. However, as most exits take place at later stage of development, mostly post-regulatory approval, CEOs of therapeutics device companies should be cognizant of undercapitalization risk and seek investors that have enough capital to support the company at least through European approval (CE-Mark) as well as engage with corporate venture firms which may have a strategic interest in investing in technologies that would feed into the pipeline of their parent company.





**Figure 5:** Sector dictates when M&As occur during product development, amount of capital needed to exit, and deal size. Deal size is shown within each circle and size of the circle is relative to M&A deal size. Oncology therapeutic exits happen earlier during product development for larger deal sizes compared to therapeutic devices that are typically approved before an exit or the limited number of exits in antibiotics. Note: M&A of therapeutic devices had completed trials and filed for approval. Data from 01/15-12/17 collected from Pitchbook and press releases.

Management must recognize and adapt to the dynamics of the sector in which it operates. It is imperative to adopt an outwardly, top-down (as opposed to technology-up), market-driven point of view from the outset. This includes developing a clear path to liquidity that is closely aligned with market characteristics or the behavior of investors as well as strategic players in your specific area. Focus on strategy first, execution second. Typically, a market segment will support a defined range of capital requirements, developmental paths and valuation inflections. While outliers do exist, a conservative strategy to follow a similar path to liquidity of the majority of benchmark companies will increase the probability of success. Entrepreneurs who evaluate their prospects based on a narrow, internally focused view, while relying on limited information and personal experience, rather than consulting the statistics of similar cases, are prone to grossly overestimate both their probability and degree of success. Management will thus be wise to avoid an internal myopic view of their company and reflect on external benchmark base rates.

The simple analysis presented here provides the base rates data for various sectors and should provide

management with a good estimation as to the required capital to achieve value-add milestones as well as the anticipated return on investment. These examples demonstrate the fundamentally different dynamics of three sectors, which will impact the reality of companies in those sectors. Substituting external formal thinking, market-driven evaluation and analysis for inward-looking and biased judgment can go a long way in crafting a mature business case for your company as well increasing the probability of success.

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