

Funding Long Shots*

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Abstract

We define long shots as investment projects with four features: (1) low probabilities of success; (2) long gestation lags before any cash flows are realized; (3) large required up-front investments; and (4) very large payoffs (relative to initial investment) in the unlikely event of success. Funding long shots is becoming increasingly difficult—even for high-risk investment vehicles like hedge funds and venture funds—despite the fact that some of society’s biggest challenges such as cancer, Alzheimer’s disease, global warming, and fossil-fuel depletion depend critically on the ability to undertake such investments. We investigate the possibility of improving financing for long shots by pooling them into a single portfolio that can be financed via securitized debt, and examine the conditions under which such funding mechanisms are likely to be effective.

Keywords: Capital Budgeting; Impact Investing; Venture Capital; Private Equity; Megafund; Securitization; Portfolio Theory; Research-Backed Obligation

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1 Introduction

The standard approach to capital budgeting and investment decisions for risky projects involves estimating a project's expected incremental cash flows, choosing an appropriate risk-adjusted discount rate, and calculating the net present value (NPV) of the project's cash flows. This approach is appropriate for many of the investment opportunities encountered in practice, such as the replacement of plant and equipment or the development of new products and services. We will refer to these as "textbook projects." Usually they are expected to lead to some level of positive future cash inflows in many states of the world, and the key issue is to determine whether these positive inflows will be sufficient to justify the initial investment when averaged across all possible states of the world. In well-functioning capital markets, a textbook project can be funded if it has positive expected NPV.

In this paper, we focus on a different type of project, which we call a "long shot." We define a long-shot investment as one with four specific characteristics: (1) it requires a large amount of initial capital; (2) it has a long gestation lag, during which no cash flows are generated and/or additional capital investment is required; (3) it has a low probability of success; and (4) if successful, its payoff is very large relative to the initial investment. Examples of long shots include drug development, alternative energy (fusion, wind, solar) technology, quantum computing, commercial space travel, and mitigating the environmental impact of climate change through geo-engineering.¹

The characteristics of long shots make them much more difficult to fund on a stand-alone basis than textbook projects. Traditionally, venture capital (VC) or philanthropic donations have been the primary sources of funding. However, some of society's biggest challenges such as cancer, Alzheimer's disease, global warming, and fossil-fuel depletion depend critically on the ability to undertake long shots, and because of the risk profile of a typical long shot, the funding requirements far outstrip the capital available from these traditional sources.

¹ See for example Fernandez, Stein, and Lo (2012) and Gaddy, Sivaram, and O'Sullivan (2016).

The simplest long shot is one in which there is a single up-front capital investment, a known project duration, and a known payoff at the end of the life if the project is successful. Suppose, for example, that a research and development (R&D) project requires an initial investment of \$200 million, lasts 10 years, and has a 5% probability of a payoff of \$10 billion, and that the project's risk is purely idiosyncratic (i.e., no priced-factor exposure). If the discount rate for the expected cash flows from this long shot is less than 9.60%, the project has a positive expected NPV. In principle, such a project should be quite attractive to investors, especially given the idiosyncratic nature of the risk and current level of interest rates.² However, such projects are, in fact, unlikely to appeal to traditional investors because of their scale, duration, and low probability of success, relative to their level of expected return.

A long shot's risk can be mitigated by forming a portfolio of many such projects. If, for example, a "megafund" of 150 statistically independent projects—each identical to the one just considered—were formed, the probability of at least one success would be 99.95% and the probability of at least four successes would be about 95%. While risk has been greatly reduced—to the point that many institutional investors would now find the investment attractive—such a portfolio would have a 10-year duration and require \$30 billion of funding. As a result, a portfolio of such scale would be virtually impossible for any single venture capitalist to fund.³

In this paper, we ask whether diversification and securitization techniques can be used to structure portfolios of long shots so as to make their risk/reward profile more attractive to a broad range of conventional institutional investors. If so, such techniques could dramatically increase the pool of available capital to fund long shots, many of which have social value far beyond their private-sector returns. Our secondary goal is to distinguish projects that can be handled by the private sector from those that must, at least in the early stages, rely on some type of government support. Although long shots may not exhibit

² The nature of much of R&D is such that the systematic risk associated with success or failure is very low. However, there may be some systematic risk associated with the value of the project in the event of success.

³ According to the *National Venture Capital Association 2017 Yearbook*, the total assets under management in the U.S. VC industry in 2016 were \$333.5 billion.

“market failures” in the traditional economic sense, i.e., externalities or public-goods aspects, we propose a new kind of market imperfection: the combination of outsized scale of investment needed to achieve acceptable levels of diversification and their high levels of risk, which make such investments difficult to undertake using current investment vehicles.

Securitization is a particularly effective tool in dealing with scale and risk.⁴ Just as a traditional asset-backed security (ABS) is used to segment the risks in a portfolio of loans or credit default swaps to appeal to a broader range of investors, a “research-backed obligation” (RBO) can be structured as a series of debt and equity tranches to distribute the risks in a portfolio of long-shot R&D projects. For example, in a simple RBO structure consisting of just three tranches—a senior tranche, a mezzanine tranche, and an equity tranche—structured under a strict priority arrangement, the cash flows from successful projects would flow first to the senior tranche until it has received its specified principal and interest payments. If there were sufficient cash flows remaining, these would then flow to the mezzanine tranche until it has received its specified principal and interest payments. Residual cash flows would then be allocated to the equity tranche.

The advantage of a securitization structure is that it has to the potential to attract a broad range of investors, thereby increasing the potential scale of overall funding. In our simple example of 150 projects, the senior tranche might be rated AAA and the mezzanine tranche BBB. The probability of default on a loan in a traditional ABS plays the same role as the probability that a long-shot project will fail. Of course, the probability of long-shot failure (95% in our example) is generally much higher than the probability of loss on a loan, but the simplest RBO structure is otherwise similar to a conventional ABS in most respects.

The analogy to an ABS also highlights the important role of pairwise correlations among projects. Our illustrative example above assumed that project successes are independent events, but this is not usually the case. “Success correlation”—the correlation between the success or failure of two long shots—is one of the critical factors in determining whether private-sector funding is feasible, as in the case of traditional ABS such as mortgage-backed securities. There are a number of reasons for positive success correlation in long-shot

⁴ See Fernandez, Stein, and Lo (2012).

projects. For example, the successes of cancer therapies being pursued by different teams using the same biological pathway are related because they depend on the therapeutic viability of that single pathway. However, unlike mortgage defaults—which became highly correlated during the national decline in home prices starting in 2006⁵—success correlations among biomedical projects are unlikely to change over time in response to market cycles.

In Section 2 we review the relevant literature and in Section 3 we describe the basic analytical framework of long shots. We then consider the application of securitization in Section 4, and show how correlation and other parameters affect the economic viability of long-shot investments. More practical aspects of securitizing long-shot portfolios are considered in Section 5, and we provide two concrete examples in Section 6, one in which securitization is effective and one where securitization fails. We conclude in Section 7.

⁵ See, for example, Lo (2012).

2 Literature Review

Funding risky ventures has traditionally been the domain of the VC industry. In 2016, the VC industry represented only \$333.5 billion of the \$4.5 trillion of private assets under management in the U.S. (National Venture Capital Association (2017), Preqin (2016)), but it has historically had a disproportionate influence on technological innovation (Kortum and Lerner (2000)). Nevertheless, long-shot investments have remained stubbornly difficult to fund, even through VC. Modern examples of long-shot investments can be found in the biopharma and energy sectors, where the lack of VC funding for expansion beyond the early-research stage is often referred to as the “Valley of Death.”

This is not a new phenomenon. The basic scale-up problem has been known for over a century within the chemical engineering sector, where the inventor of the first synthetic plastic, Leo Baekeland, gave the now-famous advice, “Commit your blunders on a small scale and make your profits on a large scale” (Baekeland (1916)).

Structural explanations for the lack of funding are common. For example, the “low-hanging fruit” or the “better than the Beatles” problem are often given as explanations for the decline in R&D efficiency within the biopharma industry (e.g., Scannell *et al.* (2012)). Rather than focusing on particular explanations for why sectors such as rare disease drug development and clean energy technologies are different from each other (Nanda, Younge, and Fleming (2015), Gaddy, Sivaram, and O’Sullivan (2016)), we propose to capture the *dynamics* of VC funding more generally via the framework of long-shot funding processes.

An enduring characteristic of the VC industry is its high volatility (Gompers and Lerner (2004), Kaplan and Schoar (2005)), although the degree to which this reflects fundamentals versus investor overreaction is still under debate in some cases (Gompers *et al.* (2008)). Many relate “hot” investment markets to less circumspect VC investment in poorer quality firms, possibly through the mechanism of herding among investors (Scharfstein and Stein (1990)). However, Robinson and Sensoy (2016) have shown that roughly three-quarters of the underperformance of VC can be attributed to co-cyclicality of public market valuations and net cash flows to VC funds.

Nanda and Rhodes-Kropf (2013) found that, although startups initially funded in hot markets were more likely to go bankrupt than those funded in less active periods, hot-market-startups that were successful had higher valuations and filed a greater number of more highly cited patents than comparable startups funded in cold markets. In other words, the outcomes for startups in more active markets were more likely to be in both tails of the distribution than those funded in less active markets. This may be indicative of heterogeneity in VC. For example, Chemmanur, Loutskina, and Tian (2014) found that corporate VC backed a proportionately larger number of startups with better patent outcomes than did independent venture capitalists, but that these startups were riskier and less profitable than their counterparts. This suggests that the lack of financing of long-shot projects may be a question of *composition* rather than base quality.

The institutional response of the VC community to reducing all-or-nothing risks to investors has been to stage investments in sequential “rounds” or “raises.” At the end of each stage, a project is abandoned, sold, or retained. Gompers (1995) showed that such staging structures have led venture capitalists to focus primarily on early stage companies. In some sectors, the market in intellectual property assets created by intermediate stages acts to counter this early-stage focus, as has been the case in the biopharma industry (Gans, Hsu, and Stern (2002)).

Gompers (1995) argues that staging is a way for venture capitalists to reduce agency costs. Kerr, Nanda, and Rhodes-Kropf (2014) view staging as a process of experimentation that allows both the investor and the innovator to negotiate in an environment of extreme Knightian uncertainty. Ewens, Nanda, and Rhodes-Kropf (2015) extend this analysis to consider how it has influenced the type of projects that are funded. They find an adaptive shift in VC strategies toward newly viable “long-shot bets,”⁶ but that this shift comes at the expense of capital-intensive projects unaffected by the innovation. Furthermore, staging can create agency costs of its own (Cornelli and Yosha (2003), Bergemann and Hege (2005)). For example, Nanda and Rhodes-Kropf (2014) observed that the mere *possibility*

⁶ Their usage of “long shot” is colloquial, unlike our more specific definition.

of financing risk in future stages provides a significant disincentive for investors to invest in first-round funding for otherwise sound projects.

To bridge the so-called “Valley of Death” in biomedicine—the preclinical stages of drug discovery through phase 2 clinical trials—Fernandez, Stein, and Lo (2012) and Fagnan *et al.* (2013) proposed combining multiple long shots into a single portfolio, and then financing that portfolio using both securitized debt and equity. Although taking “multiple shots on goal” in drug development is expensive—requiring hundreds of millions to several billion dollars (depending on the therapeutic area) to achieve sufficient risk reduction through diversification—securitization allows entrepreneurs to tap into much larger pools of capital. In 2016, the total size of U.S. debt markets was \$39.4 trillion, which is considerably larger than the VC industry’s \$333.5 billion in assets under management in that same year (of which only about \$11.7 billion was invested in the life sciences.). When one considers that, by some estimates, developing a single cancer drug can cost more than \$2 billion (DiMasi, Grabowski, and Hansen, 2016), it becomes clear that the VC community does not have sufficient capital to provide the required funding on its own.

The present paper provides a more systematic and comprehensive analysis of the opportunities and limitations of securitization in funding this type of project. Our analysis is applicable to all long shots, not just those in the biomedicine area.

3 Long-Shot Investments

Consider a project which requires an initial investment I at time 0, provides a single cash inflow at time T in the event of success, and has a T period probability of success, p . We define the investment as a long shot if the probability of success, p , is small, its life, T , is long (often five years or more), and the initial investment, I , is “large.” The motivation for our definition is to capture the unique features of investment projects that have potentially transformative payoffs, but where the required investment, risk of failure, and duration are much higher than for typical investments. The expected cash inflow, conditional on success, must of course be much larger than I , otherwise no rational investor would consider investing in the project. Examples of long shots include curing cancer, generating energy via fusion, mining asteroids and colonizing space and other planets, and geo-engineering our planet to mitigate climate change.

We argue that it is difficult for traditional financing sources involving VC and public or private equity to fund long shots and examine the role that can be played by securitization instead.

3.1 A Simple Example

To see the problems in applying traditional financing structures to long shots, consider a stylized example involving cancer drug development. Assume that the typical out-of-pocket costs for conducting clinical trials for a single anti-cancer compound are approximately \$200 million; the average duration for these trials is 10 years; and the historical success rate of cancer drug development programs is approximately 5%. If successful, a typical cancer drug might generate \$2 billion in annual profits for the remainder of its patent life of 10 years (a 20-year patent minus 10 years of clinical trials). Figure 1 provides a timeline of the cash flows.

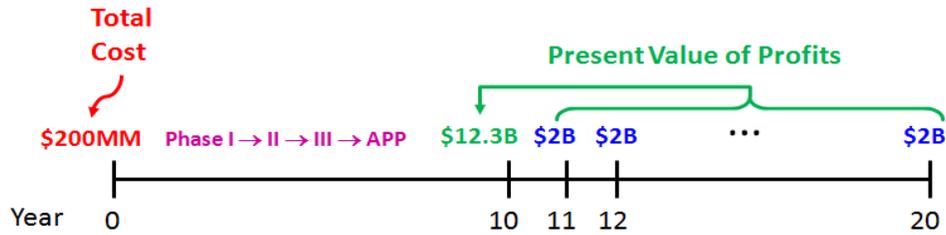


Figure 1. Timeline of revenues and costs of a hypothetical cancer drug development project.

Using a 10% cost of capital (an approximate value for the pharmaceutical industry), these profits are equivalent to a payoff of \$12.3 billion in year 10, implying an annualized expected return from the project of 11.9%.⁷ However, the 95% risk of total loss is extremely high and unlikely to interest a typical investor (especially given the 10-year gestation lag before any cash flows can begin). Therefore, entrepreneurs have difficulty attracting financing for such projects from traditional sources such as VC and public or private equity.

A natural approach to solving this problem is to combine several long shots in a portfolio. However, the low probability of success means that a large number of projects are necessary to achieve a reasonable degree of diversification. Consider an investment in a portfolio of n independently and identically distributed (IID) projects similar to the one we have just considered.⁸ The expected return from the portfolio is still 11.9%. Risk, as measured by the ratio of the standard deviation of the payoff to the expected payoff, is

$$\sqrt{\frac{1-p}{np}}$$

For values of n equal to 1, 10, 50, and 100 and $p = 5\%$, this is 4.36, 1.38, 0.62, and 0.44, respectively. As is well known, the binomial distribution approaches the normal

⁷ We define the “expected return” as the return provided by the expected payoff. This is the most meaningful measure as it corresponds to the maximum discount rate for which the project is attractive. Note that for a single-period long-shot project it is much greater than the expected internal rate of return. (The expected internal rate of return is -92.5% for the project considered here.).

⁸ In our subsequent models and simulations, we relax the IID assumption.

distribution as n increases. However, for small p , this convergence happens slowly, as is illustrated in Figure 2 which contains the probability distribution of the number of successes when there are 10, 50, and 100 projects.

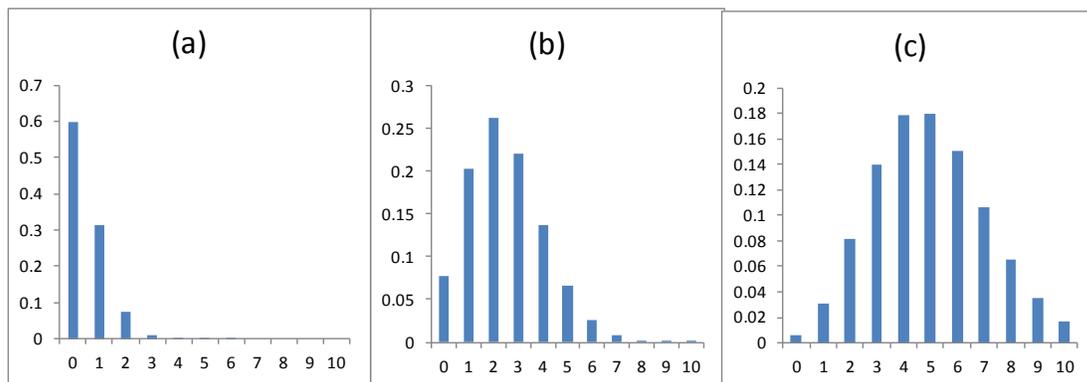


Figure 2. Probability distribution for the number of successes when the probability of success is 0.05 and the number of projects is (a) 10, (b) 50, and (c) 100.

Unfortunately, constructing a portfolio of 100 projects similar to the one we have considered requires \$20 billion, which dwarfs the assets under management of most VCs. Also, the risk-return profile is still not sufficiently favorable to attract VCs.

3.2 Project Correlation

In practice, project successes are rarely independent events. The Gaussian copula, developed by Vasicek (1987) and Li (2000), is a relatively simple way of modeling success correlation. Suppose there are n non-independent projects, each with an unconditional probability of success equal to p . The copula model associates a standard normal distribution with each project. Each project i is successful when the value V_i obtained from the normal distribution corresponding to the project is less than $N^{-1}(p)$ where N is the cumulative normal distribution function. The pairwise correlations among $\{V_i\}$ represent the factor correlations, which, suitably transformed, result in success correlations.

The correlations between the normal distributions in the Gaussian copula model can be generated using a factor model. In the case of a single common factor, V_i ($1 \leq i \leq n$) may be written as:

$$V_i = a_i F + \sqrt{1 - a_i^2} Z_i \quad (1)$$

where the a_i are constants ($-1 \leq a_i \leq 1$) while the common factor F and idiosyncratic noise term Z_i have uncorrelated standard normal distributions. The correlation between V_i and V_j , known as the copula correlation, is then simply $a_i a_j$. For convenience, it is often assumed that a_i equals a constant, a , for all i . Conditional on F , the successes are then uncorrelated with probability

$$N\left(\frac{N^{-1}(p) - \sqrt{\rho}F}{\sqrt{1 - \rho}}\right)$$

where $\rho = a^2$ is the pairwise unconditional correlation between the V_i 's.

Discretizing the normal distribution of F , the probability, $q(h)$, of exactly h successes from n projects is:

$$q(h) = \sum_{k=1}^K w_k B(h, n, p_k) \quad (2)$$

where

$$p_k = N\left(\frac{N^{-1}(p) - \sqrt{\rho}F_k}{\sqrt{1 - \rho}}\right) \quad (3)$$

and $B(h, n, \pi)$ is the binomial probability that there will be h occurrences of an event in n trials when the probability of an occurrence is π . The parameters w_k and F_k are the weights

and values when a standard normal distribution is approximated using Gaussian-Hermite quadrature and K points.⁹

The impact of correlation on the probability distribution of the number of defaults depends on the number of projects and their probabilities of success. Consider the situation where the probability of success is 10%. When there are only five projects, a copula correlation of 5% increases the standard deviation of the number of successes by only 3.5% relative to the zero-correlation case. This is due, in part, to the observation that the distribution of outcomes of five projects exhibits pronounced skewness, even with no correlation. With 25 and 50 projects, the distributions of outcomes are more symmetrical without correlation, and the increase in the standard deviation is 19.5% and 36.9%, respectively. With 100 projects (the situation in Figure 3) the standard deviation increase is 66.2%, and with 200 projects it is over 100%.

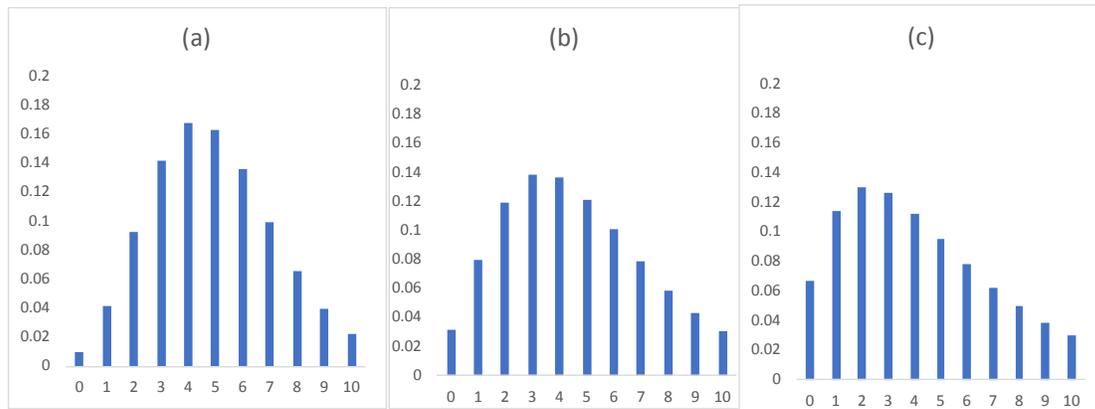


Figure 3. Probability distribution for the number of successes in a portfolio of 100 projects when the probability of success is 0.05 and the Gaussian copula correlation is (a) 0.01, (b) 0.05, and (c) 0.10.

⁹ Gauss-Hermite quadrature is an accurate way of approximating the normal distribution for the purposes of numerical integration. See, for example, Davis and Rabinowitz (1975, Ch2).

The Gaussian copula model can be generalized so that more than one factor drives the correlations. Also, other copulas with different properties can be used. One convenient way of developing other copulas is to assume non-normal, zero-mean, unit-variance distributions for F and Z_i in (1).

4 Securitization

Securitization is a well-established financing mechanism that repackages cash flows from a portfolio of assets into securities for which there is higher investment demand. Traditionally the assets have been debt instruments with regularly scheduled payments, so we begin by reviewing how securitization works in this case before moving on to consider long shots.¹⁰

Figure 4 shows a simple idealized collateralized debt obligation (CDO) in which 100 five-year loans, each with a principal balance of \$1 million and an interest rate of 5%, are transformed into three structured securities: a senior tranche with a principal balance of \$80 million, a mezzanine tranche with a principal balance of \$15 million, and an equity tranche with a principal balance of \$5 million. The tranche yields (i.e., the returns that they will receive in the absence of any losses from defaults, assuming they are sold at par) are 3%, 7%, and 25%, respectively. The weighted average yield is 4.7%. (This is less than the 5% interest rate on the loans consistent with the creator of the structure having a positive expected profit.) As the underlying loans are paid down, the principal and interest payments from those loans are used to pay debt service on the senior and mezzanine bonds, and to make equity payments.

¹⁰ See Das and Stein (2013) and Hull (2017) for a further discussion of the use of securitization and tranching for debt instruments.

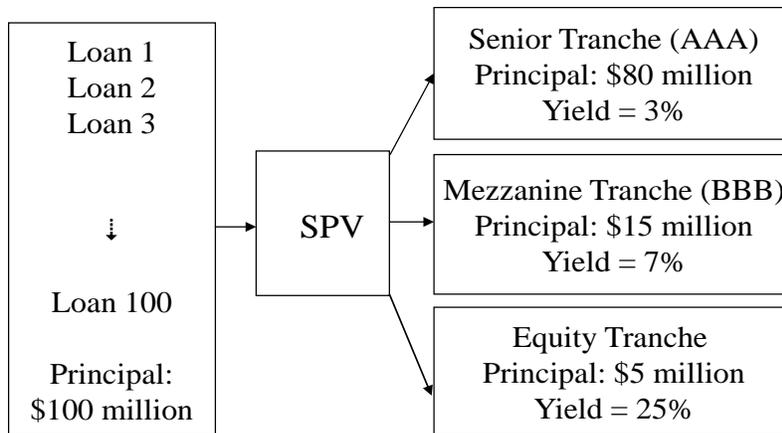


Figure 4. A simple example of a five-year structure for the securitization of debt instruments. Each loan lasts five years and carries an interest rate of 5%. The weighted average yields on the tranches is 4.7%. A strict priority rule determines how cash flows are allocated to tranches. The yield indicates the return that will be realized by a tranche if no losses are allocated to the tranche. Assuming a 50% recovery rate, the equity, mezzanine, and senior tranches will earn the specified yields if the number of defaults is less than 0, 10, and 40, respectively.

We assume a simple priority rule for both principal and interest payments on the structured securities: the senior tranche receives the first \$80 million of loan principal repayments, the mezzanine tranche receives the next \$15 million, and the equity tranche receives the last \$5 million. Similarly, interim loan interest payments flow first to the senior tranche until it has received the specified return of 3% on its outstanding principal, then to the mezzanine tranche, and if any interest cash flows remain after the mezzanine tranche has received its specified return of 7% on outstanding principal, they are used to provide a return of up to 25% to the equity tranche.¹¹

In the idealized structure in Figure 4, losses are borne first by the equity tranche. If losses reach \$5 million of par, the equity tranche is wiped out and subsequent losses are borne by the mezzanine tranche. If losses exceed \$20 million, the mezzanine tranche is also wiped out and subsequent losses are borne by the senior tranche. Suppose that the recovery rate

¹¹ Here we assume a simple zero-coupon structure for the senior and mezzanine tranches so that we may ignore the timing of interim interest payments.

in the event of a default on a loan is 50%. The mezzanine tranche will not lose any principal if the number of defaults is less than or equal to $10 = \$5\text{MM}/(0.5 \times \$1\text{M})$ and the senior tranche will not lose any principal if the number of defaults is less than or equal to 40.

In practice, the rules for distributing cash flows to the tranches in a cash CDO are more complicated than the simple structure in Figure 4. For example, there are usually more than three tranches and some over-collateralization where the principal of the loans is greater than the principal of tranches. In addition, there are numerous forms of credit enhancement beyond subordination such as coverage triggers, cash flow redirection, reserve accounts, etc. Also, there are usually some departures from the strict priority rule we have assumed. See Section 5 for a more detailed discussion.

4.1 Application to Long Shots

The use of securitization techniques to fund biomedical innovation has been proposed by Fernandez, Stein, and Lo (2012) and Fagnan *et al.* (2014). Our aim is to generalize this approach and discuss its viability and limitations in various cases.

A portfolio of long-shot projects can be financed through the issuance of an equity tranche and a number of debt tranches. The cash flows generated by successful projects are then channeled to pay principal and interest on the debt tranches. When a simple strict priority rule is used, cash inflows from successful projects go first to the senior tranche until the cash inflows have been exhausted or the senior tranche has received its specified yield. Excess cash inflows then go to the next-most-senior tranche until the cash inflows are exhausted or it has received its specified yield, and so on. As in the case of a cash CDO, the rules for allocating cash flows are usually more complicated than this (see Section 5). The model we use here is a simplification designed to explore the key factors determining the feasibility of securitization. Figure 5 shows a simple situation where, as in Figure 4, there are only three tranches: a senior tranche, a mezzanine tranche, and an equity tranche. The portfolio consists of 150 long shot projects all assumed to have identical properties. Each project requires an investment of \$200 million and has a life of five years. The probability of a successful outcome from a project is 10% and the expected annual compound return

from a project is 10%. This means that the expected cash flow from a successful project at the end of the five years is \$3.22 billion. Given that long-shot projects typically have very little systematic risk, the 10% expected return is attractive. (As mentioned earlier, the systemic risk associated with R&D projects is often low.) However, it may be difficult to obtain funding from conventional sources.

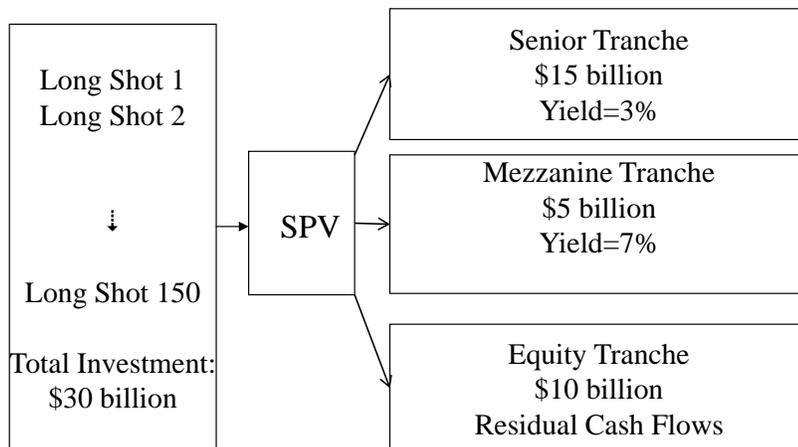


Figure 5. A simple example of a five-year structure for the securitization of long-shot projects. Each project lasts five years and requires an initial investment of \$200 million. Each project has a 10% probability of success. If successful, it gives a cash flow of \$3.22 billion in five years. If unsuccessful, it gives rise to no cash flows. The expected cash inflow therefore provides a return of 10%. A strict priority rule determines how cash inflows from successful projects are allocated to tranches. The yield indicates the return that will be allocated to a tranche if there are a sufficient number of project successes. The senior tranche will lose principal if there are less than six successful projects. The mezzanine tranche will lose principal if there are less than eight successful projects.

4.2 Analytics of Long-Shot Securitization

We now present analytics for securitizations similar to that in Figure 5. We assume that a portfolio of n projects is financed by m debt tranches and an equity tranche. We denote the probability that h of the n projects are successful by $q(h)$. (This could be determined using the copula model in Section 3.2, or in some other way.) We assume a simple priority rule, as in Figure 5, and denote by K_j ($1 \leq j \leq m$) the cash flow necessary to provide the first j tranches with their promised returns. (In the example in Figure 5, $m = 2$, $K_1 = \$15 \times 1.03^5 = \17.39 billion and $K_2 = \$17.39 + \$5 \times 1.07^5 = \$24.40$ billion.)

All projects have the same life and successful projects are assumed to give rise to identical payoff distributions at maturity. We will denote the mean and standard deviation of the payoff from a successful project by μ and σ , respectively. The coefficient of correlation between the *payoffs* from each pair of *successful projects* will be assumed to be the same and will be denoted by ρ_c .

Conditional on h successful projects, the mean and standard deviation of the total payoff available for servicing the tranches are

$$\mu_h = h\mu$$

and

$$\sigma_h = \sigma\sqrt{h + \rho_c h(h-1)}$$

respectively.

The simplest assumption would be that the payoffs from successful projects are multivariate normal, implying that the total payoff from h successes is normally distributed. However, because this assumption has the undesirable property that payoffs from successful projects can be negative, we instead assume that the payoffs from successful projects are lognormal, which appears consistent with empirical observations¹². The risk of a debt tranche is then given by Proposition 1 (all proofs are provided in the Appendix):

Proposition 1: *If the payoff from a successful project is lognormally distributed, the probability, π_j , that the j^{th} tranche will receive its promised return can be approximated as*

$$\pi_j = \sum_{h=1}^n q(h)N\left(\frac{\ln(\mu_h/K_j) - s_h^2/2}{s_h}\right) \quad (4)$$

¹² See Fernandez, Stein, and Lo (2012) for a discussion.

where

$$s_h = \sqrt{\ln\left(1 + \frac{\sigma_h^2}{\mu_h^2}\right)} .$$

The risk of the equity tranche can be approximated in a similar manner, as described in Proposition 2:

Proposition 2: *When the payoff from a successful project is lognormally distributed, the first two moments of the payoff from the equity tranche can be approximated as*

$$M_1 = \sum_{h=1}^n q(h) \left[\mu_h N\left(\frac{\ln(\mu_h/K_m) + s_h^2/2}{s_h}\right) - K_m N\left(\frac{\ln(\mu_h/K_m) - s_h^2/2}{s_h}\right) \right]$$

$$M_2 = \sum_{h=1}^n q(h) [(\mu_h^2 + \sigma_h^2)] N\left(\frac{\ln(\mu_h/K_m) + 3s_h^2/2}{s_h}\right) + K_m^2 N\left(\frac{\ln(\mu_h/K_m) - s_h^2/2}{s_h}\right)$$

$$- 2K_m \mu_h N\left(\frac{\ln(\mu_h/K_m) + s_h^2/2}{s_h}\right)$$

where

$$s_h = \sqrt{\ln\left(1 + \frac{\sigma_h^2}{\mu_h^2}\right)} .$$

Define the mean and standard deviation of the return (not annualized) to the equity tranche over the life of the project as μ_E and σ_E , respectively. If E is the investment in the equity tranche, these are related to the moments in Proposition 2 by

$$\mu_E = \frac{M_1}{E} - 1 \tag{5}$$

$$\sigma_E = \frac{\sqrt{M_2 - M_1^2}}{E} \quad (6)$$

A special case of the results in Propositions 1 and 2 is when the payoff from a successful project is assumed to be known with certainty. By letting s_h tend to zero, we see that the probability that the j^{th} tranche receives its promised return in Proposition 1 reduces to

$$\pi_j = \sum_{h|\mu_h > K_j} q(h) \quad (7)$$

The moments of the payoff to the equity tranche in Proposition 2 reduce to:

$$M_1 = \sum_{h|\mu_h > K_j} q(h) (\mu_h - K_m)$$

$$M_2 = \sum_{h|\mu_h > K_j} q(h) (\mu_h^2 + K_m^2 - 2K_m\mu_h)$$

4.3 Example

We now use the analytics in Section 4.2 to explore the properties of the securitization in Figure 5. As already noted in the structure shown in Figure 5, $K_1 = \$17.39$ billion and $K_2 = \$24.40$ billion. Also, $\mu = \$3.22$ billion. In a typical securitization of this type, the objective is to arrange for the senior tranche to have a high investment-grade rating (e.g., AAA) and for the mezzanine tranche to have a mid-investment-grade rating (e.g., BBB). When evaluating tranches, credit rating agencies compare the loss forecasted by their models with the historical loss experience on bonds and other benchmarks. Standard & Poor's (S&P) and Fitch use probability of default as the metric of interest when doing this analysis, while Moody's uses expected loss. For simplicity, we will follow the approach adopted by S&P and Fitch in what follows. Accordingly, if the loss probability corresponds to that of a AAA bond, the tranche is a candidate for a AAA rating. Similarly, if the loss probability

corresponds to that of a BBB bond, the tranche is a candidate for a BBB rating. Based on statistics provided by rating agencies, we assume in what follows that the five-year default probability must be less than 0.2% for a AAA tranche and less than 1.8% for a BBB tranche.

Consider first the case where the payoff from a successful project is known (= \$3.22 billion). From (7):

$$\pi_1 = \sum_{h \geq 6} q(h) \qquad \pi_2 = \sum_{h \geq 8} q(h)$$

If there is no success correlation, the $q(h)$ are binomial probabilities so that $\pi_1 = 0.9981$ and $\pi_2 = 0.9860$. The default probabilities on the senior and mezzanine tranches are therefore 0.19% and 1.40%, respectively. Quantitatively, this would justify considering AAA and BBB credit ratings, respectively. However, when the success correlation is modeled using (1)–(3) with a copula correlation of 5%, $\pi_1 = 0.9444$ and $\pi_2 = 0.8724$. The senior and mezzanine tranches are then no longer close to being candidates for AAA and BBB ratings. To increase the credit quality of the structured securities created from this portfolio it would be necessary to either change the capital structure of the securitization (e.g., by increasing the subordination levels) or add structural features (such as those described in Section 5), or both.

When the payoff from a successful project is uncertain, but correlation is zero, the senior and mezzanine tranches become slightly more risky, but the impact of this is much less than the impact of success correlation. For example, when there is no success correlation and no payoff correlation, increasing the standard deviation of the payoff from a success from 0% (of the expected payoff) to 25% only increases the default probability for the senior tranche from 0.19% to 0.22% and increases the default probability for the mezzanine tranche from 1.40% to 1.78%. Similar results hold for the situation where the success correlation is non-zero.

4.4 Funding Viability

If venture capitalists and other investors required compensation only for non-diversifiable risk, as theory predicts, securitization would not increase funding opportunities for long shots. We can see this immediately in the context of the Capital Asset Price Model (CAPM). Suppose that there are m tranches, all funded by well-diversified investors and that the CAPM beta of an investment in the j^{th} tranche is β_j . Then:

$$E(R_j) \geq R_F + \beta_j(E(R_M) - R_F)$$

where R_F is the risk-free rate, R_j is the return on the j^{th} tranche, R_M is the return on the market, and E denotes expected value. If a proportion γ_j of the portfolio is funded by the j^{th} tranche then, in the absence of frictions,

$$E(R_P) = \sum_{j=1}^m \gamma_j E(R_j) \geq \sum_{j=1}^m \gamma_j \beta_j (E(R_M) - R_F)$$

where R_P is the return on the portfolio. Because the beta of the portfolio equals $\sum_{j=1}^m \gamma_j \beta_j$, a well-diversified investor should be prepared to invest in the portfolio without securitization. Similar results apply for multi-factor models.

Research by Cochrane (2005) and Ewens, Jones, and Rhodes-Kropf (2013) suggest that venture capitalists and providers of private equity funding do, in fact, care about (i.e., price) diversifiable risk. Cochrane shows that individual VC projects earn large positive alphas. Ewens, Jones, and Rhodes-Kropf provide a possible explanation for this. The investors in VC and private equity funds may be well-diversified, but the funds themselves are not well-diversified.¹³ A significant part of a fund manager's compensation is related to the performance of the fund. Furthermore, the contract with investors is set in advance of deals being signed with entrepreneurs to acquire firms for the fund portfolio. This creates a principal-agent problem in which idiosyncratic risk is rationally priced by the fund

¹³ Gompers and Lerner (1999), for example, note that funds typically invest in at most two dozen firms over about three years and that the expertise of the fund managers may be limited to a particular sector of the economy.

manager even though it would not be priced by the fund's investors if they were negotiating terms directly with entrepreneurs.

To assess the viability of a securitization similar to that in Figure 5, we estimate the Sharpe ratio for the equity tranche assuming that the more senior debt tranches have been made as large as their desired credit ratings will allow. The Sharpe ratio is the excess expected return above the risk-free rate divided by the return standard deviation. It is a measure of an investment's risk/reward profile that is widely used by venture capitalists, private equity fund managers, and hedge fund managers. As a reference point, the average Sharpe ratio for the CRSP value-weighted return between 1970 and 2016 (calculated using a 60-month rolling window) was 0.37 and the average realized return during this period was 10.9%.

Define $\hat{\pi}_j$ as the maximum probability of default for debt tranche j that is consistent with its rating. From Proposition 1, the maximum value of K_j , \hat{K}_j , is given by solving

$$\hat{\pi}_j = \sum_{h=1}^n q(h) N\left(\frac{\ln(\mu_h/\hat{K}_j) - s_h^2/2}{s_h}\right).$$

The maximum size of the first tranche is \hat{K}_1 and the maximum size of the j^{th} tranche ($j > 1$), conditional on the sizes of earlier tranches being maximized, is $\hat{K}_j - \hat{K}_{j-1}$.

Assume that the minimum proportion of funding to be provided by the equity tranche is e ($0 \leq e < 1$). Suppose there are m debt tranches, T is the life of the projects, r_j is the yield on the j^{th} most senior debt tranche, and C is the total funding required. The maximum proportion of the funding that can be provided by the first (most senior) tranche is

$$u_1 = \min\left(\frac{\hat{K}_1}{C(1+r_1)^T}, 1 - e\right).$$

The maximum proportion of the funding that can be provided by the j^{th} debt tranche ($2 \leq j \leq m$) is

$$u_j = \min\left(\frac{\hat{K}_j - \hat{K}_{j-1}}{C(1+r_j)^T}, 1 - e - \sum_{k=1}^{j-1} u_k\right).$$

This leaves the size of the equity tranche to be $1 - \sum_{j=1}^m u_j$.

There are a number of alternative ways of calculating the Sharpe ratio from the mean and standard deviation of multi-year returns. We choose to define it as arithmetic average return per year minus the risk-free rate divided by the standard deviation of the return per year. For this purpose we assume that returns in successive years are independent. This means that

$$\text{Sharpe Ratio} = \frac{\mu_E/T - r_F}{\sigma_E/\sqrt{T}}$$

where, as before, r_F is the risk-free rate per year, and μ_E and σ_E are the mean and standard deviation of the cumulative return over the life of the structure which can be calculated using (5) and (6) and the results in Proposition 2.

Table 1 contains results for the case in which $m = 2$, $r_1 = 3\%$, $r_2 = 7\%$, and $T = 5$, which are the parameters corresponding to Figure 5. The risk-free rate, r_F , is assumed to be 2% and we set $e = 5\%$.¹⁴ In the top panel of Table 1, the projects are assumed to be uncorrelated while in the bottom panel, the Gaussian copula correlation is assumed to be 5%. Figure 3b illustrates the effect of this amount of correlation on the probability distribution of the number of successes when there are 100 projects and the success probability is 5%.

¹⁴ Setting $e > 0$ ensures that there is always an equity tranche and that a Sharpe ratio for it can always be calculated.

Project E[R]	Success Prob	Equity Tranche	Number of Projects					
			50	100	150	200	300	400
0% Pairwise Correlation Among Projects								
10%	5%	Min Size	100.00%	77.03%	66.17%	49.25%	30.73%	26.00%
		E[R _e]	10.00%	10.87%	12.30%	14.48%	19.68%	22.80%
		SR _e	0.23	0.28	0.35	0.39	0.46	0.56
	10%	Min Size	77.03%	46.84%	29.12%	20.26%	10.60%	5.16%
		E[R _e]	10.86%	15.62%	20.96%	26.13%	38.44%	56.49%
		SR _e	0.29	0.42	0.50	0.56	0.69	0.80
15%	Min Size	50.86%	29.12%	16.77%	10.60%	5.00%	5.00%	
	E[R _e]	13.79%	20.95%	29.48%	38.42%	57.79%	58.71%	
	SR _e	0.34	0.51	0.62	0.71	0.88	1.05	
20%	5%	Min Size	100.00%	64.52%	47.73%	21.59%	5.00%	5.00%
		E[R _e]	20.00%	25.31%	30.79%	47.28%	92.79%	94.37%
		SR _e	0.40	0.53	0.66	0.74	0.92	1.10
	10%	Min Size	64.52%	17.87%	5.00%	5.00%	5.00%	5.00%
		E[R _e]	25.31%	52.95%	93.77%	94.37%	94.37%	94.37%
		SR _e	0.55	0.78	0.97	1.13	1.38	1.60
	15%	Min Size	24.07%	5.00%	5.00%	5.00%	5.00%	5.00%
		E[R _e]	44.16%	93.77%	94.37%	94.37%	94.37%	94.37%
		SR _e	0.67	0.99	1.23	1.42	1.74	2.01
5% Pairwise Correlation Among Projects								
10%	5%	Min Size	100.00%	100.00%	84.69%	77.03%	75.43%	74.62%
		E[R _e]	10.00%	10.00%	10.54%	10.89%	11.34%	11.56%
		SR _e	0.18	0.22	0.22	0.22	0.24	0.25
	10%	Min Size	100.00%	77.03%	67.77%	67.68%	61.54%	58.46%
		E[R _e]	10.00%	10.87%	11.80%	12.31%	12.91%	13.25%
		SR _e	0.24	0.25	0.26	0.28	0.29	0.29
	15%	Min Size	84.69%	66.17%	59.99%	56.90%	53.82%	52.27%
		E[R _e]	10.52%	12.32%	13.12%	13.58%	14.07%	14.34%
		SR _e	0.27	0.30	0.31	0.32	0.33	0.33
20%	5%	Min Size	100.00%	100.00%	76.34%	64.52%	62.04%	60.79%
		E[R _e]	20.00%	20.00%	23.12%	25.34%	26.30%	26.80%
		SR _e	0.32	0.39	0.40	0.41	0.44	0.45
	10%	Min Size	100.00%	64.52%	50.21%	50.06%	40.57%	35.83%
		E[R _e]	20.00%	25.31%	29.50%	30.13%	33.88%	36.26%
		SR _e	0.43	0.46	0.49	0.52	0.54	0.54
15%	Min Size	76.34%	47.73%	38.19%	33.42%	28.65%	26.26%	
	E[R _e]	23.10%	30.80%	35.07%	37.82%	41.17%	43.15%	
	SR _e	0.49	0.55	0.58	0.60	0.62	0.63	

Table 1. Minimum size, expected returns (E[R_e]), and Sharpe ratios (SR_e) of the equity tranche. Various combinations of the number of projects, the probability of success, the expected return, and copula correlation of projects in Figure 5 are considered. Projects are assumed to last five years. The probability of loss on the senior and mezzanine tranches are less than 0.2% and 1.8%, respectively, over the five years. Tranche yields are as in Figure 5. The risk-free rate is assumed to be 2%.

The attractiveness of a securitization structure increases as the percentage of funding provided by equity declines, as the expected return on the equity tranche increases, and as the Sharpe ratio increases. Consider first the most challenging situation where the expected return is 10% and the success probability is 5%. If projects are uncorrelated, roughly 50% of a megafund of 200 projects could be financed by AAA and BBB bonds. This percentage increases as the number of projects in the fund increases, but the total amount of equity funding per project would not change substantially. The expected returns and Sharpe ratios are not unreasonable when compared with those for the CRSP value-weighted index mentioned earlier. However, when correlation between the projects is introduced, all aspects of the structure become much less attractive.

As shown in Table 1, as the probability of success increases, the size of a feasible megafund decreases and the structure becomes more attractive. For example when the success probability is 10% (the situation in Figure 5), 150 projects would create an attractive structure where about only 30% has to be funded from equity (so that 70% can be funded from AAA and BBB bonds). However, the bottom panel of Table 1 indicates that the success probability must be more than 15% when the copula correlation is 5% for such high levels of leverage.

Increasing the expected return from 10% to 20% leads to attractive structures in the cases of both 0% and 5% correlation. We conclude that this form of very simple securitization is a potentially useful tool in all situations except those where the probability of success is low and there is material correlation between the successes of different project outcomes.

4.5 Correlation Assumptions

In some situations, projects can be stratified into a small number of groups (e.g., different broad disease categories or different sources of energy). In such cases, we expect the within-group pairwise correlations to be greater than the between-group correlations. This is equivalent to assuming a multi-factor model for the latent variables, V_i , in (1). We find that similar results are obtained by replacing all correlations by the average correlation (i.e., all off-diagonal entries in the correlation matrix are replaced by the average of the off-

diagonal entries). This corresponds to the assumption that is commonly made when debt securitizations are analyzed.

5 Practical Approaches to Improving Credit Quality

The securitization model of Section 4 illustrates the relative importance of different parameters in a long-shot securitization, but is a simplification in several respects. It assumes that (a) all projects are entered into at the same time and have the same known life; (b) all the funding is provided at the beginning of a project's life; (c) a project is categorized as a success or failure only at the end of its life; (d) a success is monetized only at the end of a project's life; (e) costs are known in advance; and (f) failures are written off entirely. We have also assumed a simple zero-coupon structure for the structured debt and that there were no structural enhancements beyond subordination.

In practice, structured transactions often depart from the assumptions of our stylized models along two broad dimensions: the structure of the securities issued by an RBO, and the structure and evolution of the assets in the portfolio and the markets in which they are bought and sold.

5.1 Structure of Securities

Departures from the idealized structure of the securities primarily relate to the events on which the security payouts depend or the mechanisms that are used to protect one or more classes of investor.

Cash-flow securitizations are typically more complicated than the stylized structure in Section 4 because they distribute interim, as well as final, cash flows from a portfolio of underlying assets to investors. For example, a collateralized loan obligation (CLO) is a simple example of a cash-flow securitization where interest and principal payments from a portfolio of individual loans are used to repay principal and interest on tranches.

The strict priority rule we assumed in Section 4 typically applies to synthetic securitizations (such as synthetic CDOs), but not to cash flow securitizations. In the latter, the rules for determining how cash flows are directed to tranches can be quite complicated.

For example, cash flows are often redirected from junior to senior tranches if there is insufficient cash flow to pay all tranches and amortization schedules may be accelerated in such cases. This provides additional protection for senior tranches. However, it creates path dependence and means that analytic models such as those in Section 4 serve only as approximations. A more complete valuation generally requires a multi-period Monte Carlo simulation model.

Some of the additional credit protection mechanisms available to cash-flow securitizations include: *reserve accounts* that are pre-funded and then maintained at specific levels in expectation of future interest and principal payments or project funding needs; *coverage triggers* that require assets to be sold if specific reserves are not currently available to cover future debt payments; and *accelerated waterfalls* that require the portfolio to be prematurely liquidated to retire the bonds if certain financial criteria are not met. In addition, the terms of the debt itself may be heterogeneous, with different amortization and maturity schedules and periodic coupon payments, rather than a zero-coupon structure.

Table 2 summarizes some of the structural differences between the securities hypothesized in the stylized model of Section 4 and those typically seen in the real world.

	Stylized Model	Real-world Securitization
Debt maturity	Constant across classes	Staggered by class
Coupon timing	At maturity	Periodic
Pre-maturity cash flows	Ignored	Incorporated
Structural protection	Subordination	Subordination, cash flow triggers, waterfall acceleration
Reserve accounts	None	Debt coverage, project development

Table 2. Summary of structural differences between the stylized synthetic securitization model in Section 4 and a typical long-shot securitization structure.

5.2 Structure of Assets

In our analytic models, we assume that the assets are purchased at time 0 and then evaluated at time T , where the model time between 0 and T is considered to be a *single period*. We assumed that each asset in the portfolio either realizes its exit value or fails at time T and that there is no contingency, beyond the terminal success probability. This set of assumptions is appropriate for synthetic transactions, but in practice cash-flow securitizations are liable to be more complicated:

- There is considerable contingency built into funding decisions and thus costs, since projects that do not pass an interim phase of advancement do not require funding for future phases (prior to reaching the exit target). Conversely, funding must also be budgeted to be available at dates beyond the initial investment.
- Projects reach target exit phases at different rates. Thus, while some projects are still advancing, others may have already reached their exit target. Sales of these projects provide additional capital to fund development of remaining projects still in the portfolio. Furthermore, it is possible to exit some projects early, but still at a profit if they have advanced part-way through the development process. This is particularly helpful if additional capital is required for debt servicing. This “time tranching” also serves to reduce correlation.
- Asset sales are not necessarily instantaneous (as is the case when the assets are, for example, corporate bonds). In the case of long-shot projects, buyers must be found and terms negotiated before an exit may take place. This typically takes additional time so that there is a lag between the time a portfolio manager decides to sell a project and the time that proceeds of the sale are received.

Table 3 summarizes these and other features that differentiate typical long-shot assets from those in the stylized model of Section 4, and Figure 6 contains a schematic description of how a cash-flow securitization with coupon-paying debt might be structured for a portfolio of early-stage drug compounds. Not shown in Figure 6 are reserve accounts or the various changes to the portfolio and cash-flow structure that may occur when, for example, available funds are not sufficient to ensure that future debt payments can be made, and therefore cash flow is redirected or assets are sold early to raise capital.

Feature of assets	Stylized Analytic Model	Real-world Securitization
Timing of cash flows	Fixed	Variable
Arrival time of transitions	Fixed	Variable
Monetization	One time	Staged
Development Costs	Fixed	Variable
Payment timing for costs	One time up-front	Multiple throughout
Contingency of costs	Deterministic	Contingent
Acquisition timing	Instantaneous	Staged
Exit timing	Instantaneous	Delayed

Table 3. Summary of differences in assets between the stylized securitization model in Section 4 and a typical long-shot securitization structure.

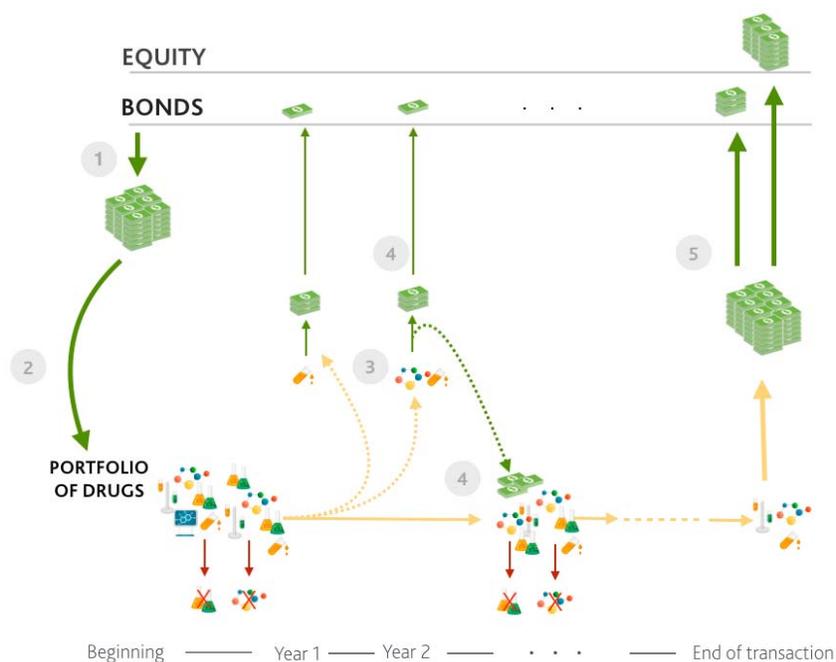


Figure 6. Schematic design of a cash-flow securitization, with coupon-paying debt, for a portfolio of early-stage drug development projects in which: (1) securities are issued; (2) proceeds from the sale of the securities are used to purchase a portfolio of candidate therapies (sometimes over a period of time); (3) as therapies move through the approval process, they gain value and are sold or they fail and are withdrawn; (4) proceeds of the sales are used to pay principal and interest and to fund trials on remaining drugs; and (5) at end of the transaction, the remaining portfolio is sold and the proceeds the distributed.

Fernandez, Stein, and Lo (2012) and Fagnan *et al.* (2014) have developed an open-source library of software tools (called *RBOToolbox*) to simulate the performance of securitization structures with behaviors such as those depicted in Figure 6. The simulation results for hypothetical megafunds in oncology and in rare diseases yield attractive risk/reward profiles when compared to current market investment opportunities. The results also suggest that the flexibility built into real-life structures often increases the protection provided to bondholders, allowing a greater percentage of funding to come from AAA and BBB bonds than suggested by the simple model of Section 4. We provide a more detailed analysis of the benefits of different components of cash flow securitization in the first example in Section 6.

However, securitization is not a panacea. In situations where the number of distinct research approaches is small and the projects' success probabilities are low, securitization is not feasible for the reasons discussed in Section 4.4. We illustrate both of these cases in the next section.

6 Illustrative Examples

To illustrate the range of applications of long-shot financing, we provide two examples at opposite extremes: a portfolio of rare-disease therapeutics and a portfolio of Alzheimer's disease (AD) therapeutics. For reasons that will become clear once we describe the risk/reward profiles of each investment, the former can be easily financed with both securitized debt and equity, particularly when additional securitization techniques such as those discussed in Section 5 are used, whereas the latter is virtually impossible to finance using any purely private-sector means.

6.1 Rare Diseases

According to the Orphan Drug Act of 1983, rare or "orphan" diseases are considered to be those that affect fewer than 200,000 patients in the U.S. Developing successful therapies for such diseases are long shots—the success rate, from the preclinical phase to FDA approval

ranges from less than 1% to 20% and higher, depending on the condition and type of therapy. This is still much higher than for many other drug development areas and is due, in part, to the scientific properties of many orphan diseases which are often caused by a single mutation in a patient's genome. This property results in two features that are particularly well-suited to portfolios. First, the research on therapies may move directly to the *treatment* of the mutation, rather than having to first establish the cause of the disease, shortening development time and increasing the odds of success. Second, because many diseases are *monogenic* (i.e., they are caused by a random mutation in a single gene), the success correlations among different therapeutic programs is likely to be low. In addition to these scientific properties, and although patient populations are often quite small, there are additional financial considerations that make these therapies more economically viable: they often receive faster regulatory approval (shorter trials), patients are often registered through foundations and can thus be pre-screened and identified (leading to smaller, cheaper trials), there are often periods of extended patent exclusivity (due to legislative actions), and patients are readily reimbursed for treatments (leading to attractive valuations upon success).

Following Fagnan *et al.* (2014) and Fagnan *et al.* (2015), we analyze a hypothetical portfolio of orphan disease therapies. The goal of such a megafund is to purchase candidate therapies at the preclinical or early phase 1 stage, where the drugs are typically very risky and therefore difficult to fund individually, and to use the fund as a vehicle to finance trials through to the much less risky phases 2 and 3 where investors have greater capacity given their risk tolerance.¹⁵

We adopt most of the calibrations in Fagnan *et al.* (2014), including: (1) the success probabilities, trial costs, and exit valuations; (2) the promised yields of the senior and subordinated debt (5% and 8%, respectively); and (3) the assumption that the target

¹⁵ In order to be approved for use in patients, a drug must undergo a number of trial phases, each of which requires a larger population of test subjects and capital to fund, but the success of which increases the probability of ultimate approval and therefore increases the economic value of the compound. In the U.S., for example, the FDA mandates that phase 1 trials test the drug's safety and dosage (typically 20-80 subjects), phase 2 trials test the drug's efficacy and side effects (hundreds of subjects), and phase 3 trials test more rigorously the drug's efficacy and further test dosing and adverse reactions (thousands of subjects).

portfolio consists of an equal number of preclinical compounds and phase 1 compounds (acquired at launch), that all compounds have target exits in phase 3, and all forms of structured exits such as deferred milestone payments, etc. are ignored. However, we modify some assumptions related to the megafund's capital structure:

Fagnan *et al.* (2014) assumed a capital structure of 15% senior debt, 20% subordinated debt, and 65% equity. Our simulations assume 30% senior debt, 20% subordinated debt, and 50% equity, which is somewhat more consistent with current market transactions.

To demonstrate the impact of different cash-flow structuring profiles, we

- structure debt as either coupon-paying or zero coupon;
- structure maturities as either concurrent or staggered; and
- include and exclude budgeting for debt service payments.

Our goal in varying the debt structure is to explore the impact that structuring can have on the credit quality of the debt. While these results are specific to the transaction structure in our example, they are directionally consistent with comparable results from other structures.

The results of our simulation are given in Table 4 (a companion table in the Appendix contains details of the structural differences between the simulations). The first rows of the table show the probabilities of default for the senior and subordinated debt tranches (“PD senior” and “PD subordinated,” respectively) along with the S&P rating that has the closest historical default rate to the estimate for the debt maturity, based on S&P's historical default studies (Standard & Poor's, 2016, Table 26). The next rows show the mean annualized return on equity (ROE) for the equity holders along with the probabilities of a loss to equity (“P(equity loss)”) and the probability of large returns (“P(ROE > 25%)”). Finally, the last row of the table shows the average number of therapies successfully advanced at least one phase through the approval process.

	(1)	(2)	(3)	(4)
	Simulation light structuring, zero coupon	Simulation light structuring, semi-annual coupon	Simulation fuller structuring, semi-annual coupon	Equity only
PD senior	9.4 %	1.2 %	7 bps	-
<i>Closest S&P historical default rate</i>	<i>BB / BB-</i>	<i>BBB</i>	<i>AAA</i>	-
PD subordinated	22.1 %	4.4 %	1.7 %	-
<i>Closest S&P historical default rate</i>	<i>B/BB-</i>	<i>BBB- / BB+</i>	<i>BBB+ / BBB</i>	-
ROE (mean)	15.0%	10.8%	13.8%	10.1%
P(equity loss)	17.3%	18.4%	14.5%	19.9%
P(ROE > 25%)	34.3%	23.2%	27.7%	9.9%
Mean drugs exiting (P2/P3)	2.7 / 4.3	3.6 / 3.5	2.9 / 4.2	0.9 / 2.4

Table 4. Summary of orphan disease megafund simulation with 1 million paths using debt structured as (1) zero coupon with no reserves or overcollateralization; (2) coupon paying debt with no reserves or overcollateralization; (3) coupon paying debt with reserves and overcollateralization; and (4) no debt but the same starting equity. The table shows the probabilities of default for senior and subordinated debt, the corresponding S&P ratings with the closest historical default rate, the mean annualized ROE for equity holders; probability that ROE < 0; and the probability that ROE > 0.25. It also shows the drugs exiting at phase 2 (P2) and phase 3 (P3). Portfolios contained an average of 16 (8) compounds when structured with (without) debt (see Appendix A.3).

As expected, the ROE results suggest that adding leverage generally increases the expected return for the transaction. However, this advantage is mediated by the tradeoff between increased purchasing power in constructing the portfolio (by virtue of a larger, levered capital base) and the need to service debt, which reduces returns both by siphoning off cash flow and by constraining portfolio growth (due either to the need to reduce development costs in order to service debt, or, in some cases, to sell assets to meet debt servicing requirements). Also, because more assets are purchased when using leverage, levered transactions advance a larger number of projects (in this case, by advancing more drugs through to phases 2 and 3).

A comparison of the columns of Table 4 suggests that the use of some of the structuring elements of Section 5 appears to improve both the credit quality of the debt and the returns to equity holders. In general, more structuring results in higher returns and lower probabilities of default, with the probability of the simple zero-coupon structure exhibiting a default probability more than two orders of magnitude larger than its more structured counterpart. In addition, the risk to equity in using debt financing tends to be improved as more structuring tools are applied, due in part to the increased diversification when a larger number of assets is purchased. In this example, the probability of a loss to equity decreases when a larger portfolio is financed (using debt), and the decrease is substantial in the case of the most structured bond (see column 3): the probability of a negative return is about 14.5%, versus 19.9% for straight equity (see column 4). It is also notable that the probability of realizing an ROE of greater than 25% rises to 27.7% for the highly structured transaction versus only 10% for the smaller, equity-only portfolio.

Note that the returns for the more fully structured case in Table 4 likely understate the performance of the transaction because we assume the same coupons on debt for all of the debt transactions, even though the more heavily structured transaction uses debt with shorter average maturities and much lower default probabilities. It is likely that the coupon on a zero-coupon bond with a five-year maturity and a 9.4% probability of default would be much higher than that of a four-year maturity bond making semi-annual payments with a default probability of just 7 basis points (bps). Such a difference in coupons for these two bonds would magnify the differences in ROE by virtue of more cash flow being directed to the portfolio and less to debt service. (The lower (higher) coupon rates would also likely reduce (increase) the default probabilities for the bonds.)

This example demonstrates the importance of including real-world features in the analysis of long-shot portfolios, but there are still more features that we have not included. For example, given the complexities in negotiating transactions for exiting investments in biomedical projects, it is likely that an initial portfolio would not be fully constructed at closing and may take several years to complete. This timing is not captured by our simulations.

More importantly, it is typical (currently about 90% of the time) for biomedical projects to exit under terms involving a combination of an up-front payment and one or more “milestone” payments that are subsequently paid to the seller upon the successful achievement of additional clinical and commercial objectives by the buyer. For example, a drug may be sold in phase 2 for \$50 million up-front and another \$25 million that is payable by the buyer to the seller if the drug achieves its phase 3 endpoints. Such deal terms have significant implications for the timing of cash flows which, in turn, affect the default probabilities of the bonds, the correlation of cash flows, and the return to equity holders.

6.2 Alzheimer’s Disease

An example of the limitations of long-shot financing can be seen in the case of drug development for AD which is studied by Lo *et al.* (2014). Because the basic biology of AD is less well developed than that of other diseases, formulating targets for drug development is more difficult. Moreover, clinical trials for neurodegenerative diseases like AD often cost more (up to \$600 million vs. \$200 million for a typical cancer drug and even less for a targeted orphan disease therapy); take longer (13 years vs. 10 years in oncology), which yields a shorter patent life upon approval; and have lower estimated probabilities of success (see below). However, given that 5 million Americans are currently estimated to suffer from AD, the earnings per year of an approved AD drug are considerably higher than those of the average cancer drug (estimated at \$5 billion vs. \$2 billion per year), yielding an NPV of \$24.3 billion at approval.

The clearest manifestation of these combined challenges is that *there have been no new AD drugs approved by the FDA since 2003.*

This is in a sharp contrast to the 36 cancer drugs approved between January 2015 and April 2017. In fact, after informally polling a number of AD experts, Lo *et al.* (2014) reported identifying only 64 potential AD targets, of which only two to three, predominantly, were being pursued by the biopharma industry. Within the months prior to this writing, there have been at least four highly visible failures of AD drug candidates in phase 3 trials (Lilly’s solanezumab in November 2016, Lundbeck’s idalopirdine and

Merck’s verubecestat in February 2017, and Axovant’s intepirdine in September 2017), raising further doubts in the minds of investors about this therapeutic area.

To examine what this implies for long-shot financing, we performed a variation of the simulation in Lo *et al.* (2014). Consider a stylized megafund of 64 AD drug candidates with the cost and revenue parameters in Table 5:

Cost per project	\$600 million
Clinical trial duration	13 years
Remaining patent life	7 years
Earnings per year	\$5 billion
Cost of capital	10% ¹⁶

Table 5. Parameters used for analysis of Alzheimer’s megafund.

The total cost of constructing the portfolio of 64 AD candidate therapies is $64 \times \$600$ million = \$38.4 billion and the NPV of the payoff for a single successful project is \$24.3 billion, so that at least two successful projects are required just to recover the initial investment (assuming no other fees or expenses). In the scenario of two successful drugs, the investor would receive \$48.6 billion in NPV, yielding a *total* return (not annualized) for the 20-year investment of $R = \frac{48.6}{38.4} - 1 = R = \frac{48.6}{38.4} - 1 = 26.6\%$, or just over 1% per year annualized.

The only two remaining parameters needed to simulate the investment performance of an AD megafund are the probability of success of each project and the pairwise correlation among projects, if any. Because there have been no successful AD drugs developed over the last 14 years, the probability of success is difficult to estimate. In the most recent published study, Cummings, Morstorf, and Zhong (2014) estimate a failure rate of 99.6% for a 0.4%

¹⁶ Note that the 10% assumption for cost of capital is generous. For example, Kerins, Smith, and Smith (2004) and Moeza and Sahut (2013) both find that for diversified biotechnology venture investors, a gross cost of capital in the range of 13% to 15% is reasonable.

probability of success using a sample of 413 AD trials from 2002 to 2014.¹⁷ For simplicity, we run simulations with $p = 1\%$, 5% , and 10% for illustrative purposes. With respect to pairwise correlation, we follow Lo *et al.* (2014) and use equicorrelated multivariate normal latent variables to simulate correlated Bernoulli trials.¹⁸

The cumulative distribution functions (CDFs) for the total number of successes (out of 64 trials) are displayed in Figure 7 for various pairwise correlation assumptions. The red line shows the results when using average estimated pairwise correlations provided by several AD experts, while the interpretation of the others is given in the legends.

We also show results for the success correlation, ρ , ranging from 0% to 75% —Figure 7a contains the CDFs for $p = 1\%$, and the two remaining subfigures contain the CDFs for $p = 5\%$ and 10% . These figures show that the distribution of the total number of successes depends heavily on ρ . With $\rho = 0\%$ and $p = 1\%$, the probability of at least one success out of 64 trials is 47.5% ; with $\rho = 5\%$, this probability becomes 43.7% ; with $\rho = 10\%$, this probability becomes 40.2% ; and with $\rho = 75\%$, this probability declines to 9.9% .

Of course, the impact of higher pairwise correlation is diminished when the probability of success for each Bernoulli trial is higher. For example, Figure 7c shows that when $p = 10\%$, the probability of at least one success ranges from 99.9% with $\rho = 0\%$ to 45% with $\rho = 75\%$, almost as high as in the case with $p = 1\%$ and $\rho = 0\%$. Therefore, the impact of success correlation on default probabilities can be mitigated by selecting projects with higher probabilities of success. However, doing so is akin to identifying investments with positive “alpha”; it is easier said than done.

¹⁷ Using the “Rule of Threes,” the naïve 95% upper bound on the estimate of the success rate, having observed zero successes in 413 trials, would be $3/413 = 0.07\%$. By similar calculations, a naïve 99% upper bound on the success rate would be 1.1% and a 99.9% upper bound would be 1.7% (assuming no correlation).

¹⁸ This is equivalent to the Gaussian copula model (1).

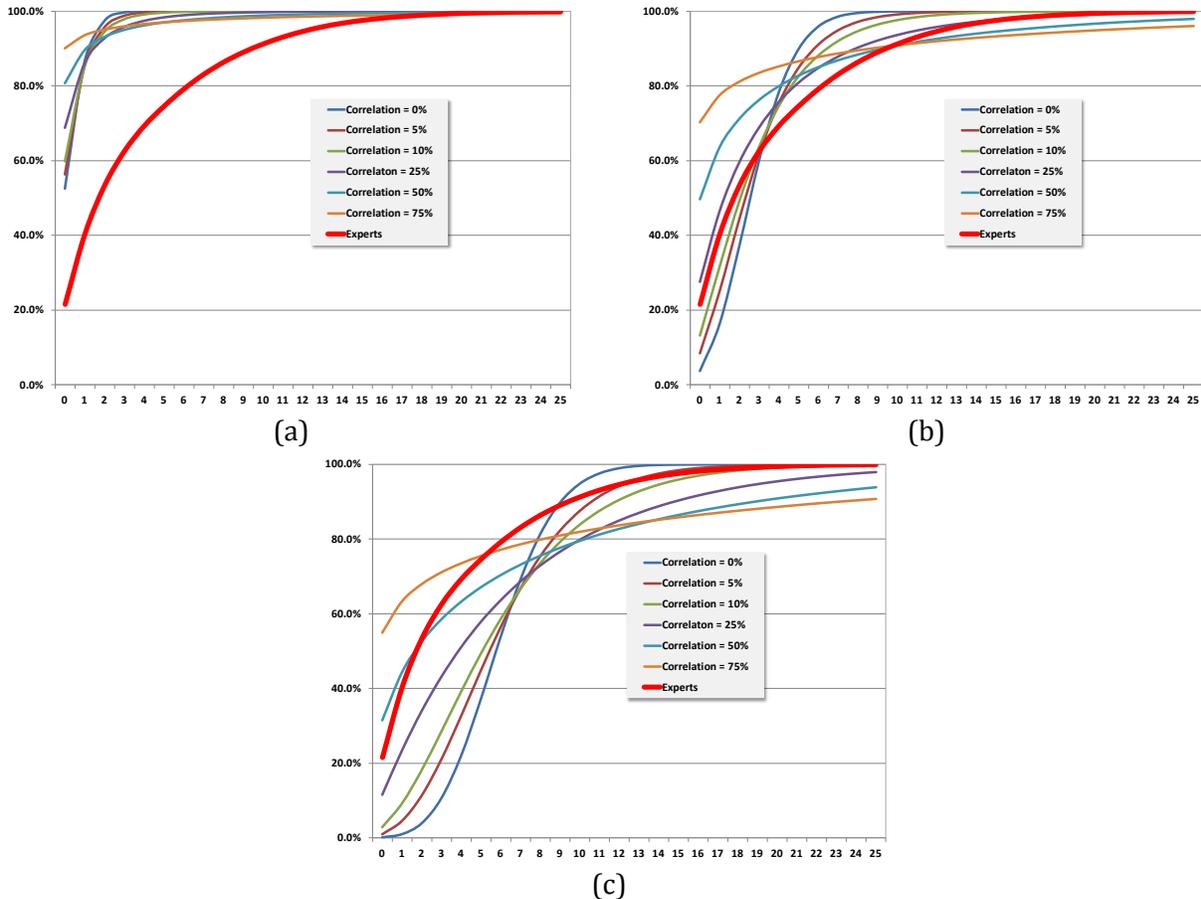


Figure 7. Cumulative probability distribution functions for the number of successes, k , in 64 trials with equal pairwise correlation ranging from 0% to 75%, and correlation determined by averaging expert opinion (see Lo et al., 2014), for probability of success p equal to (a) 1%; (b) 5%; and (c) 10%. To show more detail in the left tail of the distribution functions, the graphs display only up to $k = 25$.

The performance results for the hypothetical AD megafund are contained in Table 6. With $p = 1\%$ and $\rho = 0\%$, the expected annualized return is -53.4% with an annualized standard deviation of 49.1% . And this is the best-case scenario for the fund when $p = 1\%$ —as ρ increases, the fund’s performance becomes worse, yielding an expected return of -89.5% with $\rho = 75\%$. With such performance, no rational investor would participate in this fund, hence securitization is not a feasible alternative.

Performance improves somewhat when $p = 5\%$. With no pairwise correlation, the expected return in this case is 1% and the standard deviation is 20.3% . However, with even the slightest positive correlation, the fund’s expected return becomes negative. Only when the probability of success reaches 10% does megafund financing become feasible. But even

in this extreme case, once pairwise correlations reach 25%, the expected return becomes negative and megafund financing is again infeasible.

There is, of course, some level of p beyond 10% for which the expected return is positive, but in the context of AD, such levels are currently unrealistic.

p	ρ	Prob at				SD[R]	p	ρ	Prob at				SD[R]
		E[hits]	least 1 hit	E[R]	SD[R]				E[hits]	least 1 hit	E[R]	SD[R]	
1%	0%	0.6	47.5%	-53.4%	49.1%	10%	0%	6.4	99.9%	10.6%	5.3%		
1%	5%	0.6	43.7%	-56.9%	49.0%	10%	5%	6.4	98.9%	9.0%	12.4%		
1%	10%	0.6	40.2%	-60.2%	48.6%	10%	10%	6.4	97.2%	6.7%	19.2%		
1%	25%	0.6	31.3%	-68.7%	46.6%	10%	25%	6.4	88.4%	-3.3%	35.7%		
1%	50%	0.6	19.3%	-80.2%	40.6%	10%	50%	6.4	68.4%	-24.8%	51.7%		
1%	75%	0.6	9.9%	-89.5%	31.8%	10%	75%	6.4	45.0%	-49.5%	56.4%		
5%	0%	3.2	96.3%	1.0%	20.3%	Experts		3.8	78.5%	-16.7%	44.0%		
5%	5%	3.2	91.6%	-4.0%	29.6%								
5%	10%	3.2	86.7%	-9.0%	36.0%								
5%	25%	3.2	72.5%	-23.7%	47.4%								
5%	50%	3.2	50.3%	-46.3%	53.7%								
5%	75%	3.2	29.7%	-67.4%	50.5%								

Table 6. Performance statistics of a hypothetical portfolio of 64 AD drug candidates over a 13-year investment period, each with probability of success, p , ranging from 1% to 10% and pairwise correlations, ρ , ranging from 0% to 75%, and with success probabilities and correlations determined by experts. E[hits]: expected hits; E[R]: expected returns; SD[R]: standard deviation.

Motivated by the results above, an alternative strategy to “picking winners” is to construct portfolios containing many different therapeutic approaches, which can reduce correlation. At one extreme, if all projects are perfectly correlated, the probability of one success is the same as the probability of 64 successes. By investing in a more diverse portfolio, perhaps containing more unconventional approaches, the portfolio’s expected returns may be improved due to the reduction in correlation. These more unorthodox therapies may have lower probabilities of success. However, the diversification benefit they confer could overcome their (relatively) lower likelihood of paying off, particularly for portfolios with such low initial probabilities of success. This technique—trading asset quality for portfolio diversification—is routinely employed by credit portfolio managers in managing more conventional fixed-income portfolios (Bohn and Stein, 2009). However, an important constraint on our results is the availability of viable AD therapies in which to invest. In

practice, we are limited simply by the small number of distinct targets, mechanisms of action, and researchers in the field.

Although AD therapies currently do not appear to be conducive to a purely private-sector funding model, this should not be interpreted as motivation to divest from AD therapeutics (although several large pharma companies seem to be doing just that). Instead, it underscores the need for some sort of government intervention to address this societal challenge. In fact, Lo *et al.* (2014) show that, from a public policy perspective, government investment in an AD megafund may yield potentially highly attractive rates of return when we include the projected cost savings to taxpayers of delaying the onset or slowing the progression of AD (e.g., according to the Alzheimer's Association (2017), the projected 2017 spending on AD by Medicare and Medicaid alone is \$175 billion).

Additional research can lead to both improved probabilities of technical success (as the scientific community expands its knowledge of the biology of AD) and a more diverse set of therapeutic alternatives (as funding becomes available to finance research on novel scientific approaches). Through more creative government-backed programs such as long-term AD bonds backed by government guarantees (such as those described in Fagnan, *et al.*, 2013), these dual outcomes may serve, over time, to transform AD drug development to a purely private-sector pursuit.

7 Conclusions

Long shots play a key role in innovation—they are the means by which some of society's biggest challenges will be met. In this paper, we propose the use of securitization to finance long shots, a well-established financing technique uniquely suited because of the scale and scope of debt markets and their risk-sharing capacity.

The viability of the securitization structure we have proposed depends critically on the number of available projects, their probabilities of success, the costs of development, the relative relationship between these costs and the payoff upon success, and the correlations between projects. Because of the sensitivity of default probabilities to these correlations, it is important to maximize diversification among the projects chosen for the portfolio. Of

course, greater diversity also means greater expertise required to manage the portfolio, hence a balance must be struck.

We also show that in some settings, credit quality may be improved dramatically through the use of more involved structuring techniques. While such techniques cannot turn a negative NPV investment positive, they do permit more efficient use of the returns generated by portfolios of positive NPV projects to service structured debt backed by the portfolio. This may result in significant increases in the credit quality of the structured debt, even when projects are correlated. We provide an example of such performance improvement on portfolios composed of identical assets, but differing structures and structural enhancements.

Finally, our analysis has the potential to allow us to distinguish projects that can only be funded by the government from those that can be funded by the private sector. For long shots that yield a much higher return to society than to the private sector, government funding must be used to bridge the financing gap, perhaps in the form of public/private partnerships. Except for these cases, however, it appears feasible to finance long shots through private-sector securitization as described in this paper.

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APPENDIX

A.1 Proof of Proposition 1

To prove Proposition 1 we note that the sum of variables that are multivariate lognormal is approximately lognormally distributed. Appropriate parameters for the lognormal distribution of the sum can be determined by moment matching.¹⁹ Define m_h and s_h as the mean and standard deviation of the logarithm of total payoff from h successes. From the properties of the lognormal distribution, we require

$$\mu_h = \exp(m_h + s_h^2/2)$$

$$\sigma_h^2 = \mu_h^2[\exp(s_h^2) - 1]$$

so that

$$s_h = \sqrt{\ln\left(1 + \frac{\sigma_h^2}{\mu_h^2}\right)}$$

$$m_h = \ln(\mu_h) - 0.5s_h^2$$

Conditional on h successes, the probability that the payoff will be greater than K_j is

$$N\left(\frac{m_h - \ln(K_j)}{s_h}\right)$$

The result in Proposition 1 follows from substituting for m_h .

A.2 Proof of Proposition 2

To prove Proposition 2, define P_h as the payoff conditional on h successes and $f_h(P_h)$ as its probability density. From Proposition 1

¹⁹ This approach was suggested by Fenton (1960) and is known as the Fenton-Wilkinson approximation. It is commonly used when pricing derivatives such as basket and Asian options and provides good accuracy in a wide range of situations.

$$\int_{K_m}^{\infty} f_h(P_h) dP_h = N\left(\frac{\ln(\mu_h/K_m) - s_h^2/2}{s_h}\right)$$

From results in Aitchison and Brown (1957)

$$\int_{K_m}^{\infty} P_h f_h(P_h) dP_h = \mu_h N\left(\frac{\ln(\mu_h/K_m) + s_h^2/2}{s_h}\right)$$

$$\int_{K_m}^{\infty} P_h^2 f_h(P_h) dP_h = (\mu_h^2 + \sigma_h^2) N\left(\frac{\ln(\mu_h/K_m) + 3s_h^2/2}{s_h}\right)$$

The first moment of the distribution of the cash flow to the equity tranche is

$$M_1 = \int_{K_m}^{\infty} (P_h - K_m) f_h(P_h) dP_h = \int_{K_m}^{\infty} P_h f_h(P_h) dP_h - K_m \int_{K_m}^{\infty} f_h(P_h) dP_h$$

The second moment is

$$\begin{aligned} M_2 &= \int_{K_m}^{\infty} (P_h - K_m)^2 f_h(P_h) dP_h \\ &= \int_{K_m}^{\infty} P_h^2 f_h(P_h) dP_h + K_m^2 \int_{K_m}^{\infty} f_h(P_h) dP_h - 2K_m \int_{K_m}^{\infty} P_h f_h(P_h) dP_h \end{aligned}$$

Proposition 2 follows.

A.3 Additional Parameters for Orphan Drug Megafund Simulation

	(1)	(2)	(3)	(4)
	Simulation light structuring, zero coupon	Simulation light structuring, semi-annual coupon	Simulation fuller structuring, semi-annual coupon	Equity only
Fund Characteristic				
Total capital	\$575 MM	\$575 MM	\$575 MM	\$ 287.5 MM
Senior debt	\$287.5 MM	\$287.5 MM	\$287.5 MM	-
Subordinated debt	\$172.5 MM	\$172.5 MM	\$172.5 MM	-
Equity	\$115 MM	\$115 MM	\$115 MM	\$ 287.5 MM
Average number of drugs acquired (Pre/P1)	8.0/8.0	8.0/8.0	8.0 / 7.9	4.0/3.9
Senior bond				
Maturity	5 yrs	4 yrs	4 yrs	NA
Coupon payment schedule	Terminal per	Semi-annual	Semi-annual	NA
Amortization	Terminal per	2 yr straight line	2 yr straight line	NA
Subordinated bond				
Maturity	5 yrs	6 yrs	6 yrs	NA
Coupon payment schedule	Terminal per	Semi-annual	Semi-annual	NA
Amortization	Terminal per	2 yr straight line	2 yr straight line	NA
Budget for future trials	No	No	Yes	NO
Senior debt coverage requirement	NA	NA	1.75	NA
Subordinated debt coverage requirement	NA	NA	2.75	NA
Number of periods of P&I reserved	0	0	2	NA

Table A.1 Additional details of orphan disease megafund simulation with 1 million paths using debt structured as (1) zero coupon with no reserves or overcollateralization; (2) coupon paying debt with no reserves or overcollateralization; (3) coupon paying debt with reserves and overcollateralization; and (4) no debt but the same starting equity. P&I: principal and interest payments.