The Hypervelocity Innovation Model: A Blue Print for Drug Development in Pandemics

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Abstract

The branded pharmaceutical industry is a slow innovation industry, because of the long time to market of new molecular entities (NME). On average, it takes ˜10-15 years from concept to product, at a cost of ˜$1-5 billion, and a failure rate of ˜90% [1]. There are generally two reasons why the timelines are long. One involves the linear phase sequencing of clinical trials and the other, is around financial risks around probability of technical and regulatory success. A perhaps more proximal issue is that pharmaceutical R&D enterprises are organized around prioritized investments, working on assets with the greatest return of investments. There is much less appreciation or flexibility in leveraging expertise around priorities that are often thrust on the system by external forces, such as the current pandemic. Addressing emerging public health concerns, including preparedness for epidemic/pandemic situations, requires a hypervelocity mindset, which the current apparatus is least prepared for. This commentary offers insight into the organizational preparedness into mobilizing resources and scientific creativity for accelerated timelines in response to pandemics.

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The branded pharmaceutical industry is a slow innovation industry, because of the long time to market of new molecular entities (NME). On average, it takes ˜10-15 years from concept to product, at a cost of ˜$1-5 billion, and a failure rate of ˜90% [1]. There are generally two reasons why the timelines are long. One involves the linear phase sequencing of clinical trials and the other, is around financial risks around probability of technical and regulatory success. A perhaps more proximal issue is that pharmaceutical R&D enterprises are organized around prioritized investments, working on assets with the greatest return of investments. There is much less appreciation or flexibility in leveraging expertise around priorities that are often thrust on the system by external forces, such as the current pandemic. Addressing emerging public health concerns, including preparedness for epidemic/pandemic situations, requires a hypervelocity mindset, which the current apparatus is least prepared for. This commentary offers insight into the organizational preparedness into mobilizing resources and scientific creativity for accelerated timelines in response to pandemics.

An Organizational Appraisal of Innovation: Drivers of Risk Based Innovation

Innovation requires the ability to take higher order risks. In drug development, there is often a defensive mindset at play and such a risk posture can hamper innovation and reduce productivity [2]. Using the validated scale of Hansen and Birkinshaw [3], a survey based analysis in which a myriad of pharmaceutical companies participated, the survey revealed high scores on two dimensions, namely, difficulty with which ideas got funded, and that there was a risk averse attitude towards investing in novel ideas [2]. The survey revealed that in general there was a good degree of collaboration across units and businesses. Idea sources appear to transcend specific organizational boundaries – originating from within and beyond firm's immediate environment. There was a good degree of idea sourcing within the organization and there is sufficient agility in the organization to leverage fast to patients. These observations suggest that ideation and diffusion are not problem areas in an innovation enterprise.

Because the analysis revealed two potential weak links, difficulty in getting ideas funded and a risk-averse attitude, firms are conversion-poor [3], which is validated in the industry analysis by others [1,4]. It is poor in *selection* of concepts for further advancement. This aspect warrants an understanding of how innovation occurs within an enterprise, and more importantly, what change situations do to the organizations. A change situation is one where an organization reacts to a certain situation that could affect the ways of the firm in unprecedented ways, e.g., the coronavirus pandemic. This aspect is further analyzed as follows.

Facilitating change to process hypervelocity conditions

The speed of drug development is often informally characterized as velocity, wherein there is a passage of new drugs through a stage-gate process. Increasing the velocity of the pipeline flow is often achieved by including innovative tools, either decisionable biomarkers, or using modeling and simulations. The term hypervelocity is usually referenced in space research, and signifies super high velocity. The author introduces a new use of the term hypervelocity to describe the pressing patient need in pandemics, which require a heightened sense of speed and resource mobilization in the backdrop of significant uncertainty, to deliver therapeutics in the face of pandemics.

Issues that may have contributed to poor conversion rates is the lack of agility in the organization and tolerance towards risks. A risk-averse culture may reflect the presence of greater bureaucracy stifling innovation. The inherently large failure rates for NME development (one in 10 compounds reach the market as a drug [4]) coupled with the slow innovation nature of the NME business [1] predisposes an innovation enterprise to stage its investments carefully. Such a predisposition contributes to an organizational lethargy, which in the context of the short window of opportunity that exists for opportunistic investments may create an unsustainable barrier to value maximization.

Hansen and Birkinshaw [3] indicated conversion-poor companies will benefit from multichannel funding and safe havens. Let us further examine these aspects.

In a pipeline-centric model (as we call prioritized-investments model), there is a single pipeline and single

funding and resource pool. For example, a firm may opt for a particular therapeutic area focus for such investments. When a change situation occurs (e.g., a repurposed product for a new indication) the new situation now competes with the prioritized investments for resources and funding. Invariably, the new drug candidate for that therapeutic area gets a higher priority and the repurposing of the molecule may receive a lower priority. While the former provides an anticipated benefit more than 10 years in the future, the latter provides a more imminent benefit in enhancing patient value.

In a patient-centric model (as we define hypervelocity model), there may be multiple pipelines and multiple resourcing models created with more directed investment funding pool established to support emerging diseases or pandemics. The funding of such ideas is at a noticeable fraction of that required for the NME, and can be stage-gated to weed out the low probability ideas and select ones with high probability of technical and commercial successes for full development.

The hypervelocity enabling apparatus should be nimble, leveraging the power of "skunkworks" [5], with little managerial oversight to avoid hindering its mission. This creates a safe haven for emerging realizable opportunities which may fall by the wayside in the firm's current organizational structure [3].

The cultural environment within the patient-centric apparatus will be entrepreneurial in nature. Individuals, teams, and managers will be expected to exercise entrepreneurial alertness and attitudes towards risk taking [6,7]. Like Hamel [8] proclaims, entrepreneurs create new wealth while stewards conserve. Over time, the conserving attitudes paralyze the organization's ability to remain vigilant to new business opportunities. There may be hybrid models where there may be a primary pipeline apparatus that plays a conserving role, while a second pipeline apparatus be opportunistic, tolerant to risk-taking, and be entrepreneurial. Creating an overall organizational balance between these two forces will also develop agility in thinking while creating a buffer between long range and short-range goals.

Such an organizational mindset change will be more aligned with a *"play-to-win"* strategy [9], where winning is improving quality of life for patients. It will be incumbent upon firms to establish patient-centric innovation as a priority for the company, and directly take ownership for innovation productivity. This will send strong signals aligning innovation priorities as a key link to company business strategy to the rest of the organization on enhancing product and patient value. **Table 1** summarizes the critical determinants of successful innovation performance.

Tactical action plan to improve creativity and innovation for hypervelocity investments

There are three principal areas of improvement. These are:

- Creating an agile process that enables rapid screening of ideas into full development at low investment costs – is the idea feasible? If not, terminate quickly.
- Developing innovation teams ("skunkworks" [5]) that are small in size, with sufficient authority to rapidly generate concepts into decisions
- Creating an enabling culture and a decision framework that provides innovation teams with less constraining oversight to chase hypervelocity conditions [10,11].

These areas are further expanded below.

Agile Process Development

The innovation value chain is divided by distinct stages separated by a gate which filters the concepts. This process allows measuring the probability of success of any given idea as it moves through the process and allows decisions to be made in a timely fashion. There is evidence that such a model can balance creativity and value capture [12]. The degree of uncertainty will reduce as the idea moves through the various stages of the value chain. A hypervelocity poster organization should transition from reactive thinking to proactive thinking, as it relates to managing an innovation model within a stage-gated process.

A crowd-sourcing model can be used to generate ideas. Ideas for these opportunistic investments can come from internal and external sources, including pre-competitive knowledge sharing networks or public-private

partnerships or consortia. Simple rules can be readily applied including refraining from criticism, allowing freewheeling and idea improvements [13]. Once ideas are brainstormed, a next step may be understanding the whitepaper feasibility of that idea. The primary goal of this stage is to complete a theoretical feasibility analysis. The advantage of this stage is to identify showstoppers immediately and identify whether a concept may technically necessitate an unusually high resource requirement (such as a unique or somewhat inaccessible patient population). Once the idea is deemed feasible, the concept is reviewed by a network of experts before transitioning into experimental investigations. During the experimental phase, prototypes of the product concepts are developed and tested to see if the product meets desired objectives (e.g., designing a proof of concept trial for a vaccine for coronavirus). Once the data are available from such a trial phase, a technical review is initiated and a recommendation is made for full development leveraging big data and real world evidence.

Innovation teams

Another critical organizational improvement is in developing the right team to execute on the opportunistic-investments model, modeled after the "skunkworks" concept by Rich and Janos [5]. This will facilitate a change form reactive to proactive thinking [14]. The NME product development teams (NME teams) are positioned in a way that embodies linear thinking. Such linear thinking is a constraint for creativity and innovation.

More specifically, these innovation teams need to exercise creative realism in the Finke's creativity model as opposed to the conservative realism that exists in asset development teams [15]. This is because innovation teams need to be highly imaginative and highly connected to the expert knowledge to be able to visualize the full scope of the patient and product value [16]. Innovation teams are to exercise divergent thinking, again contrasting to convergent thinking that may exist in asset development teams [17]. In Clark and Wheelwright [18] typology, these innovation teams are autonomous teams.

Summary

The author has proposed firm level enhancements for enhancing hypervelocity creativity and innovation, such as those necessary for pandemics. These modifications are designed to increase the conversion rate of ideas into viable products in the shortest possible time.

Three key lessons emerge from this analysis. These include:

- Innovation builds on existing incremental knowledge – The success of the opportunistic-investments strategy is deeply linked to prior knowledge from the product and therapeutic area expertise. Making pandemics as future-proof as possible is an example of incremental innovation. Sawyer [19] suggests this is an action theory where execution is essential in the creative process.
- Leverage the power of collaboration – creativity is enhanced in groups, the source of intangible synergy of teams. Building internal and external networks and collective creative cognition is key to "mining group gold" as Kayser [20] indicates, leading to generation of dynamic capabilities, core competence and resilience of the organization [21, 22]. This coupled by crisis leadership will enable the hypervelocity model.
- Compatibility to the external context – This is an essential attribute to a hypervelocity strategy, which relies on what patients want and at what speed.

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Table 1: Drivers for innovation performance for the hypervelocity innovation model

Strategy
Hypervelocity Strategic alignment between accelerated innovation and business strategy (i.e., plan to win) Accountable inno

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