

The art of **COLLABORATION**

Partnering and licensing have become paramount in a pharmaceutical industry that is under inordinate pressure to fill pipelines and increase the number of approved new molecular entities. This article discusses how Novartis has gone about addressing this issue.

There is a great deal of focus on discovering innovation in the pharmaceutical industry today. In a perfect world, all new compounds would come from a company's in-house R&D operations. Yet, research and development efforts face higher hurdles than ever: advancing science, increasing costs, a more demanding regulatory environment.

In fact, the Boston Consulting Group pegs the increase in the industry's R&D spending at an annual 11% compounded over the past 15 years, to more than \$40 billion a year. Nevertheless, the number of new molecular entities approved by regulators has been flat, similarly that of incrementally modified drugs.

For Novartis, innovation is at the core of our strategy. We first focus on internal innovation, utilising the resources that already exist within Novartis, and then we work to complement our efforts with external activities. We look to find ways to further complement and continue to strengthen our already full pipeline. We believe that a strong, pro-active business development and licensing (BD&L) programme can be an effective, profitable complement to internal research. According to consultants Wood Mackenzie, by 2010 in-licensed product sales in the pharmaceutical industry will equal the growth contribution of internal products. Both will exceed the contribution of mergers and acquisitions to growth.

There are a variety of benefits to BD&L. BD&L

acts as back-up system, as externally derived compounds can take a good portfolio of internally derived medicines and make it a great one. But BD&L's value is also in how you deploy it. At Novartis, even with a large R&D strategy, we can't always cover all the disease areas that become interesting. We use BD&L to look for products in areas, such as anti-infectives, that have not been core to us in the past but have been to certain biotechnology companies.

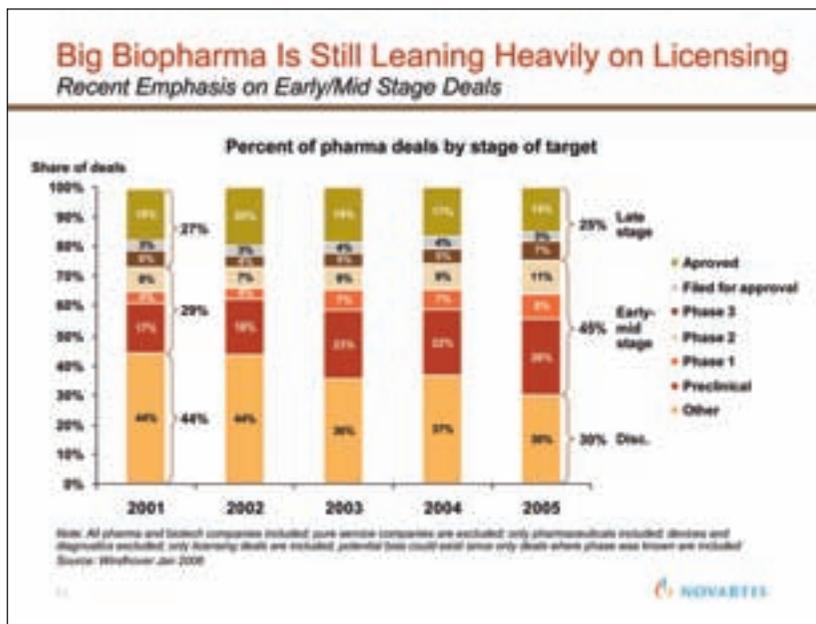
We can also use in-licensed compounds to more effectively cover a time horizon. If, for example, our in-house researchers are working in the pre-clinical stage on a cardiovascular medicine that wouldn't come to market for a decade, we might look to partner on a cardiovascular compound from outside Novartis that is in later-stage trials, meaning it would come to market in only five years' time. We may avoid duplication in terms of time, but not in terms of concepts. We also pick up key learnings for our own earlier-stage compounds that way.

BD&L strategy

At Novartis, our BD&L philosophy is a simple one: provide a win/win solution for both us and our partners; share profits according to contribution; and seek to establish true long-term partnerships. We provide value to our partners, engage them in continuing dialogue, and negotiate fair terms.

**By Anthony
Rosenberg**

Business



This philosophy also complements biotech's goals. A BCG survey last year showed that downstream capabilities are biotech's highest priority. The three specific components biotech wants more than anything else from a deal with a pharmaceutical company? Sales and marketing capability; nurturing (the ability of the biotech to develop and prosper); and clinical/regulatory expertise.

We believe the Novartis approach is working. The 2006 BCG survey found Novartis the best at deal-negotiation responsiveness; leadership committed to partnering; easiness to work with;

What Can Big Pharma/Biotech Do Better?

<p>...to make itself more attractive to a licensing partner?</p> <ul style="list-style-type: none"> Show flexibility, and responsiveness during the negotiation process, as well as post-deal signing Have effective mechanism for responding to initial inquiries Consider creative deal structures, e.g. with equity investment or with options for co-development and co-promotion that a smaller partner can exercise later Be the highest bidder 	<p>...to improve the deal making process?</p> <ul style="list-style-type: none"> Move more quickly to execute an agreement, once the process has started Assemble the right team quickly to evaluate the opportunity, including R&D and Commercial Have clear points of contact for each TA. Be clear about the overall process (e.g., hurdles to get to a CDA, decision making bodies and timing) Transparent and speedy (decision) process Act in true win-win spirit
<p>...to improve its alliance management capabilities?</p> <ul style="list-style-type: none"> Provide a clear picture of expectations and timetables from a business perspective, not just R&D management Do not bail right away if things do not go well - that affects future perception by other companies Design alliance management and conflict resolution into the contract and ensure that there are true decision-making capabilities of the team that do not require disagreements to go to arbitration Do not try to avoid paying royalties or renegotiate contracts Make alliance management a key responsibility of senior management, don't just delegate to low-powered people 	

Source: BCG survey, BCG Interview

alliance management; expertise within therapeutic areas of interest; and tied with Pfizer in clinical/regulatory expertise.

At Novartis, we believe three approaches make our BD&L programme successful: we are quick and flexible in our decision-making; we provide value; and we are a true partner.

Timing

The timing of a deal involving Novartis BD&L can be as short as 5-6 weeks from start to fruition, or as long as 8-12 months. We do put an emphasis on speed, where appropriate, but also on due diligence; the two don't have to be mutually exclusive. Unlike some pharmaceutical companies, which send 50 or 60 people into a small potential biotech partner, we do quick, highly focused due diligence. We send in relatively small teams, who really know what questions to ask and are highly professional. In fact, we now have teams for each therapeutic area dedicated to due diligence.

Providing value

Biotech companies in the process of developing compounds often find that bringing a drug to market is about far more than just discovering a workable compound. The drug-development process now is highly complicated, both in terms of interactions with authorities and in the global implementation of clinical trials (Europe, Asia and the United States, simultaneously). There are very few biotech companies that have real global development capacity; small biotech often struggle with the production, chemistry manufacturing and controls, and technical operational components of the drug-making process.

That is where we come in, offering an industrial-scale process with the ability to tap thousands of patients, collect their data, interpret it, and so on. Put simply, we specialise in development, production and marketing capacity and expertise. If a biotech needs a mass market for its medicines, we have the thousands of sales representatives to detail a product. Unless a biotech is in a very, very specialised market, odds are that it needs a partner.

True partnership

At Novartis, we treat our partners equally, independent of their size. We recognise that a compound in question, once licensed, is still not all our asset; it is very important to the biotech company, and since we like to work with companies on second and tertiary partnerships, we conduct ourselves accordingly. Biotech appreciate this, and a number of them have come back to us with

multiple products after the initial alliance. We dedicate special teams to each product, with a dedicated alliance manager to each project, available full-time for both Novartis and the partner company. Of late, we have extended our BD&L vision to include venture-capital companies, which ask us to assess the achievements of their portfolio companies, as opposed to our licensing specific products.

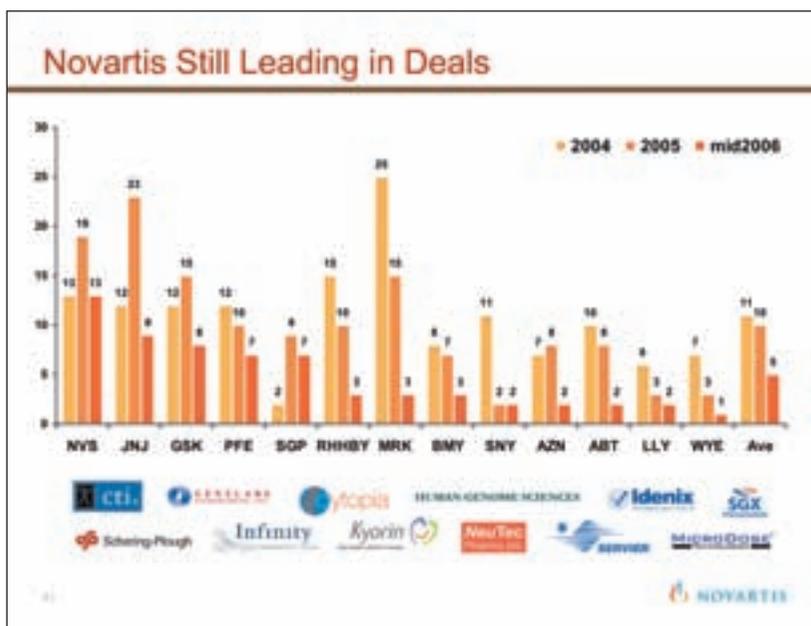
Making a deal

How does a deal happen at Novartis?

Once a year we go through what is called a ‘disease area process,’ so that each of our therapeutic areas can address its needs on a fairly long-term basis. Our cardiovascular team, for example, will look at its plan for the next five-to-seven years, at a minimum. It will identify the most interesting segments of cardiovascular medicine, the segments we most want to be in, hypertension, congestive heart failure, etc. The team will then, based on its own experience and a review of the scientific community and the marketplace, home in on the modes of action most likely to meet the market needs of the future within these segments. In the entire BD&L process, we put tremendous emphasis on modes of action.

At this point, we run through our internal capabilities. If we have a strong internal capability and believe products will be delivered to meet the needs of the marketplace within or close to that timeframe, we will concentrate our energies on the internal product. If the timing of an internal product does not fall into the timeframe, however, or there is a compelling mode of action that we have not explored internally, any product that meets these criteria becomes a licensing target. We then screen all companies with possible targets, and initiate conversations. (Roughly 60% of our BD&L deals start with us approaching biotech, about 30% with biotech approaching us, and the remaining 10% emanate from various sources, personal contacts, partnering and industry meetings.)

After meeting with a potential partner and signing a Confidential Disclosure Agreement, the partner would then send us confidential information, and within a week to 10 days, our technical and marketing experts will do an initial evaluation of a possible deal. If there are big red flags around, for example, intellectual property or patents, the deal is unlikely to progress past this stage. If, on the other hand, the project starts to take shape as something more serious, we then send in a due diligence team. In most cases, an assessment is ready in 3-4 weeks.



If a compound and its licensor are still attractive after due diligence, it then comes back to the Novartis business franchise in question, which will then perform external market research to validate our market assumptions asking, among other things, how the medicine would look to physicians and patients. A Novartis development team, meanwhile, will work up a preliminary development case and assess costs. If the potential costs and revenue make sense, the franchise decides whether or not to go forward. If the answer is yes, we inform the potential partner that we are very serious, and

What Novartis offers its partners

Advancing Science

We are at the forefront of science

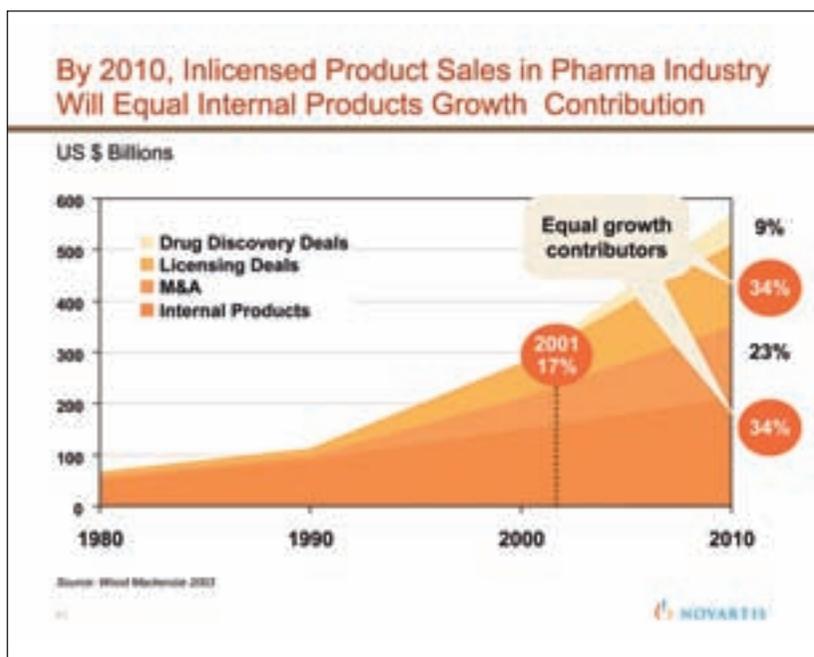
Advancing Compound Development

We are an industry leader in development time using state-of-the-art technology
 We have excellent regulatory contacts optimising chances to obtain approvals
 We have outstanding manufacturing capabilities with an impeccable safety record

Advancing Sales Performance

We excel in commercialisation with global reach consistently outperforming average market growth

Business



then the process above is repeated in much more detail. At this point, we start to consider concerns over-and-above technical and marketing considerations. These would include production issues and toxicology work already performed.

If no red flags appear through this juncture, we will bring the potential deal to the Novartis Deal Review Committee once, for a negotiation mandate. This usually, but not always, occurs within 2-3 months of the project's inception. Internally, we discuss our starting position, our walk-away posi-

tion, how adjustable we are in-between, and then the negotiating team takes these parameters and proceeds to negotiation. It is in this final process that the phrase 'one man's ceiling is another man's floor' becomes particularly apt. While we have stayed away from a number of recent industry deals for technical reasons, we have also pulled out of some over valuation.

Pricing

It is part of the Novartis BD&L philosophy to pay fair value in a licensing deal. We do not approach negotiations with an ulterior motive, whether to take over the target company at some point, or to wring absolute maximum profit out of the deal at any cost. We would rather our partners return to us for future profitable deals, safely knowing we are interested in a win-win situation.

When we consider what to pay for a compound, ie, how to distribute its value in monetary terms, we reflect not only on its market potential, but also on what has been put and what will be put into the therapy, intellectually, during development and commercialisation. We tend to look very systematically at each company's contribution and work from there, leading not to overpayment or underpayment, but rather to a fair and specific value.

Dialogue

Dialogue is very important to the BD&L process. It is vital to us that we keep a very strong interaction going with all, or at least the vast majority, of the CEOs of the companies that we partner with. As noted earlier, the BCG survey found Novartis ranked as the top pharmaceutical company in terms of deal-negotiation responsiveness, leadership committed to partnering, easiness to work with, and alliance management. All of these are so-called 'soft' issues, but the personal touch is crucial not only in making a deal go through, but also in helping the final product succeed. A good existing working relationship between partner companies is where future deals start.

Strong dialogue is also important internally at Novartis. We have arranged for our search-and-evaluation negotiation people to be very entrenched in their business franchises. A BD&L cardiovascular expert's office is located with the cardiovascular franchise, not with BD&L, so that they really seem part of the business, even sitting on the business franchise's board. This way, they fully understand what the franchise strategy is, know exactly what it is they should be looking for in a deal partner – and what not to look for – so that when they do their search-and-evaluation

Why Establish Alliances with Novartis?

- We are committed to establishing alliances
- We are an integral part of the business
- We have a clear mandate
- We are clear about what we want
- We have established processes and quality standards
- We respect cultural differences and are determined to establish longterm win win relationships

NOVARTIS

projects, they won't waste anyone's time. Our negotiation people, for their part, become much more familiar than they otherwise would be with our development capacities, development budgets and issues of co-promotion. Our alliance managers, however, are only partially franchise-based; they are also company-based, such that even if we have multiple partnerships with one company, there is only one alliance manager, with rare exception. This helps keep confusion to a minimum.

Personnel qualities

As head of the Novartis BD&L unit, I am often asked what characteristics make a good BD&L person. When I look at the best qualities of the people in my department, I notice certain personality elements are there, across the board: perseverance; an external focus; and an innate ability to manage internal dichotomies.

Perseverance is key because, frankly, most deals don't get done. Most sales and evaluation people will trace 100 leads to get five or six due diligence negotiation mandates, out of which we might get one deal. Implicit in this, then, is that most of the time, sales and evaluation people are looking at either products that are not all that good, or a deal that is likely to break down on our side or on the potential partner's.

An external focus is just as important. Licensing, by definition, means two companies are working together to bring a product to market; it does not work to have BD&L associates confined to an office, sifting through impersonal databases. While databases are necessary and do help, sales and evaluation specialists have to get out of the office, talk to people, meet people, expand their knowledge of biotech, and understand when a company will or won't want to partner.

Having a strong internal network, meanwhile, is crucial. Deals have to be sold internally as well as externally, and it is only natural in a big company – any big company – to find some reluctance, a key person who might say the in-licensed product will compete with an internal one, perhaps take its resources, slow it down. In the industry, this is known as the 'not invented here' syndrome. This is not a serious problem at Novartis, but it is at other big pharmaceutical companies; either way, it is still necessary to have very keen internal-stakeholder-management abilities, such as a strong network of allies, good selling skills and very good scientific and technical skills.

Measurement

BD&L, like any other function at any company, is ultimately measured by the results it achieves. But

Case study: Using BD&L to help build an anti-infectives business

The goal

A few years ago, Novartis made the decision to try to become the world leader in medicines to fight hepatitis by 2015, and to be a top-five producer of anti-viral medicines.

The strategy

We first defined our investment needs and time horizons on a research, development and commercial basis. We then assessed our internal assets and capabilities, for example, Biochemie, part of our Sandoz generics division, has significant capability in antibiotic production. We decided to build our capabilities and product offerings through internal development, in-licensing, mergers and acquisitions and a reorganisation.

We invested in research at both our Cambridge, Massachusetts, and Singapore locations, and acquired Famvir® from GlaxoSmithKline in 2001 to gain both knowledge and revenue. We amplified our efforts to manufacture and help distribute our antimalarial drug, Coartem®, in many developing nations. And we signed a deal with Idenix Pharmaceuticals, of Cambridge, Massachusetts, to launch our hepatitis business.

Our relationship with Idenix is a broad co-development/co-commercialisation alliance for 'selected compounds'. We paid \$255 million, plus contingent milestone payments, for a majority position in Idenix stock, the rights to two hepatitis B anti-virals and the exclusive option to a hepatitis C anti-viral and other compounds.

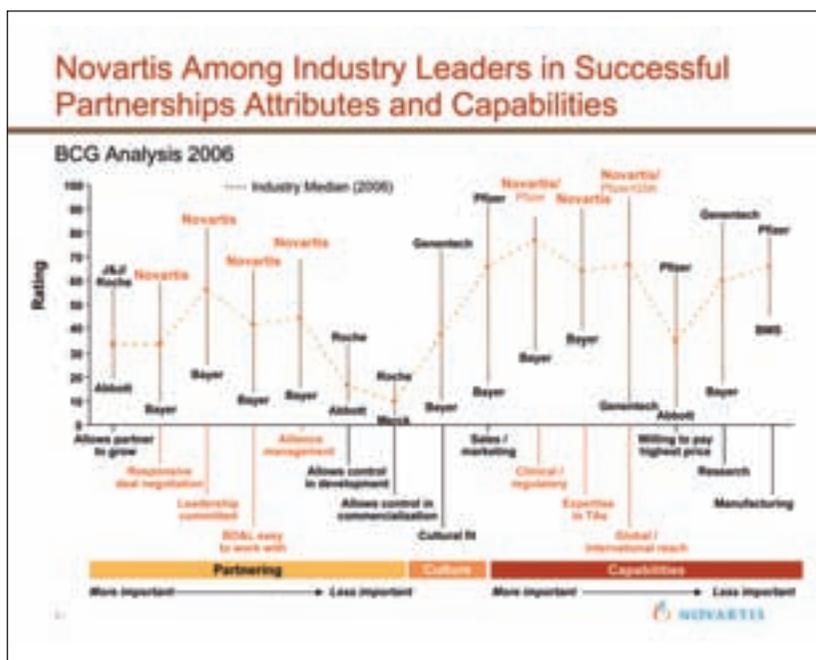
After the Idenix transaction, we reorganised all Novartis Infectious Disease assets into a separate business franchise focused on anti-virals, anti-bacterials and tropical medicine. We ultimately decided to build critical mass and exploit synergies by merging the Infectious Disease business franchise, part of our General Medicines portfolio, with our Transplantation and Immunology activities to create one specialty business unit with more than \$1 billion in revenues. Combined, each operation receives more senior management attention than they received alone, and with overlapping customer groups, this leveraging of existing commercial infrastructure fosters a greater chance of success.

We have taken particular care to build our hepatitis C portfolio with complementary modes of action. Pursuant to this, since the Idenix deal, we have made further transactions with Human Genome Sciences, Anadys, Arrow Therapeutics, Genelabs Technologies, NeuTec Pharma and Chiron. Many of the products involved in these deals would be first-in-class if approved by regulators.

The results

The Novartis Infectious Disease Transplantation and Immunology pipeline is now set to offer one launch per year through 2010 and, we expect, for years after.

Business



licensed including FTY720 for multiple sclerosis; Lucentis® for wet age-related macular degeneration and Telbivudine for hepatitis B. We have prepared well and picked out good products and paid fair prices for them with partners who want to be associated with us. And our business licensing and development has allowed us to expand into therapeutic areas we otherwise would probably not have engaged, allowing us to supplement our strong research operations. **DDW**

there are challenges inherent in BD&L – particularly pharmaceutical BD&L – that aren't found in many other functions, most importantly the long development time needed to bring a product to market, and a fair accounting of the long odds against doing just that. If it takes, say, six years to bring a product to market after it is in-licensed, many of the people involved in the original deal may no longer be involved in either of its parties.

At Novartis, we try to keep our measurement of success simple, and focus on how many deals we do each year, at what minimum sales potential. There is an allowance for the difference between a mass-market compound and a specialist medicine. We have some exciting compounds that were in-

Anthony Rosenberg, Head of Business Development and Licensing for Novartis AG, has overseen several major in-licensing transactions in areas such as respiratory, infectious disease, transplant and ophthalmology. Rosenberg, who first joined Sandoz in 1980, has a BSc (Biological Sciences) from the University of Leicester, and an MSc (Physiology) from the University of London.

ADVERTISEMENT INDEX

Amphora Discovery Corporation	6	Fisher Biologics ApS	55	Molecular Devices Corporation	13,35
BD Biosciences	15	GE Healthcare	4	Novartis AG	3
Beckman Coulter, Inc	42	Genetix Ltd	67	PerkinElmer Life Sciences	8,59
Bentham Science Publishers Ltd	33,IBC	Greiner Bio-One GmbH	40	Thermo Electron Corporation	16,OBC
BioDot, Inc	65	Hamamatsu Photonics KK	IFC	TTP Labtech	38
BioFocus DPI Plc	52	IBC USA	29	Velocity II	51
Caliper Life Sciences, Inc	45	ID Business Solutions Ltd	22		
CISBIO International SA	56	Invitrogen Corporation	25		