interview

Joseph Miletich talks about big Pharma, biotech and the future of Amgen

Interview by **Steve Carney**

Joseph P. Miletich
Senior Vice President of Research, Amgen

Joseph P. Miletich is Senior Vice President of Research at Amgen and is a member of Amgen's senior management team. He directs the company's drug discovery efforts in basic research, as well as preclinical development and medical sciences worldwide.

Miletich joined Amgen from Merck Research Laboratories, where he was Senior Vice President of worldwide preclinical development. Before joining Merck, Miletich was Professor of Internal Medicine and Pathology at the Washington University School of Medicine in St Louis and he held the additional position of Chief of the Division of Laboratory Medicine. He also served as Director of Laboratories at Barnes–Jewish Hospital in St Louis. Miletich received his MD and PhD in molecular biology from Washington University in St. Louis and trained in internal medicine at the University of California, San Francisco. He has authored numerous peer-reviewed manuscripts in the field of hematology and pathology and has served with distinction on expert scientific review groups and editorial boards.

Is there a danger of losing the nimble entrepreneurial spirit as a company gets bigger?
Absolutely. But we take enormous strides not to lose that spirit as we grow. First and foremost, we spend a great deal of effort in communication, so that all of our staff have a genuine understanding of where they fit in the company and what we're trying to do overall. We try to let everybody know what the most critical issues are at each point in time, who is dependent on whom, and how we want to move together. We call this 'seamless integration'. The company is committed to it, from our CEO down, and our people spend significant time and energy to make sure that it happens.

We also spend a lot of time with our staff in training and development. We treat it not as a passive activity, but a core responsibility of every staff member. Without a common willingness to speak our minds, we risk thinking in silos, and that's a threat to nimble decision-making.

Finally, for a company of our size, scale and global reach, we are still relatively small. Even with revenues exceeding US$12 billion in 2005, and operations in so many countries around the world, our employee base is just over 16,000. That's a lot smaller than many other companies of our capacity and reach. So it makes our task a lot easier.

Do you think that a company with origins in biotechnology retains a different culture – with respect to innovation – from big Pharma, even though you probably draw your workforce from a similar pool?
Yes, I think there is a difference. Many people have joined Amgen from big Pharma companies, myself included. Most have done so to recapture that younger entrepreneurial spirit and culture. The difference is in the execution and how we pull it off – how we embrace change, how we treat staff, how we communicate.

While we pull some talent from big Pharma, we also draw from other biotech companies, and some staff are new to the industry. We benefit tremendously from having a blend of staff from a wide range of backgrounds. Diversity of thought and diversity of background and culture are enormously valuable resources for us.

Do you think that size in itself is a factor in innovation and risk management?
I don't accept the premise that risk aversion is an inevitable consequence of a company's growth. I do see a gravity that can draw growing companies in that direction. The bigger they get, the more they worry about what can go wrong; they buy insurance policies and become conservative.

"At Amgen we work enormously hard to become an ever better partner"

But it doesn't have to be that way. The management of the company can make the difference. Being conscious of those tendencies, a growing company can still maintain an innovative, change-embracing culture.

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Certainly, the line must be drawn at anything that might put patients at risk. We'd certainly never want to step into those waters. We only embrace risk by placing bets that don't put people in danger.

What do you see as the future for Pharma–biotech alliances? Do you think we'll see a shift towards earlier stage licensing as big Pharma need to fill their pipeline?
That shift has already begun. There are not enough late stage opportunities to go around, to fill everybody's demand. There is more attention and focus on the earlier stage candidates. I know that at Amgen, we work enormously hard to become an ever better partner. We currently have over 100 active collaborations, and in a given year we examine more than 2000 opportunities.

We know that no single company can do a large fraction of the world's scientific and medical discovery. Even with our resources, we are too small compared to the world's needs. So it's absolutely imperative for us to be a good collaborator, respectful of our partners' goals and their ambitions. We look for opportunities everywhere we possibly can.

Do you think that as a biotech company you have a different approach – perhaps as a 'poacher turned gamekeeper' – to alliances with companies compared with Merck?
Part of being 25 years young is that we still have many people who were with Amgen at its beginning, who remember what it's like to be small. I think that helps us to be a better partner. We know what a smaller company might be looking for, and can feel some of the same aspirations and pressures. That perspective helps us craft partnerships, collaborations, deals and even occasionally acquisitions that are ultimately beneficial to both parties.

What would you say are the potential jewels in the crown for Amgen?
Our most visible product that we hope to bring to market in the near term is denosumab, the fully human monoclonal antibody that we have previously referred to as AMG 162. Denosumab is a monoclonal antibody that works against bone resorption. We're studying its action in every setting in which there is more resorption of bone than deposition – from osteoporosis to treatment-induced bone loss and metastatic bone cancers.

It's an extremely attractive molecule. Our clinical activity has spanned more than 10,000 patients worldwide, and we have fully enrolled our Phase III studies in osteoporosis. We now have a couple of years' data on of our Phase II studies that give us every reason to believe that, based on bone markers and bone density scans, denosumab is a safe and effective therapeutic that is enormously convenient for patients.

A simple injection twice a year is sufficient to give extremely promising results in osteoporosis. We expect denosumab to have a better safety and tolerability profile than selective estrogen-receptor modulators or bisphoshonates, and with much more convenience. We also believe it will show improved efficacy, but we'll have to demonstrate that in the final studies themselves. In all, it should be a superior treatment in just about every dimension.

> *"I don't think the door is ever closed to innovation"*

You have a lot of products in the cancer and connective tissue areas. Are these the two areas that you see Amgen continuing with in the future?
We are bringing forward panitumumab, which is our fully human monoclonal antibody that targets the epidermal growth factor receptor, and we have recently announced very promising results in colorectal cancer. We also have AMG 706, our multikinase inhibitor that targets angiogenesis, along with a few other kinases that are prominent in tumor proliferation. And there are five more targeted biologic therapies in early clinical trials, plus we are investigating our platelet-stimulating agent, AMG 531, and denosumab, in oncology. So we certainly do have a focus on cancer therapeutics.

We also have an enormous interest in inflammatory diseases with our flagship product, Enbrel®, in the USA. Behind that, we now have AMG 108, a fully human monoclonal antibody that targets the interleukin-1 pathway for the potential treatment of inflammatory diseases, and AMG 623, a unique biologic we are currently studying in patients with lupus. In partnership with Genmab, we are working on AMG 714, which targets interleukin-15, another inflammatory target.

But we also have significant programs in diabetes, asthma, chronic neuropathic and inflammatory pain, and neurodegenerative disorders. So in all, we have a wide spectrum of molecules designed to treat serious illnesses.

Are there areas that you see the company developing into in the future? I saw that you recruited Chris Fibiger. Does that mean that you may have plans to explore psychiatric or neurological medicines in the short term?
Chris joined us about two years ago. We do believe that there is great promise in neurosciences, and Chris is working very hard to build up our capabilities. Our aspiration is to become the best human therapeutics company, and wherever we believe we can bring a competitive advantage to the field, and speed new products along to help patients with serious illnesses, we will try to do so.

Amgen have been in existence for 25 years and you have been at the centre of the biotechnology and information technology boom. Do you think that in the next 25 years another organization could develop in a similar way, or has the door closed?
I don't think the door is ever closed to innovation. I would rather characterize our position in the way that my boss has: 'If a new door opens up, we want to walk through it'. We want to be part of all these innovations.

Certainly, across the next 20 or 25 years we will see enormous possibilities that will expand the potential for improving the quality of human life. That is the hope and promise of the future, and I'm a great believer in it.

> *"Our aspiration is to become the best human therapeutics company"*

In 1980 nobody could have foreseen the future success of biotechnology. What do you see as the new directions that will be adopted in the next 25?
It's a very interesting question, and many who have speculated on it in the past have been wrong. It's difficult to know where the next disruptive technology will come from. A lot of attention has been paid to the fact that with advances in nanotechnologies and information technologies, we should be able to make great progress in systematically understanding more of human biology. We should make strides in personalizing medicine to develop much more specific, individualized, targeted therapies. It's hard to predict what the timing of that will be, and exactly what disruptive change will begin a steep upward slope of progress. But certainly, in the next 20 or 30 years, it will come.

As therapeutics become more specific and the therapeutic areas more fractionated, do you think that the unit costs of biologics could come down significantly and do we stand the risk of not being able to recoup the investment costs for the drug?

What you point out is certainly a challenge, but I'm unwilling to say that it will stop us. Whenever new things become possible, we always find a way to make them work. Progress can move in stutter steps at times, while we wait for an additional breakthrough – to make unit costs come down, for example. But over the long horizon, I'm quite optimistic.

In the meantime, I can say with absolute clarity that I would never quit working on the problem for fear that we won't find a way of dealing with it. We have to keep pressing forward, and we will do that with all of our energy and talent.

It's not easy to map out completely now but I'm confident that, in the future, we will be able to bring the cost down. In our current state, it is quite expensive to produce a biologic but we continue to learn more and more and advance the science year after year.

> *"I would never quit working on the problem for fear that we won't find a way of dealing with it"*

As biologics make up a greater percentage of new drugs in the near term, do you think there is a danger that we will break the bank?

One very important element of bringing new therapeutics forward, especially biologics, will be to demonstrate their value. At Amgen, we have put an enormous focus on working with governments and agencies around the world to design programs that will demonstrate that there is economic value of our therapeutics. In the outcomes research that we do, we see that the impact on quality of life – and therefore productivity – warrants investment in some of these new molecules.

Nonetheless, there will always be some struggles as we push through this. But I'll go back to what I said before – knowing that there are hurdles should never keep us from running the race. We'll continue striving to bring the most innovative medicines forward that we can, helping to change the practice of medicine and make the quality of life better for those who suffer from diseases that would otherwise limit them.

> *"I'd rather focus my attention on making sure that we are going to be leading the pack in innovation"*

Do you feel that in the future, the bulk of R&D will be done in biotech companies and licensed by big Pharma?

I have enormous respect for all of my colleagues in big Pharma companies, and I think that they will become more agile and continue to work on their innovative ideas as well. So I'm not sure that I want to speculate on how it's all going to turn out. People are resilient in all industries. I'd rather focus my attention on making sure that we are going to be leading the pack in innovation, embracing change. It's actually good to be in a race, as long as the footsteps you hear are behind you.

Do you think perhaps that there will be less generic competition on biologics in the future than we see for small organics at present?

The pressures will certainly be different for biosimilars entering the field than they have been for generics in the small-molecule arena. For small molecules, generics can be identical copies, and it is reasonably well understood how to ensure that a small molecule generic can deliver the same safety, tolerability and efficacy profile as the original. The manufacturing costs can then be brought down into ranges that make it possible for a small molecule generic to come in quickly and at significant cost reduction.

However, biosimilars are not identical copies, so the same elements aren't true for them. To protect the patient, it is much more important to ensure that the safety, tolerability and efficacy profiles are all well-established for any biosimilar product.

The combination of having to develop the complex processes, invest in them, and perform appropriate clinical trials to assure safety and efficacy will increase both the timelines and the investment costs for biosimilars. All of those things should act in concert to reduce the impact over time of the cost reduction that comes into play.

Having said all that, there could be a place for biosimilars that can reach those targets and actually demonstrate those properties. They might be able to reduce cost per patient and make room for further innovations. That's a good thing for patients and a good thing for companies.

> *"It's actually good to be in a race, as long as the footsteps you hear are behind you"*

What do you see as the future of the pharmaceutical industry over the next 10 years?

I see the future as being incredibly bright. I'm optimistic in spite of all the hurdles we have talked about – issues around paying for drugs, demonstrating their true value, and perhaps turning public perception around as to the real intent and motives of the human therapeutics industry.

In spite of all this, although, the opportunity has never been greater to introduce safe and effective molecules that can help us understand human biology and what goes wrong in serious illnesses. I've never been more optimistic in our ability to increase our understanding at a pace that we can communicate and demonstrate to people everywhere. Confidence will be restored, interest will be renewed, and appropriate resources will be allocated to embrace the changes that are coming forward. I'm very optimistic.