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Today scientists have poor frustration tolerance: Glivec discoverer

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Dr Alex Matter, CEO, Experimental Therapeutics Center, A*Star, Singapore, is among the pioneers of the world's first targeted cancer therapy, imatinib mesylate, also known as Glivec. His discovery turned chronic myeloid leukaemia (CML) from a deadly disease into one that can be treated with an oral pill with nearly 90 percent long-term survival rate.

Dr Matter has played an important role in the success of several anticancer drugs, including Tasigna, and has been instrumental in building and leading teams that discovered novel anticancer drugs. Dr Matter was appointed director of Novartis Institute for Tropical Diseases (NITD), Singapore, in 2003.

Before moving to Singapore, Dr Matter was global head of oncology research for Novartis Pharmaceuticals, head of Novartis Institutes for BioMedical Research in Basel, and global head of translational research. Dr Matter is also spearheading D3-Drug Discovery and Development, an initiative to boost drug discovery landscape in Singapore. D3- Drug Discovery and Development is jointly funded by A*Star and Singapore's National Medical Research Council (NMRC) and National Research Foundation, Singapore (NRF).

In an interview with *BioSpectrum Asia*, Dr Matter shares his perspective on the drug development potentials of Singapore, challenges prevailing in the ecosystem and ways to boost the novel drug development.

Tell us something about the 'Glivec development days'. What change do you see in the attitude of today's scientists?
It took a long time to develop Glivec. It involved 18 years of R&D and not too many companies had the breadth and patience

to do it. It was the first time that such a project was being undertaken and many people said that it would fail and will not be successful.

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There were published article that it cannot be done so we swam in the opposite current. We worked in a small team as compared to today's pharmaceutical laboratories where the size of team is really big. One has to be smart. One has to stand up to convictions, which lacks in youngsters today. They don't have the patience to accept fall outs. A good drug dies five times before it goes to the market.

Tell us about the activities taking place in D3. What success has been achieved so far?
D3-Drug Discovery and Development, is a virtual company that develops drugs, goes into preclinical and clinical trials, and can go up to proof-of-concept level. A team of experts in D3 focus on taking projects through the development process from preclinical development candidates to 'proof-of-concept' (PoC) studies in humans, with the overall goal of developing treatment modalities for Singaporean patients, generating major economic benefit through licenses and potentially creating new intellectual property. D3 translates R&D for biomedical discoveries made in Singapore and is striving to build a seamless value chain from biomedical discovery, or even a mere concept, to a clinical application.

By working closely with other A*STAR institutes, D3 is building a bridge between basic science and clinical translation. D3 also collaborates with other research groups in Singapore, such as Singapore Clinical Research Institute (SCRI), Investigational Medicine Units of the Singapore Health Services, Changi General Hospital and National University Health System, as well as industry partners.

In the first half of 2013, D3 advanced into an H1N1 influenza virus-like particle vaccine project from preclinical to clinical development. Jointly developed with the ETC, the Singapore Immunology Network (SIgN), the Duke-NUS Graduate Medical School (Duke-NUS), the DSO National Laboratories and biopharmaceutical company Cytos Biotechnology, the project enabled a collaboration between D3 and the ETC.

D3 enables a seamless transition of a molecule preclinical target identification, assay development, lead optimization to preclinical-development activities. Anybody with novel molecule identification that can go up to pre-clinical trial can approach D3 and if it is a worthwhile project, then it can be adopted for further progress.

Is Industry-academy collaboration the only viable model for drug discovery? Is Singapore on the right path to emerge as a drug development hub in the region?
Traditionally, Singapore has not been a place for drug development and it is still growing to become one. Singapore has lot of building blocks such as investigational units, clinical research organizations (CROs), Clinical research centers and regulatory bodies such as Health Science Authority (HSA) and one needs to bring them together.

All the institutes or different research centers in Singapore need to club together to present a combined image and must learn to work in teams, a large multi-disciplinary team for long years. Currently, Singapore is driven by principal investigator (PI) research model where there is just one PI and a whole group is following. This model needs to be changed and a bigger involvement of all researchers is required.

What are the current challenges that Singapore is facing in the domain of drug discovery?
Singapore's biggest challenge is the availability of the right set of human resources, manpower and skilled researchers. Researchers today must learn to do applied research and not basic research. Also, the goal of researchers should not solely be to publish papers. Today researchers have poor frustration tolerance and in drug discovery lot of things go wrong. If a progress is not being followed in a positive way, it needs to be terminated and replaced with another project.

A PI driven group stays with the same specialty area for over many areas. Ideally one should stick with a project for long years only if it is successful or should terminate it otherwise. Singapore needs to build a tradition to implement this kind of model. It takes a long time and does not come by itself. These things are not taught in any university and cannot be bought from anywhere. It has to evolve.

Do you think Asia can contribute in replenishing the drying globval novel drug pipeline?
Academia is under huge pressure and pharmaceutical companies of the US are suffering at investor's hands. Asia could play a distinctive role, if it learns the trade. Asia has the capital, talent, and infrastructure but needs leadership to accomplish drug discovery targets.