Transcript of interview with Professor Luca Pani, Director General of the Italian Medicines Agency (Agenzia Italiana del Farmaco – AIFA)

You are seen as a thought leader in Europe on the development of adaptive licensing. Why have you and the Italian Medicines Agency (AIFA) taken a proactive approach to this issue?

AIFA's commitment to the shaping of a new licensing approach in Europe stems from our interpretation of what is a regulator's duty. The main duty of a regulatory agency, for us, is to provide 'the right treatment to the right patient at the right time'.

Regulators are not expected merely to keep 'bad medicines' off the market anymore. They must align drug licensing with patients' needs by granting them timely access to new technologies. Early access to medicines for a restricted population will imply stricter monitoring and data generation throughout the entire life-span of a drug through various modalities, such as monitoring registries, additional studies and so forth.

The EMA [European Medicines Agency] is at the forefront of this wave of regulatory innovation having launched a pilot project for adaptive pathways that is a first major step in the right direction.

Much of the success of this strategy will depend on whether or not the European Commission, the EU Member States and relevant stakeholders will be able to find a suitable political and legal framework for adaptive pathways.

How do you see adaptive licensing integrating into Italian healthcare strategy?

The challenge of personalised medicine is well recognised by all of our stakeholders and AIFA has never failed to deliver its views on amendments to the regulation that will be needed in the near future.

I went on the record many times about the need for flexible authorisation models. This problem has sparked a lively public debate and we hope that this will lead in a short period of time to the development of new paradigms for evaluation and reimbursement of innovative molecules.

Have you seen an evolution of thought through various administrations in Italy?

Having been at the helm of AIFA for almost four years I had the privilege to liaise and work with three different governments. There were certainly many hurdles along the way, namely the economic crisis that affected Italy, as well as the whole of Europe, in recent years.

Managing ever-decreasing pharmaceutical budgets in the era of spending cuts while ensuring that innovative medicines, like the new anti-HCV drugs, make it to the market was, and still is, an extremely difficult challenge.

I am particularly grateful to the current administration and especially to the Minister of Health, Beatrice Lorenzin, that has supported us during the infamous "Stamina" case. It was a critical time for science in Italy. This so called "method" was advertised as a miraculous cure, despite the lack of any kind of scientific evidence nor clinical trials. At a certain time it was even allowed to be given to patients in Italy.

AIFA stood up for science during the whole ordeal and tirelessly fought to make sure that EU regulations regarding advanced therapies and the scientific method were respected. Last month, as you probably know, the case ended and the founder of the Stamina Foundation pleaded guilty to a charge of fraud.

In terms of adaptive licensing, what sort of evidence do you think will be important in the years ahead?

The short answer is that we need as much 'real world' data as possible. The bottom line is that an innovative drug should be licensed and reimbursed only if proven effective. That makes identification of responders absolutely paramount.

AIFA has established a wide range of monitoring registries. Our registries are dynamic tools placed in the early phases after marketing authorisation of new drugs. They have a clear purpose and typically a short defined lifespan, which is designed to measure real world safety and effectiveness and apply the Managed Entry Agreements' procedures.

I am pretty confident that tools like these are the solution to the problem of evidence generation in the context of adaptive licensing. We need to have granular, real-time data on prescription, adherence, effectiveness and safety in order to allow a higher degree of uncertainty, which can never mean a higher level of risk.

How might this new approach affect the pricing discussion?

Although this new approach to drug licensing only concerns prospective therapies, it has the potential to become a new paradigm for regulators, payors, patients and drug companies. The pricing and, I may add, reimbursing of drugs approved under this new programme is surely one of the hardest puzzles to solve.

From the payors' perspective it poses a clear challenge to the tools currently in use to assess a drug's value. Currently, the latter is agreed on based on evidence presented by companies after many years of clinical trials. This could not be the case for drugs approved on the basis of adaptive licensing.

As with any innovation there are still potential roadblocks that need to be removed but I am confident that we will be able to overcome them by working together with our stakeholders.

In general do you see the price of medicines rising or falling in the coming years?

Many regulators – myself included – have voiced concerns over the high price of innovative molecules designed to target chronic diseases with high prevalence. It takes a company a minimum of 15-20 years, with the enormous risks it entails, to bring a drug to the market. Regulators, payors (or insurers depending on the market) are all aware of the need to remunerate the hard labour, research, and risk taking that went into drug development.

On the other hand companies are aware of budget constraints and the burden that such high prices imply for universal healthcare systems like the one in place in Italy. Furthermore, there is still a knowledge gap regarding the methodology used by companies to determine a fair price for an innovative drug.

I said publicly that more transparency is needed especially regarding potential conflicts of interests with the medical community. It appears that we still have many issues to confront on both sides regarding drug pricing.

Will adaptive licensing lead to more dynamic pricing?

If we are able to move from adaptive licensing to an adaptive reimbursement type of system – this is the aim of the game. In the adaptive phase, if you put the price of drug at €50 and can then provide additional data [showing positive results] the price could go to €100.

Usually payors are not used to giving you a certain reimbursement price and then scaling up – they tend to go for €100 and if the drug expands to a wider population they go down to €50. The real problem is that vast majority of payors will say that in the adaptive license phase they paid a price of €100 and then, if the company proves everything, they will give a price of €50. They say 'I gave you earlier reimbursement and you have gained 3, 5, or maybe 10 years'.

What can industry do to facilitate the kinds of shifts you describe?

Industry needs to start changing the type of trials it conducts. This means moving away from the approach taken in the past. Naturally some might say 'we have always done it like this' but it cannot go on without changes.

We need innovators inside the industry. That might sound a bit awkward but even innovative industries like biotech do not always have an innovative approach to pricing and reimbursement. They do incredible things in mechanisms of action, quality control, pharmacokinetics – but then come with a dossier for reimbursement and they take a classical approach.

There is usually a lot of money spent on clinical trial execution. We ought to spend a lot of time and resources on the strategic part of the clinical trial: how to design it; what are the population sub-clusters we are interested in; what are the endpoints.