THE OPHTHALMOLOGY MARKET has expanded significantly in recent years. Many eye diseases have a major impact on healthcare costs; while some are associated with ageing, such as macular degeneration (AMD – the most common cause of blindness in the Western world), diabetic retinopathy, glaucoma and dry eye syndrome, and others, such as retinitis pigmentosa and tumours of the eye, can lead to loss of vision at any age.

Nanomedicine has also grown rapidly over the past few years, producing tangible solutions through innovative approaches generated by improved knowledge and ability to control matter at the nanoscale. As researchers aim to develop effective drug therapies and delivery systems for ophthalmological purposes, nanomedicine is increasingly playing a key role.

NANOMEDICINE TOOLS
There are a number of next generation nanomedicine tools offering innovative solutions to ophthalmological issues. There are nanomachines for monitoring the physiology of tissues and cells (intraocular pressure or oxygen tension); valves for glaucoma drainage; prosthetics for ion channels that are sensitive to light and can cure blindness; and many novel tools for surgery, such as nanoneedles and nanotweezers. In terms of drug delivery devices, a small, refillable and implantable ocular drug pump has been developed that is capable of dispensing nanoliter-sized doses of drugs for the treatment of glaucoma and AMD.

Scaffolds based on nanostructured matrices (such as a range of biocompatible polymeric materials and/or nanowires) have also been proposed for the regeneration of functional tissue, to promote cell transplantation and to induce cell differentiation and repair. These are engineered either for cell-based therapy in pathologies involving the retina, or for the regeneration of axons following injury of the optic nerve.

NANOMEDICINE DRUG DELIVERY SYSTEMS
Eye drops are easy to use and, as such, ensure high levels of patient compliance. For this reason, innovative formulations of nanoparticles (NPs) as eye drops are promising systems for ophthalmological drug delivery. Colloidal systems, both in liquid form (such as micro/nanoemulsions) and in solid form (such as NPs), have excellent potential for interaction with the eye; due to their size and the characteristics of their surface, they are strongly up-taken by the cornea, forming a drug reservoir and thus improving permanence of drugs at the aqueous and vitreous humour levels and enhancing efficacy in treating diseases of the anterior eye.

Meanwhile, cationic gelatine-based NPs loaded with plasmid coding a modified MUC5AC glycoprotein, having gel-forming properties, are well tolerated in animal models and induce MUCSA expression in ocular surface tissue, leading to inflammation reduction. Moreover, they also have the potential to bring different types of molecules to the retina through simple topical administration: for example, we have produced NPs that, in addition to showing extremely favourable toxicological profiles due to being made from natural lipids, can be used to deliver a new molecule, myriocin, that is able to reduce degeneration of photoreceptors in retinitis pigmentosa, to the eye. The effectiveness of this therapy has been demonstrated in mouse models of the disease. Nanovectors allow the loaded molecule to reach the retina and exert its biochemical protective action there, preserving cones from degeneration and maintaining better visual acuity in treated mice.

In another pathology, functionalised polymeric NPs incorporating anti-vascular endothelial growth factor intraceptor plasmid have been demonstrated to increase gene expression in retinal vascular endothelial cells and to inhibit the progression of laser-induced choroidal neovascularisation in a rodent model after intravenous administration.

FRESH PERSPECTIVES
The external and confined position of the eye facilitates its study with local, focused and minimally-invasive treatments, making ophthalmology an interesting field for testing innovative nanomedical technologies. Many novel products are expected to appear in this field in the near future. Furthermore, rare diseases in ophthalmology are excellent targets for the development of nanomedicine, due to the facilitated regulatory pathways and intrinsic specificity of the requested approach. This particular topic is described in a new call in Horizon 2020, underlining the urgency of this approach and the need for new therapies in such fields.

Paolo Gasco and Claudia Musicanti from Nanovector srl, an Italian SME member of the European Technology Platform on Nanomedicine, give an overview of nanomedicine-based solutions in ophthalmology and their hopes for the future of this field

the last word:
Opening eyes to nanomedicine