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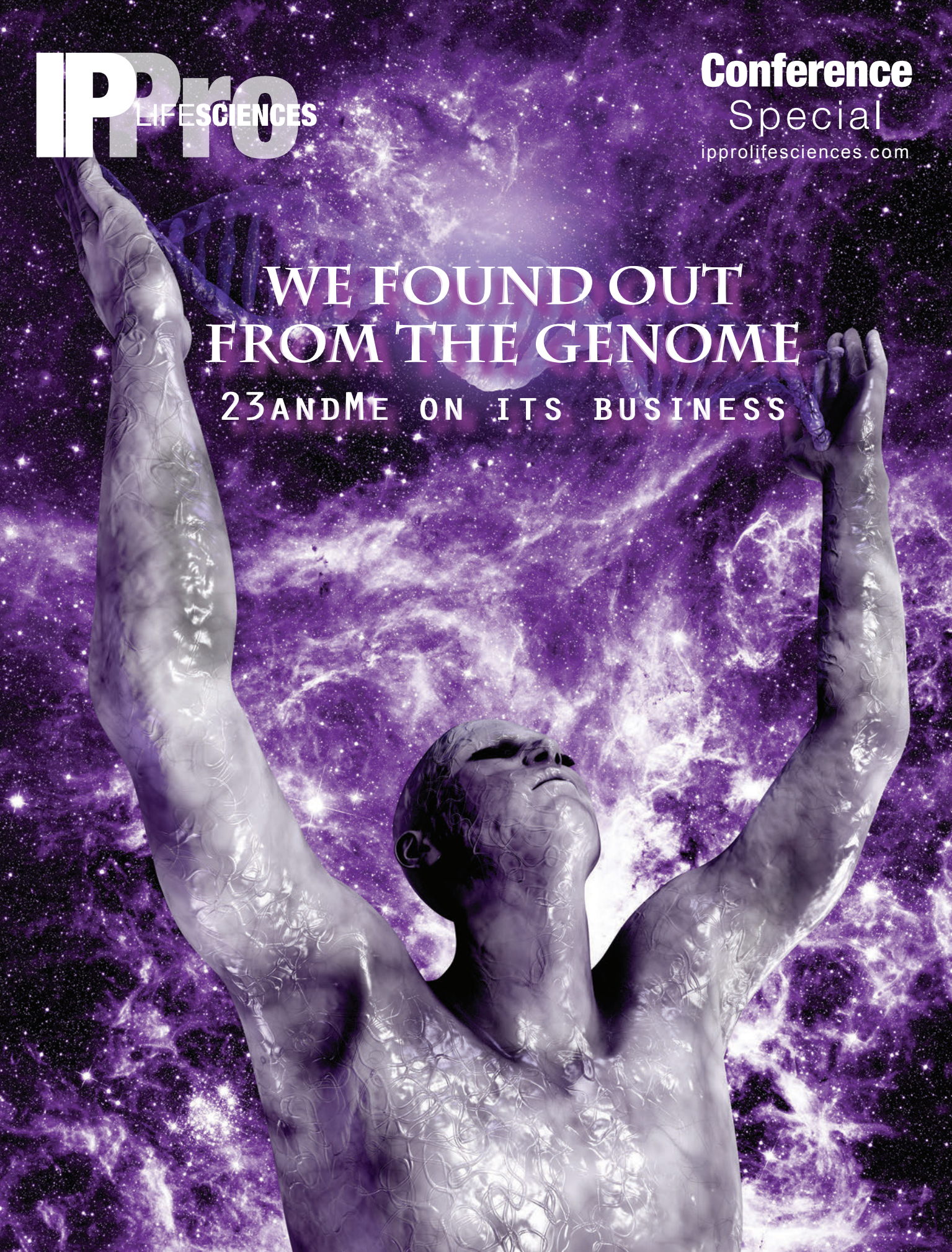

Another patent caught in the tangled web of Section 3(d)

India's Section 3(d) is at it again, but the reasoning is sound, say Manisha Singh Nair and Zoya Nafis of LexOrbis

The controversial Section 3(d) of the Indian Patents Act again came into the limelight when the Indian Patent Office recently revoked a patent for asthma drug Spiriva, which was held by German pharmaceutical company Boehringer Ingelheim, following the evaluation of a post-grant opposition filed by Indian generic drug maker Cipla. The revocation was based on the ground that the patent lacked inventive step and failed to demonstrate therapeutic efficacy as required under Section 3(d) of the Indian Patents Act.

Spiriva (tiotropium bromide) is a respiratory drug and is highly beneficial for curing chronic obstructive pulmonary disease (COPD). While assessing the post-grant opposition, the patent office observed that the compound tiotropium bromide is already known in the prior art, including the specifications as to its quantity and size, and Boehringer failed to show any inventive advancement in this regard.

The patent's claims were deemed to be obvious to a person skilled in the art and there was no inventive step involved.

While deciding on the efficacy of the proposed substance, the patent office relied on well-established law in India that a patent must show significant and necessary improvement of substantial or therapeutic efficacy as compared to the known form of the particular substance.

But Boehringer's patent related to the crystalline tiotropium bromide monohydrate, which is a polymorph of tiotropium bromide, and failed to disclose any substantial efficacy compared to its structurally similar known compound, tiotropium bromide, so it could not survive the test imposed by Section 3(d).

In its order, the patent office reiterated the fact that efficacy is not related to the following factors: particle size; stability of the polymorphic form of the drug substance during or after micronisation or grinding; stability of the polymorphic form during formulation of the inhalable product; and reaching the targeted size to treat the disease.

All of these factors will influence the bioavailability of the drug rather than its therapeutic efficacy. The physical stability of the compound during formulation cannot be a sole factor for improvement of therapeutic efficacy of the drug as required under Section 3(d) of the act.

Boehringer argued that efficacy has to be interpreted on a case-to-case basis. Specifically, in terms of respiratory diseases, the efficacy of the drug is measured in terms of FEV1 (or forced expiratory volume of the lungs within one second), which depends on the drug reaching the desired locations in the lungs.

The claimed crystalline form results in improved FEV1 and therefore enhances therapeutic efficacy, according to Boehringer Ingelheim, but the patent office disagreed.

Boehringer's argument, even if it was taken into consideration, does not have legal standing without clinical trials or research data demonstrating the fact that the newly formed crystalline tiotropium bromide monohydrate is more efficacious than tiotropium bromide.

Although the German pharma company tried to demonstrate that the number of particles reaching the lungs is higher, it failed to address the requirement of showing enhanced therapeutic efficacy.

While Boehringer achieved a reduced particle size to effectively penetrate the lungs, it was not a demonstration of enhanced therapeutic activity over the known substance.

The patent office even made a reference to an order passed by the Supreme Court of China rejecting a patent for crystalline tiotropium bromide monohydrate filed by the Boehringer, because it lacked unexpected technical effects and was not creative.

As a result, the patent office revoked the patent as it lacked inventive step and failed demonstrate any therapeutic efficacy as required under Section 3(d).

Proving therapeutic efficacy has already been upheld by the Supreme Court of India in the landmark Novartis judgement, in which the court made it clear that an increase in certain properties by a derivative substance must show an enhancement in therapeutic efficacy. It observed in its judgment that in case of chemicals, especially pharmaceuticals, if the product for which patent protection is claimed is a new form of a known substance with known efficacy, then the product in question must clear the test of enhanced efficacy.

The term "efficacy" that is used in Section 3(d) of the Indian Patents Act implies "therapeutic efficacy" only, and nowhere includes physicochemical properties.

But the Supreme Court of India made it clear that the present interpretation of Section 3(d) does not mean that patent protection for all incremental inventions of chemical and pharmaceutical substances would be barred. **IPPro**

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