PROTACs and Patents: Navigating a Complex Landscape

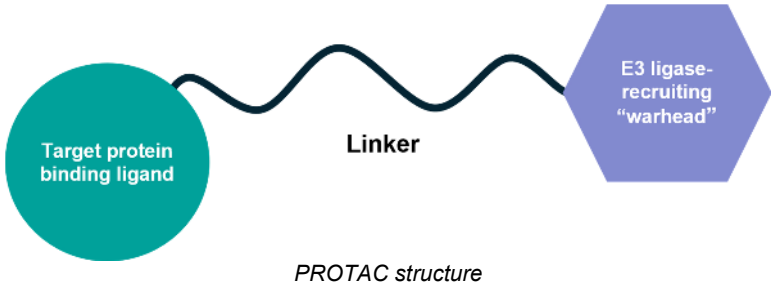
On 1 May 2026, Arvinas' vepdegestrant (Veppanu) received FDA approval for the treatment of adults with ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer following progression on at least one prior line of endocrine therapy. Vepdegestrant is the first FDA-approved Proteolysis Targeting Chimera (PROTAC), marking a major milestone for targeted protein degradation following years of growing scientific interest and investment.

The emergence of PROTACs as a clinically validated therapeutic modality has also given rise to significant intellectual property considerations. Given their unique architecture, PROTAC technology raises distinct issues concerning filing strategy, freedom-to-operate, inventive step, sufficiency, and claim breadth.

Background

Unlike conventional small molecules inhibitors which generally rely on occupancy of a functional binding site, PROTACs induce targeted protein degradation by harnessing the endogenous ubiquitin–proteasome system. Their bifunctional architecture generally comprises three key components:

(i) a target protein binding ligand (TBL),
(ii) an E3 ligase-recruiting "warhead" or "degron", and
(iii) a linker connecting the two moieties.



PROTAC structure

The target-binding ligand selectively engages the protein of interest (POI), while the E3 ligase ligand recruits an E3 ubiquitin ligase, thereby promoting formation of a POI–PROTAC–E3 ligase ternary complex. Within this complex, the E3 ligase catalyses ubiquitination of the POI, thereby marking it for recognition and subsequent degradation by the 26S proteasome.

Targeted protein degradation offers several potential advantages as a therapeutic modality. One of the most significant is its catalytic mechanism of action: following ubiquitination and degradation of the target protein, the PROTAC dissociates and can engage additional POI molecules, enabling multiple rounds of degradation and a potent or prolonged pharmacological effect. Furthermore, because PROTACs do not depend on binding sites directly associated with enzymatic activity, they can potentially be used to target proteins previously considered difficult to inhibit using conventional active-site approaches.

PROTACs and Platforms: Subject Matter for Protection

Compared to traditional therapeutics, the modular nature of PROTACs introduces additional complexity when considering patent filing strategy. This stems from the fact that innovations involving any individual component of the degrader – be it the TBL, warhead, or linker – may independently constitute a patentable invention. Conversely, the invention might lie in the combination of components, such as a specific TBL-warhead pairing.

Accordingly, parties may seek to protect a development in just one component of a PROTAC. Applications to this effect are often described as "platform" applications and are generally filed at an earlier stage when the applicant is seeking protection for a technical concept that may be employed across multiple targets or degrader designs. Platform filings typically rely on structural delineation for the innovative aspect (for example, using a Markush structure), while defining the remaining

components using broad, functional language – for instance, a moiety capable of binding to a target protein or recruiting a particular E3 ligase.

PROTACs may also be protected through conventional small-molecule applications ("PROTAC filings") defining the entire degrader structurally. Although this approach provides narrower protection than broader platform functional claims, it often facilitates prosecution and enforcement. In particular, claims to a defined chemical structure are generally less vulnerable to objections relating to sufficiency, clarity, and inventive step.

In practice, many portfolios benefit from both types of filings. A layered strategy is typically adopted in which early platform filings establish broad conceptual protection, and later filings focus on optimised lead degraders.

For platform filings, one key point to consider is that the functional language commonly employed can pose additional challenges during prosecution. While such definitions are in principle allowable under European law, the EPO requires that the skilled person is able to perform the invention across substantially the entire claimed scope without undue burden.

The EPO has become increasingly demanding where broad functional definitions are supported by only limited examples. Applicants should therefore provide substantial structural diversity and experimental evidence demonstrating that the claimed technical effect can reasonably be achieved across the breadth of the claims. Inclusion of representative examples spanning different linker types, warheads, and TBLs may improve prospects of satisfying sufficiency and inventive step requirements.

In practice, securing granted platform patents with elements defined in purely functional terms can be difficult, even for a well-exemplified application. Nevertheless, even pending or provisional protection derived from such applications may still provide a meaningful strategic deterrent, particularly by discouraging third parties from operating within the same chemical or biological space.

Filing Strategies and Considerations

In the field of PROTACs, it is common practice to file platform applications, followed by applications to specific, optimised degraders. This provides broad, conceptual coverage, complemented by follow-on filings relating to lead compounds, formulations, and therapeutic applications. However, the successful implementation of this approach requires careful foresight and strategic management.

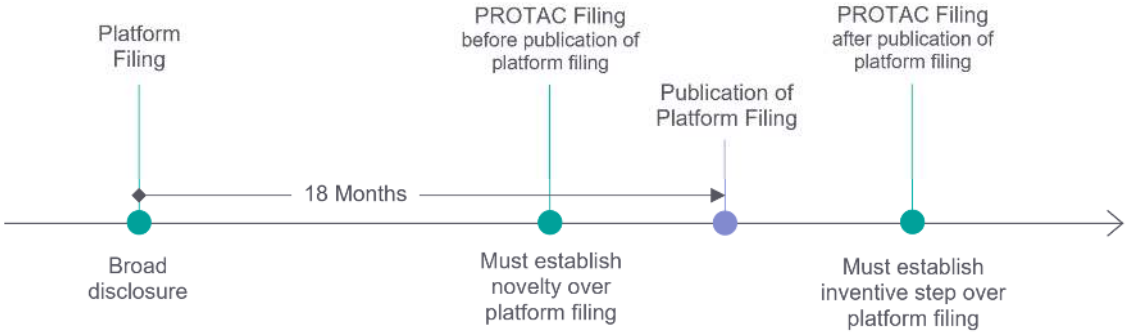
Under EPO standards, a generic disclosure only anticipates a later specific embodiment if that embodiment is directly and unambiguously disclosed. A broad degrader platform therefore will not usually destroy novelty of a later, specific PROTAC. However, such applications may still be highly relevant to inventive step. For instance, the same exemplary degraders that are necessary to support sufficiency and enablement of a broad platform filing may later be relied upon as closest prior art. This creates a risk that a subsequent application directed to specific degraders could be found obvious over the applicant's own prior art, especially where the modifications are considered a matter of routine optimisation.

Accordingly, due consideration must be given to the examples included in platform applications. In particular, attention should be given to which exemplary degraders are disclosed, and whether their inclusion could create difficulties for the patentability of later-filed applications directed to specific compounds which may include the clinical candidate.

Applicants must also carefully manage the timing of their filing strategy, including publication schedules. Where a later application is filed before the earlier platform application is published, the earlier application will not form part of the state of the art for inventive step purposes under EPO law. Thus, one potential strategy is to file downstream applications prior to publication of the platform application. This may help to avoid the earlier disclosure being cited against later filings. In parallel, consideration may be given to disclaiming compounds exemplified in the platform application, to mitigate potential novelty or anticipation issues in follow-on applications.

Conversely following publication of an earlier platform application, any later-filed PROTAC applications must be found novel and inventive over the earlier disclosure. In such a case, unexpected technical effects – such as improved degradation efficiency, selectivity, pharmacokinetics, or reduced toxicity –

can be useful in supporting the inventiveness of the later application. Comparative experimental data showing the improvement relative to the closest compounds in the platform filing are therefore highly valuable in supporting inventive step arguments.



Exemplary PROTAC filing timeline

Applicants should also consider how later-generated data may be used during prosecution. Where improved degradation, selectivity, pharmacokinetics or toxicity is likely to become important, the application as filed should include a clear technical rationale, and preferably supporting data, for those effects. This may assist in relying on post-filed evidence under **G 2/21**, if further comparative data is generated after filing.

Platform applications should therefore be drafted with care. A balance needs to be struck between adequate exemplification, while having due regard for any potential future filings.

Freedom to Operate (FTO) Considerations

FTO analysis is especially complex in the PROTAC field because multiple proprietary elements may coexist within a single degrader molecule. A commercial PROTAC may need to be assessed against patents claiming the TBL, the E3 ligase warhead, and the linker.

This issue is amplified by the concentration of early foundational patents around commonly used E3 ligase binders such as cereblon and VHL ligands. Even where a company develops a novel degrader structure, use of a patented warhead or linker technology may still present infringement risks. Accordingly, FTO analysis in Europe often requires careful assessment of overlapping patent estates owned by different entities.

Supply-chain and indirect infringement issues may also arise in certain jurisdictions. In a modular technology such as PROTACs, potential exposure may not be limited to the entity marketing the final degrader. The supply or offer of a ligand, linker, intermediate, or other component may require consideration where that component relates to an essential element of a patented invention and the supplier knows, or should have known, that it is suitable and intended for putting that invention into effect.

European FTO also requires attention to where and how rights may be enforced. Although the EPO centralises examination, grant and opposition procedures, infringement and post-grant validity may be litigated before national courts and, where applicable, before the Unified Patent Court.

Finally, the doctrine of equivalents may broaden infringement exposure beyond literal claim language in certain European jurisdictions. Given the modular and substitutable nature of PROTAC components, patentees may argue that modified linkers or related ligands remain equivalent to claimed structures if they preserve the same overall degradation strategy.

Conclusion

PROTAC technologies present substantial opportunities for strategic patent protection but also raise complex issues under European patent law. Equivalent-infringement analysis should be performed jurisdiction by jurisdiction and, where relevant, under developing UPC case law. The modular nature of

these molecules supports layered filing strategies combining broad platform protection with narrower compound-specific filings. At the same time, the fragmented ownership landscape creates significant FTO challenges.

From an EPO perspective, successful prosecution often depends on careful consideration of claim breadth and experimental support. Broad functional claims may offer valuable commercial coverage, but they must be supported by credible technical teaching across the claimed scope. In parallel, later-filed specific degraders can still obtain meaningful protection where they demonstrate distinct structural and technical advantages over earlier generic disclosures.

Furthermore, as more clinical data are published, the breadth of the disclosure that the EPO considers justifiable might change. Therefore, it is essential that patent applications and granted patent claims include intermediate fallback positions that can narrow the scope in case the EPO's approach becomes stricter or certain components are found to be inactive.

As the European PROTAC patent landscape continues to mature, applicants will increasingly need sophisticated drafting and portfolio strategies that anticipate both prosecution scrutiny and future enforcement considerations.