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# Benzimidazole scaffolds in emerging trends for therapeutic develeopment: A comprehensive review

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**Abstract**
Heterocyclic compounds constitute a central class of aromatic molecules in medicinal chemistry with benzimidazole derivatives emerging as one of the most significant and versatile scaffolds in modern drug design. First synthesized in the late nineteenth century, benzimidazole is a fused bicyclic system comprising a benzene ring and an imidazole ring and it is among the earliest nitrogen-containing heterocycles reported. Owing to its structural similarity to purine bases such as adenine and guanine, benzimidazole exhibits favourable physicochemical properties including tautomerism, that enable effective interactions with diverse biological targets such as enzymes and receptors. This structural advantage has positioned benzimidazole as a privileged pharmacophore in the development of bioactive molecules.
Extensive research over recent years has demonstrated that benzimidazole derivatives possess a wide spectrum of pharmacological activities, including anthelmintic, antibacterial, antifungal, antidepressant, anticancer, anticonvulsant, anti-inflammatory, antioxidant, antitubercular and antiviral effects. Numerous studies reported between 2022 and 2025 highlight the synthesis, characterization and biological evaluation of novel benzimidazole-based compounds, many of which exhibit comparable or superior activity to standard reference drugs across *in vitro*, *in vivo* and in silico models. Furthermore, several benzimidazole-containing drugs such as albendazole, mebendazole, omeprazole, telmisartan, candesartan and bendamustine are already established in clinical practice, underscoring the therapeutic importance of this scaffold.
This review provides a comprehensive overview of recent advancements in the synthesis and pharmacological evaluation of benzimidazole derivatives, emphasizing their broad biological potential and reinforcing the role of benzimidazole as a promising core structure for the development of future therapeutic agents.

**Keywords:** Benzimidazole, antioxidant activity, antiviral activity, anti-microbial activity, antidiabetic activity, anthelmintic activity

## Introduction

Among the many families of aromatic chemicals, heterocyclic compounds stand out as a leading theme and represent one of the most promising structural units found in a wide range of clinically important drugs [2]. Hoe Brecker first prepared benzimidazole in 1872 and shortly after, Ladenburg and Wundt achieved the same synthesis in 1878, establishing it as one of the earliest nitrogen containing heterocycles ever reported [3].
Benzimidazole is a notable heterocyclic compound in which a phenyl ring is fused to an imidazole ring at the 4- and 5-positions. Its derivatives display a broad spectrum of medicinal activities within the pharmaceutical industry [1]. The IUPAC numbering for benzimidazole is shown in Figure 1 [8]. When a hydrogen atom is attached to the nitrogen at position 1, the molecule can easily shift its double bonds (tautomerize). This basic "6 + 5" ring framework is also found in natural compounds like adenine and guanine, which are the building blocks of nucleic acids [1, 4].

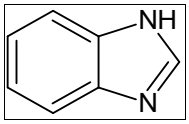



**Fig 1:** Benzimidazole

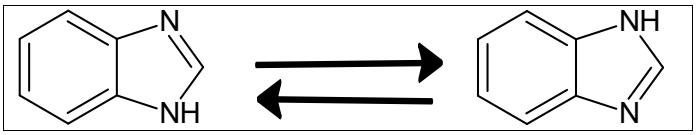
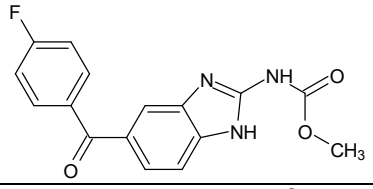
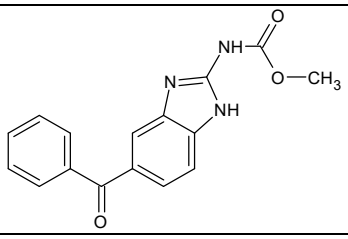
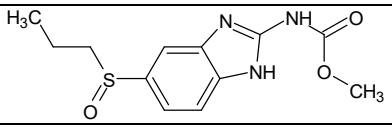
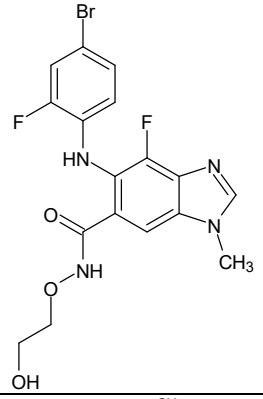
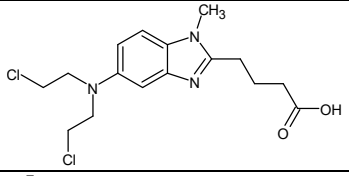
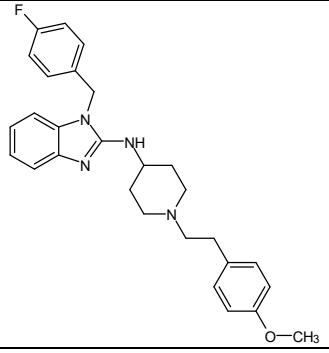
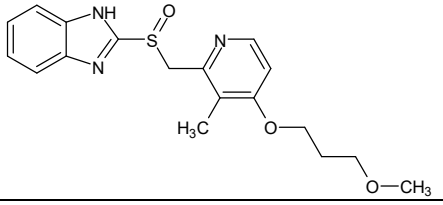


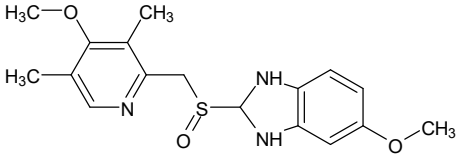
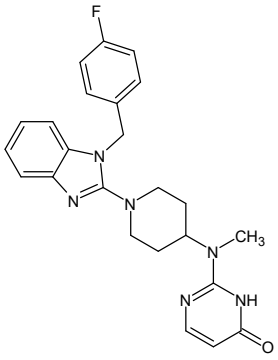
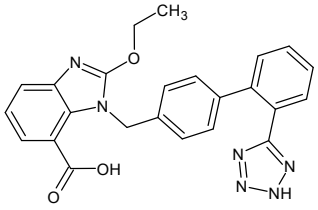
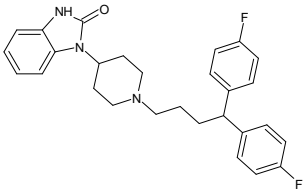
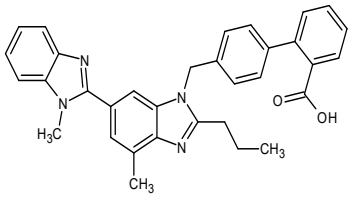

**Fig 2:** Benzimidazole possessing tautomerism

Benzimidazole is a privileged heterocyclic scaffold in medicinal chemistry due to its structural resemblance to purine bases, which are fundamental components of DNA and RNA [5]. This similarity allows benzimidazole derivatives to interact effectively with various biological targets, including enzymes and receptors involved in disease processes. Over the last few decades, benzimidazole has emerged as a core structure in the design of many bioactive molecules [6, 7].
The benzimidazole scaffold functions as a versatile pharmacophore, granting its derivatives a broad range of biological effects such as anti-inflammatory, analgesic, anti-ulcer, antimicrobial, anthelmintic, anticancer, anti-asthmatic, antidiabetic, antitubercular, antiprotozoal

and antiviral activities [9, 10]. Several drugs already available in clinical use like Omeprazole and rabeprazole are employed for gastric ulcers; telmisartan and candesartan target hypertension; astemizole and mizolastine address allergic rhinitis; and albendazole, oxibendazole and mebendazole are used against parasitic infections [9]. And also, bendamustine is approved for treating chronic lymphocytic leukaemia and non-Hodgkin's lymphoma [11]. Therefore, Benzimidazole serves as a potential therapeutic agent.

**Table 1:** FDA-approved, commercially available drug products

| SI NO. | DRUG NAME | STRUCTURE |
|---|---|---|
| 1 | Flubendazole |  |
| 2 | Mebendazole |  |
| 3 | Albendazole |  |
| 4 | selumetinib |  |
| 5 | Bendamustine |  |
| 6 | Astemazole |  |
| 7 | Rabeprazole |  |

| | | |
|---|---|---|
| 8 | Omeprazole |  |
| 9 | Mizolastine |  |
| 10 | Candesartan |  |
| 11 | Pimozide |  |
| 12 | Telmisartan |  |

**Pharmacological activity**

**Anthelminthic activity**

1. Kameliya Anichina [12] *et al., (*2025) reported the synthesis of two groups of methanimines and hydrazones heterocyclic containing benzimidazole derivatives and evaluated for their *in-vitro* anthelminthic activity. Among those Compound 1a & Compound 1b exhibit potent activity against trichinella spiralis (80.5% at 100µg/mL after48h) and T. spiralis L(57.5%at100µg/mLafter48h) compared with standard albendazole. Fig.no:3

**Antibacterial activity**

2. Hayrani Eren Bostancı [13] *et al.,* (2025) present a new hybrid structure containing benzimidazole and thiadiazole units were synthesized and structural analysed by using 1H-NMR, 13C-NMR, HRMS and elemental analysis. The antimicrobial, antioxidant and *in vitro* anti-cancer activities of all compounds were investigated. Among that Compound 2g bearing 4-methoxyphenyl derivative showed the best activity with 32 µg/mL against S. aureus ATCC 29213 and P. aeruginosa ATCC 27853 by using broth microdilution method & Compound 2a-c showed more antioxidant properties than vitamin E by using Ferric Reducing method. Fig.no:3
3. Pragya Kawde [14] *et al*., (2023) described a Novel N-substituted Benzimidazole derivative were synthesised, characterized and evaluated for antibacterial activity on gram positive bacteria (Staphylococcus aureus MTCC 740 and Bacillus subtilis MTCC 121) and gram-negative bacteria (Escherichia coli MTCC 1302 and Pseudomonas aeruginosa MTCC 741) by disc diffusion method. Among those Compound 3a, 3b, & 3c was more active against growth of Staphylococcus aureus, Bacillus subtilis, Escherichia coli and Pseudomonas

aeruginosa respectively, when compared to Ciprofloxacin as standard drug. Fig.no:3

**Antifungal activity**

4. Dr. N. Krishnarao [15] *et al*., (2024) reported a synthesis of N-substituted benzimidazole derivatives were characterized and carry out anti-fungal activity on sabouraud Dextrose Broth media. Among that Compound 4(a-e) possessed best activity against Candida albicans compared with standard fluconazole with a MIC of 12.5µg/ml. Fig.no:4

**Anti-depressant activity**

5. Rubina Chowdhury [16] *et al*., (2024) synthesized 2-styryl-1H-benzo[d]imidazole derivative and assessed an *in-vitro* antidepressant activity. Among those Compound 5a ((E)-5-(2-styryl-1H-benzo[d]imidazol-1-yl) pyrimidine-2,4(1H,3H) -dione) & Compound 5b ((E)-1-(4-bromophenyl) -2-styryl-1H-benzo[d]imidazole) showed good activity with IC50 values of 367.19 µM/mL and 184.56 µM/mL against MAO-A and MAO-B, respectively Fig.no:4.

**Anticancer activity**

6. Mohamed Oussama Zou Aghi [17] *et al., (*2024) reported a new benzimidazole derivatives were synthesized and evaluated for *in-vitro* anticancer activity by MTT assay against various cell line like (MDA-MB-231, MCF-7, HT-29 and healthy cell line (HF). Among that, (3-(4-chlorobenzyl)-1-(2-morpholinoethyl)-5,6-dimethylbenzimidazoliumchloride) Compound 6 showed relative significant higher cytotoxicity with $IC_{50}$ values of 165.02µM (MDA-MB-231), 175.02µM (MCF-7), 219.37 µM(HT-29) and 225.8µM (HF cells), which can be compared against reference drug cisplatin. Fig.no:4

**Anti-convulsant Activity**

7. Sonakshi Tyagi [18] *et al.,* (2024) demonstrated a novel quinoline-benzimidazole hybrids were synthesized, characterized and evaluated for anti-convulsant activity by *in-silico* studies on the Swiss albino mice using the subcutaneous pentylenetetrazol method. Among those Compound 7a-c showed potent activity at a dose of 30mg/kg after 0.5 hr as well as 4 hr when compared with standard carbamazepine. Fig.no:4

**Anti-inflammatory activity**

8. Shaher Bano [19] *et al*., (2024) reported a series of 2-substituted benzimidazole derivatives was synthesized & evaluated for *in-vitro* &*in-vivo* anti-inflammatory activity by using luminol-chemiluminescence and paw edema assay. Among that Compound 8 shows highest activity with (IC50=2.4 ± 0.2µg/ml) compared against standard Ibuprofen with an (IC50Value of11.2 ±1.00µg/ml). Fig.no:5
9. Muftia Arubah Basri [20] *et al., (*2025) presented a new 2-((1H-benzo[d]imiadazol-2-yl) thio)-1-3, 5 diphenyl-1h-pyrazol-1-yl) ethenone derivative was synthesised, characterized and evaluated for *in-vitro* anti-inflammatory and anti-arthritic activities by Carrageenan induced paw edema method. Compound 9 (36.88 ± 0.782) ($p < 0.001$) shows good reduction activity against TNF-α & IL-6 cells, when compared with piroxicam (32.82 ± 1.044) ($p < 0.001$) as a standard. Fig.no:5
10. Haseeb Ahmad [21] *et al.,* 2025 described the evaluation of the benzimidazole derivative BMZ-AD in an FCA-induced arthritic model. The compound was prepared & administered at graded doses for activity testing. The study groups were compared directly with the standard drug piroxicam. This compound lowered inflammatory signals such as TNF-α & IL-6 during the study and they also reduced PGE2 formation, showing strong calming action. So overall, Compound 10 exhibited promising anti-arthritic potential against induced disease. Fig.no:5

**Antioxidant activity**

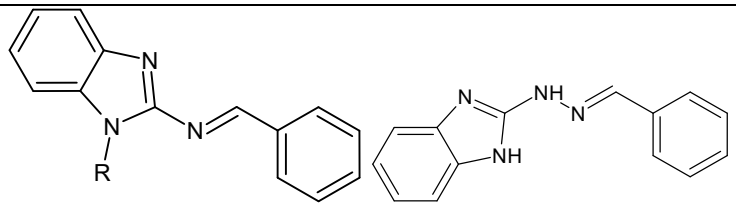
11. Hafiz Aamir Ali Kharl [22] *et al.,* (2025) worked on benzimidazole-pyrazole hybrids (M3a–M3t) for biological screening. They prepared the new molecules and confirmed their purity by spectral data. Among the series, Compound 11 M3e, M3i and M3m showed strong antioxidant action with low $IC_{50}$ values. In that Carbonic anhydrase inhibition was marked for M3e and M3m when compared with the standard drug acetazolamide. So overall, M3m displayed the highest activity in the entire group. Fig.no:5
12. Mithun Rudrapal [23] *et al*.,(2025) demonstrated a new benzimidazole derivatives were synthesised, characterised and evaluated for their the toxicity, molecular interactions with NAD(P)H oxidase and antioxidant potential by DPPH (1,1-diphenyl-2-picryl hydrazyl) radical scavenging assay. Among these Compound 12 exhibited good activity with $IC_{50}$ values 53.21 µg/mL when compared to the standard drug, ascorbic acid with $IC_{50}$ value of 11.95 µg/mL. Fig.no:6

**Antitubercular activity**

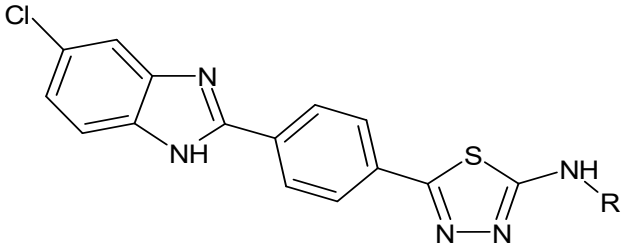
13. Berfin Sucu [24] *et al*., (2025) reported a series of benzimidazolium derivatives were synthesised and evaluated for *in-vitro* antitubercular activity by using the BACTEC MGIT 960 system. Compound 13 (1-(2-Hydroxyethyl)-3-(3-methylbenzyl)-1H-benzo[d]imidazole-3-ium bromide) demonstrate strong activity against Mycobacterium tuberculosis H37Rv with MIC value of 2 µ g/ml. Fig.no:6
14. Nombulelo T.P. Nyoni [25] *et al*., 2023 developed benzimidazole-1,2,3-triazole-quinoline hybrids through a multi-step synthetic method. The synthesized molecules were tested for *in-vitro* antimycobacterial activity against the H37Rv strain. The hybrids produced strong responses with $MIC_{90}$ values between 1.07 and 8.66 µM showing better action Among the tested series, Compound 14a ($MIC_{90}$ = 1.54 µM) and Compound 14b ($MIC_{90}$ = 1.49 µM) showed the highest inhibition when compared to the standard drug Ethambutol ($MIC_{90}$ = 9.54 µM). Fig.no:6

**Anti-viral activity**

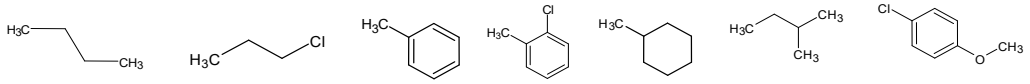
15. Prafullya Kumar Mudi [26] *et al*., (2022) developed synthesis of 5-membered heterocycle-substituted benzimidazole derivatives, characterized by using spectroscopic technique. And evaluated for *in silico* anti-SARS-CoV-2 proficiency against main protease (M pro) and non-structural proteins (nsp2 and nsp7) of SARS-CoV-2. Compound (2-(thiophen- 2-yl)-1-((thiophen-2-yl) methyl)-1H-benzo[d]imidazole) shows good activity on M pro. Fig.no:6



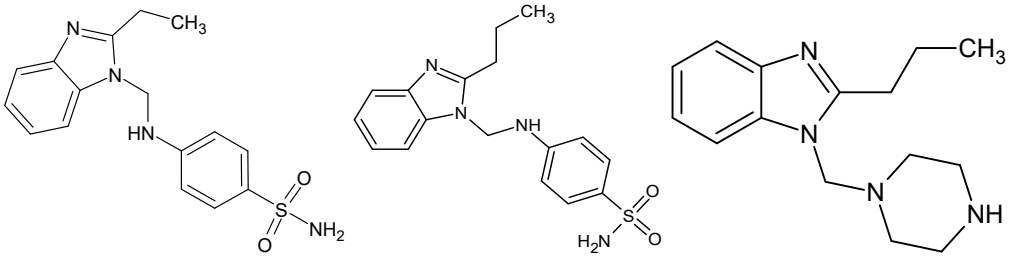
**Compound 1a Compound 1b**



**Compound 2a -g**

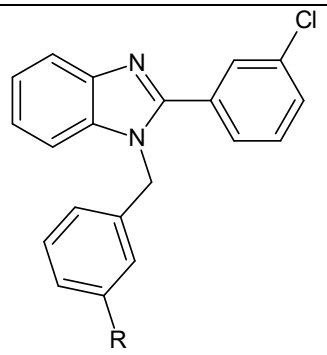


**R** = 2a 2b 2c 2d 2e 2f 2g



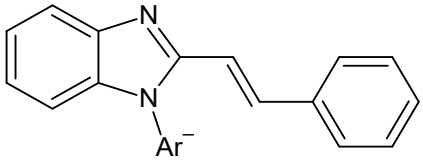
**Compound3a Compound3b Compound 3c**

**Fig 3:** Pharmacological activity of benzimidazole derivatives



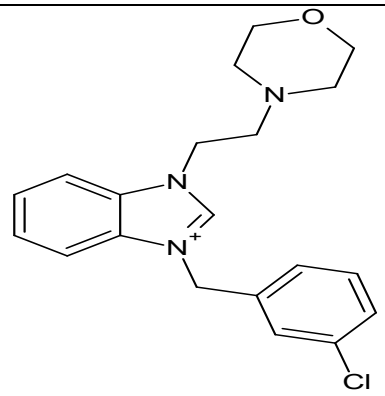
**Compound 4a-e**

R=H, 4-OCH3, 4-Cl, 4-CN, 4-NO

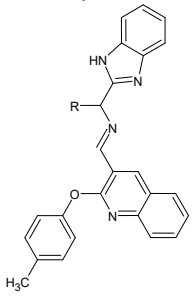


**Compound 5a-5b**

Ar =5 bromouracil, 1,4 dibromo benzene



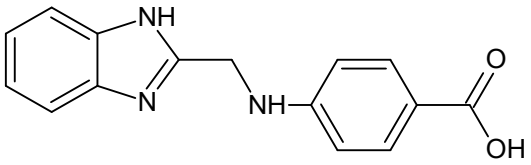
**Compound 6**



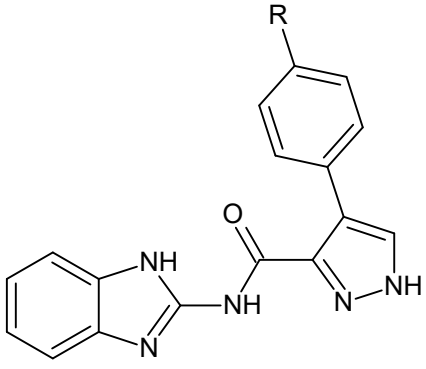
**Compound 7a-c**

R = H, $CH_3$, $-CH(CH_3)_2$

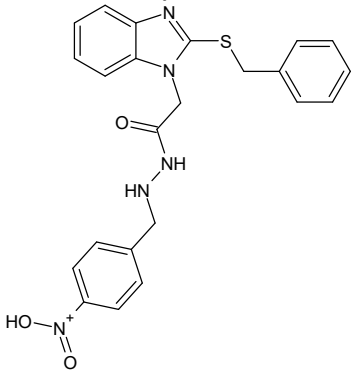
**Fig 4:** Pharmacological activity of benzimidazole derivatives



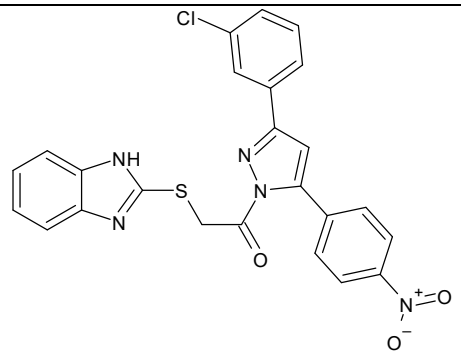
**Compound 8**



**Compound 9**

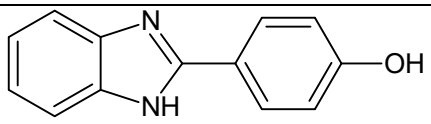


**Compound 10**

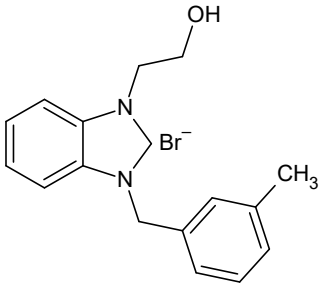



**Compound 11**

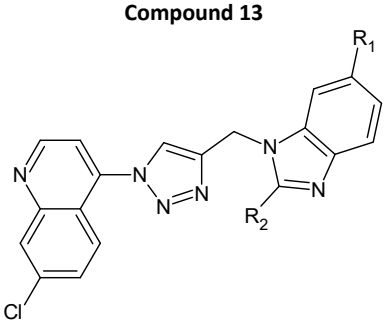
**Fig 5:** Pharmacological activity of benzimidazole derivatives




**Compound 12**

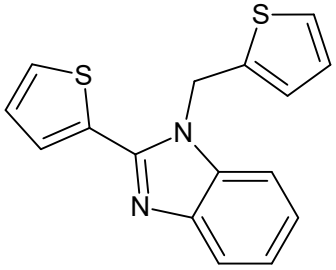



**Compound 13**




**Compound 14a** = $R_1$ -$NO_2$ $R_2$-H

**Compound 14b** = $R_1$-$NO_2$, $R_2$-$CH_3$




**Compound 15**

**Fig 6:** Pharmacological activity of benzimidazole derivatives

## Conclusion

The benzimidazole nucleus has proven to be a privileged pharmacophore, enabling the design of a broad spectrum of bioactive molecules with excellent yields and functional-group tolerance. The compiled studies demonstrate that subtle modifications of the benzimidazole scaffold can yield compounds with remarkable potency across multiple disease models, from parasitic infections to neurodegenerative and inflammatory disorders. Notably, several derivatives exhibit activities comparable or superior to standard reference drugs, highlighting their therapeutic promise. However, further optimization is required to improve selectivity, pharmacokinetic profiles and *in-vivo* efficacy. Future work should focus on rational drug design,

mechanistic investigations of target interactions and advanced pre-clinical evaluations to translate these promising leads into clinically viable therapeutics.

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